Joint ECDC-WHO Regional Office for Europe Mpox Surveillance Bulletin

04 April 2023

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SURVEILLANCE SUMMARY

A total of 25,874 cases of mpox (formerly named monkeypox) have been identified through IHR mechanisms, official public sources and TESSy up to 4 April 2023, 14:00, from 45 countries and areas throughout the European Region. **Over the past 4 weeks, 28 cases of mpox have been identified from 7 countries and areas.**

Case-based data were reported for 25,763 cases from 41 countries and areas to ECDC and the WHO Regional Office for Europe through The European Surveillance System (TESSy), up to 4 April 2023, 10:00.

Of the 25,763 cases reported in TESSy, 25,584 were laboratory confirmed. Furthermore, where sequencing was available, 489 were confirmed to belong to Clade II, formerly known as the West African clade. The earliest known case has a specimen date of 07 March 2022 and was identified through retrospective testing of a residual sample. The earliest date of symptom onset was reported as 17 April 2022.

The majority of cases were between 31 and 40 years-old (10,146/25,731 - 39%) and male (25,268/25,701 - 98%). Of the 11,256 male cases with known sexual orientation, 96% self-identified as men who have sex with men. Among cases with known HIV status, 38% (4,042/10,623) were HIV-positive. The majority of cases presented with a rash (15,303/16,027 - 96%) and systemic symptoms such as fever, fatigue, muscle pain, chills, or headache (10,855/16,027 - 68%). There were 783 cases hospitalised (6%), of which 271 cases required clinical care. Eight cases were admitted to ICU, and six cases of mpox were reported to have died.

To date, WHO and ECDC have been informed of five cases of occupational exposure. In four cases of occupational exposure, health workers were wearing recommended personal protective equipment but were exposed to body fluid while collecting samples. The fifth case was not wearing personal protective equipment. The WHO interim guidance on clinical management and infection prevention and control for mpox remains valid and is available at [https://apps.who.int/iris/handle/10665/355798](https://apps.who.int/iris/handle/10665/355798).
INTRODUCTION

PURPOSE AND SCOPE

This report provides an overview of the total number of cases of mpox (formerly named monkeypox) identified by ECDC and the WHO Regional Office for Europe through IHR mechanisms and official public sources and case-based data through The European Surveillance System (TESSy) up to 4 April 2023.

The first summary table and maps (first two tabs) describe the number of cases identified through the different platforms. The following figures and tables describe national case-based data for surveillance of mpox reported in TESSy from all the countries and areas of the WHO European Region, including the 27 countries of the European Union (EU) and the additional three countries of the European Economic Area (EEA).

Case Report Form Data are submitted through the case-based record type mpox (MPX) to The European Surveillance System (TESSy) database hosted at ECDC.
CASE DEFINITION (WHO and ECDC)

As of 22 December 2022

Cases of mpox should be reported to TESSy if they meet any of the WHO, ECDC or national case definitions.

Confirmed case

- A person with laboratory confirmed MPXV infection by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)\(^1\) and/or sequencing.

Probable case:

- A person presenting with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region 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 One or more of the following:

- has an epidemiological link\(^2\) to a probable or confirmed case of mpox in the 21 days before symptom onset;
- identifies as gay, bisexual or other cis or trans man who has sex with men;
- has had multiple and/or casual sexual partners in the 21 days before symptom onset;
- has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody\(^3\) (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titer based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the absence of a recent smallpox/mpox vaccination or other known exposure to OPXV;
- has a positive test result for orthopoxviral infection (e.g., OPXV-specific PCR without MPXV-specific PCR or sequencing)\(^1\).

Suspected case

- 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 (\(\geq 38.5^\circ\text{C}\)), headache, myalgia (muscle pain/body aches), back pain, profound weakness or fatigue.
OR

• A person presenting since 01 January 2022 with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region 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, 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.

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\(^1\).

• Conversely, 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.

The previous WHO and ECDC case definitions can be found in the Annex.

1. PCR on a blood specimen may be unreliable and should also not be used alone as a first line diagnostic test. If blood PCR is negative and was the only test done, this is not sufficient to discard a case that otherwise meets the definition of a suspected for probable case. This applies regardless of whether the blood PCR was for OPXV or MPXV specific.
2. The person has been exposed to a probable or confirmed monkeypox case.

3. Serology can be used for retrospective case classification for a probable case in specific circumstances such as when diagnostic testing through PCR of skin lesion specimens has not been possible, or in the context of research with standardized data collection. The primary diagnostic test for monkeypox diagnosis is PCR of skin lesion material or other specimen such as an oral or nasopharyngeal swab as appropriate. Serology should not be used as a first line diagnostic test.
KEY INDICATORS

IHR SUMMARY

Table 1: Summary of number of cases of mpox identified through IHR mechanisms and official public sources and reported to TESSy, European Region, 2022–2023

Countries and areas reporting new cases in the past 4 ISO weeks are highlighted in blue
<table>
<thead>
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<th>Country/Area</th>
<th>Number of new cases identified through IHR, official public sources and TESSy in the past 4 ISO weeks</th>
<th>Cumulative number of cases identified through IHR, official public sources and TESSy</th>
<th>Cumulative number of cases reported through TESSy</th>
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<td>Total</td>
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<td>25874</td>
<td>25763</td>
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MAPS

ECDC Map

Map Figure 1a: Distribution of new cases of mpox reported in the past 4 ISO weeks, European Region, TESSy, 2022–2023, ECDC borders

Geographical distribution of confirmed mpox cases in the EU/EEA, Western Balkans and Türkiye, 6 Mar 2023-2 Apr 2023 as of 04 Apr 2023

- ≥100 cases reported
- 50-99 cases reported
- 20-49 cases reported
- 10-19 cases reported
- 1-9 cases reported
- No reported cases
- Not included

Countries not visible in the main map extent
- Malta
- Liechtenstein

Administration boundaries: © EuroGeographics
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 04 Apr 2023
Map Figure 1b: Distribution of all cases of mpox, European Region, TESSy, 2022–2023, ECDC borders

Geographical distribution of cumulative confirmed mpox cases per 1,000,000 population in the EU/EEA, Western Balkans, and Türkiye, as of 04 Apr 2023

- ≥100 cases per 1,000,000
- 50-99 cases per 1,000,000
- 10-49 cases per 1,000,000
- ≤10 cases per 1,000,000
- No reported cases
- Not included

Countries not visible in the main map extent:
- Malta
- Liechtenstein

Administration boundaries: © EuroGeographics
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 04 Apr 2023
Map of WHO European Region

Map Figure 1c: Distribution of cases of mpox, European Region, TESSy, 2022–2023

Mpox total cumulative incidence and new cases reported in the last 4 weeks as of 04 April 2023

Data source: WHO European Region IHR Database
Contact: euroinfo@who.int
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EPICURVES

Date of notification is defined as the date when the case report is notified for the first time to the place of notification, date of diagnosis is defined as the first date of clinical or laboratory diagnosis, and date of onset as the date of onset of any symptoms.

Overall by date of notification

Figure 2: Overall number of cases of mpox, per date of notification, European Region, TESSy, 2022–2023
Figure 3: Overall number of cases of mpox, per date of symptom onset, European Region, TESSy, 2022–2023
By date of onset and by country or area

Figure 4: Number of cases of mpox, per ISO week and per country/area of notification, European Region, TESSy, 2022–2023

Week of symptom onset (or earliest of week of diagnosis or notification if missing)

Number of new cases

Andorra
Austria
Belgium
Bosnia and Herzegovina
Bulgaria
Croatia
Cyprus
Czechia
Denmark
Estonia
Finland
France
Georgia
Germany
Gibraltar
Greece
Hungary
Iceland
Ireland
Israel
Italy
Latvia
Lithuania
Luxembourg
Malta
Netherlands
Norway
Poland
Portugal
Republic of Moldova
Romania
San Marino
Serbia
Slovakia
Slovenia
Spain
Sweden
Switzerland
Türkiye
Ukraine
United Kingdom
By date of onset and by country or area - country/area level

Figure 5: Number of cases of mpox, per ISO week and per country/area of notification, European Region, TESSy, 2022–2023
Week of symptom onset
Number of new cases

Georgia
0
200
400
600
800

Germany
200-W09
200-W10
200-W11
200-W12
200-W13
200-W14
200-W15
200-W16
200-W17
200-W18
200-W19
200-W20
200-W21
200-W22
200-W23

Gibraltar
0
200
400
600
800

Greece
200-W09
200-W10
200-W11
200-W12
200-W13
200-W14
200-W15
200-W16
200-W17
200-W18
200-W19
200-W20
200-W21
200-W22
200-W23

Hungary
0
200
400
600
800

Iceland
0
200
400
600
800

16
Sweden

Switzerland

Türkiye

Ukraine

United Kingdom

*Week of symptom onset or earliest of week of diagnosis or notification if missing
### SUMMARY TABLE

Table 2: Summary of number of probable and confirmed cases of mpox as well as deaths, by reporting country/area, European Region, TESSy, 2022–2023

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<th>Probable cases</th>
<th>Total cases</th>
<th>Total deaths</th>
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<td>Serbia</td>
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<td>0</td>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>Slovakia</td>
<td>14</td>
<td>0</td>
<td>14</td>
<td>0</td>
</tr>
<tr>
<td>Slovenia</td>
<td>47</td>
<td>0</td>
<td>47</td>
<td>0</td>
</tr>
<tr>
<td>Spain</td>
<td>7547</td>
<td>2</td>
<td>7549</td>
<td>3</td>
</tr>
<tr>
<td>Sweden</td>
<td>260</td>
<td>0</td>
<td>260</td>
<td>0</td>
</tr>
<tr>
<td>Switzerland</td>
<td>552</td>
<td>0</td>
<td>552</td>
<td>0</td>
</tr>
<tr>
<td>Türkiye</td>
<td>12</td>
<td>0</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Ukraine</td>
<td>5</td>
<td>0</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>3541</td>
<td>148</td>
<td>3689</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>25584</td>
<td>179</td>
<td>25763</td>
<td>6</td>
</tr>
</tbody>
</table>
Figure 7: Age and gender distribution of cases of mpox, European Region, TESSy, 2022–2023

Gender from 12 cases is reported as Other and these cases are not depicted on this graph. Information on gender is missing for 50 cases and information on age is missing for 32 cases.

Data on gender is collected as Female, Male, Other (e.g., transgender man, transgender woman and collected as free text), or Unknown.
CLINICAL DESCRIPTION

The median time between symptom onset and diagnosis was 7 days.

**Figure 8: Distribution of symptoms among those reporting at least one type of symptom (N=16027), European Region, TESSy, 2022–2023**
Table 3: Distribution of rash and systemic symptoms among those reporting at least one type of symptom (N=16027), European Region, TESSy, 2022–2023

<table>
<thead>
<tr>
<th>Any type of rash</th>
<th>Systemic Symptoms*</th>
<th>Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Absent</td>
<td>Absent</td>
<td>144 (0.9%)</td>
</tr>
<tr>
<td>Absent</td>
<td>Present</td>
<td>580 (3.6%)</td>
</tr>
<tr>
<td>Present</td>
<td>Absent</td>
<td>5,028 (31.4%)</td>
</tr>
<tr>
<td>Present</td>
<td>Present</td>
<td>10,275 (64.1%)</td>
</tr>
<tr>
<td>Total</td>
<td>-</td>
<td>16,027 (100%)</td>
</tr>
</tbody>
</table>

*Fever, fatigue, muscle pain, chills, headache

Detection of asymptomatic cases is dependent on testing guidelines which currently do not recommend testing asymptomatic persons.
### OUTCOME, HIV STATUS

**Table 4: Summary of outcome and HIV status of cases, European Region, TESSy, 2022–2023**

<table>
<thead>
<tr>
<th></th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admitted to ICU</td>
<td>8 (0.1%)</td>
<td>7,041 (99.9%)</td>
<td>7,049 (100%)</td>
</tr>
<tr>
<td>Hospitalized*</td>
<td>783 (6.4%)</td>
<td>11,452 (93.6%)</td>
<td>12,235 (100%)</td>
</tr>
<tr>
<td>Died</td>
<td>6 (0.0%)</td>
<td>18,027 (100%)</td>
<td>18,033 (100%)</td>
</tr>
<tr>
<td>HIV-Positive</td>
<td>4,042 (38.0%)</td>
<td>6,581 (62.0%)</td>
<td>10,623 (100%)</td>
</tr>
</tbody>
</table>

*Includes cases hospitalized for isolation or treatment (187 cases were hospitalized for isolation purposes, 271 required clinical care and 325 were hospitalized for unknown reasons).*
SEXUAL ORIENTATION

Sexual orientation in TESSy is defined according to the following non-mutually exclusive categories:

- Heterosexual
- MSM = MSM/homo or bisexual male
- Women who have sex with women
- Bisexual
- Other
- Unknown or undetermined

Sexual orientation is not necessarily representative of the gender of the person the case had sex with in the past 21 days nor does it imply sexual contact and sexual transmission.

We summarize here the sexual orientation that male cases identified with.

**Table 5: Summary of reported sexual orientations among male cases of mpox, European Region, TESSy, 2022–2023**

<table>
<thead>
<tr>
<th>Sexual Orientation</th>
<th>Count (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSM</td>
<td>10,792 (42.7%)</td>
</tr>
<tr>
<td>Bisexual</td>
<td>130 (0.5%)</td>
</tr>
<tr>
<td>Heterosexual</td>
<td>334 (1.3%)</td>
</tr>
<tr>
<td>Unknown or undetermined</td>
<td>2,744 (10.9%)</td>
</tr>
<tr>
<td>Not reported</td>
<td>11,268 (44.6%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>25,268 (100%)</strong></td>
</tr>
</tbody>
</table>
**MICROBIOLOGICAL ANALYSES**

**SPECIMEN TYPES**

Table 6: Summary of specimen types with positive test result used for diagnosis of mpox, European Region, TESSy, 2022–2023

<table>
<thead>
<tr>
<th>Specimen type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lesion swab</td>
<td>5,336 (58.7%)</td>
</tr>
<tr>
<td>Lesion crust</td>
<td>2,833 (31.1%)</td>
</tr>
<tr>
<td>Oropharyngeal swab</td>
<td>580 (6.4%)</td>
</tr>
<tr>
<td>Rectal swab</td>
<td>221 (2.4%)</td>
</tr>
<tr>
<td>Genital swab</td>
<td>94 (1.0%)</td>
</tr>
<tr>
<td>Urine</td>
<td>21 (0.2%)</td>
</tr>
<tr>
<td>Serum</td>
<td>13 (0.1%)</td>
</tr>
<tr>
<td>Semen</td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>9,098 (100%)</strong></td>
</tr>
</tbody>
</table>
Phylogenetics of mpox virus

Phylogeny of human monkeypox virus was performed using Nextstrain. Briefly, genome sequences were extracted from Nextstrain repository comprising the curated NCBI GenBank sequences and metadata that were quality assessed using Nextclade\(^1\). The sequences were filtered for the Nextstrain curated exclusions, minimum length of 10000 bp, collected from 2017 and subsampling of 40 samples per country during the same sampling month and year. The phylogenetic analysis was performed using Nextalign (masking specific sites), IQTREE to construct the tree and TreeTime to refine the tree and visualized using Microreact\(^2\).

There are two genetically distinct clades described for monkeypox virus: Clade I and Clade II with sub-clades IIa and IIb\(^3,4\). The current outbreak falls within Clade IIb and following the nomenclature used in Nextstrain, a majority of the 2022 sequences belong to lineage B.1\(^4,5\). A few sequences do not cluster with the outbreak sequences but fall into lineages A.2 and A.3\(^6-8\). Figure A shows a phylogeny based on sequences from Clade IIb. The phylogeny is also visualized in Microreact along with the sequence metadata. Sequences from 2022 and 2023 are indicated with coloured circles and the binary heatmap shows sequences submitted after 16 January 2023.

**Figure A. Phylogenetic tree of monkeypox virus sequences of Clade IIb as of 30 January 2023.**

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5. Nextstrain Genomic epidemiology of monkeypox virus. Available at: https://nextstrain.org/monkeypox/hmpxv1


DISCLAIMERS AND ACKNOWLEDGMENTS

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ACKNOWLEDGMENTS

We gratefully acknowledge the Nextstrain team, the authors, originating and submitting laboratories of the genetic sequences and metadata (NCBI Genbank) for sharing their work.
ANNEX

WHO and ECDC case definition prior to 22/12/2022

Cases of monkeypox should be reported to TESSy if they meet any of the WHO, ECDC or national case definitions.

Confirmed case

- Laboratory confirmed monkeypox virus infection by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)\(^1\) and/or sequencing.

Probable case:

- A person presenting with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region or elsewhere on the body. Mucosal lesions may include single or multiple oral, conjunctival, urethral, penile, vaginal, or ano-rectal lesions. Anorectal lesions can also manifest as ano-rectal inflammation (proctitis), pain and/or bleeding.

AND One or more of the following:

- has an epidemiological link\(^2\) to a probable or confirmed case of monkeypox in the 21 days before symptom onset;
- identifies as gay, bisexual or other man who has sex with men;
- has had multiple or anonymous sexual partners in the 21 days before symptom onset;
- has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody\(^3\) (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titre based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the absence of a recent smallpox/monkeypox vaccination or other known exposure to OPXV; *has a positive test result for orthopoxviral infection (e.g. OPXV-specific PCR without MPXV-specific PCR or sequencing)\(^1\).

Suspected case

- A person who is a contact of a probable or confirmed monkeypox 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.
• A person presenting since 01 January 2022 with an unexplained acute skin rash, mucosal lesions or lymphadenopathy (swollen lymph nodes). The skin rash may include single or multiple lesions in the ano-genital region 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, 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 monkeypox 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 coinfections have been identified.

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\(^1\).
• Conversely, 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.

Both the previous WHO and ECDC case definitions can be found in the Annex.

---

1. PCR on a blood specimen may be unreliable and should also not be used alone as a first line diagnostic test. If blood PCR is negative and was the only test done, this is not sufficient to discard a case that otherwise meets the definition of a suspected for probable case. This applies regardless of whether the blood PCR was for OPXV or MPXV specific.
2. The person has been exposed to a probable or confirmed monkeypox case. Please see below definition of a contact.

3. Serology can be used for retrospective case classification for a probable case in specific circumstances such as when diagnostic testing through PCR of skin lesion specimens has not been possible, or in the context of research with standardized data collection. The primary diagnostic test for monkeypox diagnosis is PCR of skin lesion material or other specimen such as an oral or nasopharyngeal swab as appropriate. Serology should not be used as a first line diagnostic test.

**ECDC case definition for monkeypox prior to 08/09/2022**:

**Confirmed case**:

A person with a laboratory-confirmed monkeypox infection (1) monkeypox virus specific PCR assay positive result or (2) orthopoxvirus-specific PCR assay positive result which is then confirmed by nucleotide sequence determination of the detected virus as MPXV) with symptom onset since 1 March 2022.

**Probable case**:

(1) A person with an unexplained rash\(^1\) on any part of their body AND one or more other symptom(s) of monkeypox infection\(^2\) with symptom onset since 1 March 2022

AND one of the following:

- has a positive laboratory test result on orthopoxviral infection (e.g., orthopoxvirus-specific positive PCR without sequencing, electron microscopy, serology);
- has an epidemiological link to a confirmed or probable case of monkeypox in the 21 days before symptom onset;
- reports travel to MPX endemic countries in the 21 days before symptom onset;
- is a person (of any sexual orientation) who had multiple or anonymous sexual partners in the 21 days before symptom onset;
- is a man who has sex with men.

OR

(2) A person with an unexplained generalized or localized maculopapular or vesiculopustular rash with centrifugal spread, with lesions showing umbilication or scabbing, lymphadenopathy and one or more other MPX-compatible symptoms\(^2\).
1. Since EU/EEA countries are just starting to identify cases and if testing capacity is sufficient, the above more sensitive case definition can be used. In countries with limited testing capacity for orthopoxviruses, the following description can be added to characterize the rash: ‘unexplained localized or generalized maculopapular or vesiculopustular rash potentially with umbilication or scabbing’.

2. Fever (usually higher >38.5°C), headache, back ache, fatigue, lymphadenopathy (localized or generalized).

**WHO case definition for monkeypox prior to 25/08/2022:**

**Confirmed case**

- Laboratory confirmed monkeypox virus by detection of unique sequences of viral DNA by real-time polymerase chain reaction (PCR)\(^1\) and/or sequencing.

**Probable case:**

- A person meeting the case definition for a suspected case

**AND One or more of the following:**

- has an epidemiological link [prolonged\(^2\) face-to-face exposure in close proximity, including health workers without appropriate PPE (gloves, gown, eye protection and respirator); direct physical contact with skin or skin lesions, including sexual contact; or contact with contaminated materials such as clothing, bedding or utensils] to a probable or confirmed case of monkeypox in the 21 days before symptom onset;
- has had multiple or anonymous sexual partners in the 21 days before symptom onset;
- has detectable levels of anti-orthopoxvirus (OPXV) IgM antibody\(^3\) (during the period of 4 to 56 days after rash onset); or a four-fold rise in IgG antibody titre based on acute (up to day 5-7) and convalescent (day 21 onwards) samples; in the absence of a recent smallpox/monkeypox vaccination or other known exposure to OPXV;
- has a positive test result for orthopoxviral infection (e.g. OPXV-specific PCR without MPXV-specific PCR or sequencing) \(^1\).
**Suspected case**

- A person of any age presenting since 01 January 2022 with an unexplained acute rash or one or more acute skin lesions

**AND one or more of the following signs or symptoms:**

- headache, acute onset of fever (>38.5°C), lymphadenopathy (swollen lymph nodes), myalgia (muscle pain/body aches), back pain, asthenia (profound weakness)

**AND for which the following common causes of acute rash or skin lesions do not fully explain the clinical picture:**

- varicella zoster, herpes zoster, measles, herpes simplex, bacterial skin infections, disseminated gonococcus infection, primary or secondary syphilis, chancroid, lymphogranuloma venerum, 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 monkeypox 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 coinfections have been identified.

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- 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\(^1\).
- Conversely, 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.

---

1. PCR on a blood specimen may be unreliable and should also not be used alone as a first line diagnostic test. If blood PCR is negative and was the only test done, this is not sufficient to discard a case that otherwise meets the definition of a suspected for probable case. This applies regardless of whether the blood PCR was for OPXV or MPXV specific.
2. Evidence is currently lacking as to the duration of exposure necessary for infection by the respiratory route, including how it relates to the severity of the index case’s disease. Characterization of this parameter is one of the goals of the case investigation form described below.

3. Serology can be used for retrospective case classification for a probable case in specific circumstances such as when diagnostic testing through PCR of skin lesion specimens has not been possible, or in the context of research with standardized data collection. The primary diagnostic test for monkeypox diagnosis is PCR of skin lesion material or other specimen such as an oral or nasopharyngeal swab as appropriate. Serology should not be used as a first line diagnostic test.