22-ID-10

Committee: Infectious Disease

Title: Public Health Reporting and National Notification for Monkeypox Virus Infection

☐Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: _N/A____.

Synopsis: This position statement creates a standardized surveillance case definition for infection with monkeypox virus and recommends that monkeypox be made nationally notifiable.

I. Statement of the Problem

Beginning in May 2022, multiple countries that do not usually have monkeypox began to report cases, including the United States. Most of these cases were not associated with travel to parts of West or Central Africa where the disease is endemic. Many, but not all, cases were in gay or bisexual men, or other men who report sex with men (MSM),[1] suggesting new risk factors for the disease. Between May 13 and June 2, 2022 the World Health Organization reported 780 cases in 27 countries.[2] The unprecedented rapid increase in cases occurring over a widespread geographic area in people without traditional risk factors indicates an emerging public health concern requiring standardized surveillance data collection to describe the extent of the problem and case reporting to public health to facilitate response.

II. Background and Justification

Monkeypox is a rare zoonotic disease that is caused by infection with monkeypox virus. Monkeypox virus (MPXV) belongs to the *Orthopoxvirus* genus in the family *Poxviridae*. The *Orthopoxvirus* genus also includes variola virus (which causes smallpox), vaccinia virus (used in the smallpox vaccine), and cowpox virus. Monkeypox was first discovered in 1958 when two outbreaks of a pox-like disease occurred in monkeys kept for research. The first human case of monkeypox was recorded in 1970 in the Democratic Republic of the Congo (DRC) during a period of intensified effort to eliminate smallpox. Since then, monkeypox has been reported in people in several other central and western African countries: Cameroon, Central African Republic, Cote d'Ivoire, Democratic Republic of the Congo, Gabon, Liberia, Nigeria, Republic of the Congo, and Sierra Leone.[3]

Until May 2022, monkeypox cases in people outside of Africa were linked to international travel or imported animals from endemic areas in Africa. Cases in the United States in 2003 were linked to imported rodents from Ghana;[4] two cases in 2021 were linked to international travel.[5] Israel, Singapore, and the United Kingdom have also had cases linked to international travel.[5] Beginning in May 2022, multiple countries that do not usually have monkeypox, including the United States, began to report cases not associated with the traditional epidemiologic risk factor of travel to places where the disease is endemic. Many, but not all, cases were in gay or bisexual men, or other men who report sex with men (MSM), suggesting possible new risk factors for the disease.[1]

At this time, testing for MPXV is not commercially available but can be conducted through public health laboratories that are part of the Laboratory Response Network (LRN). These laboratories can provide real-time polymerase-chain-reaction (RT-PCR) to detect the presence of non-variola orthopoxvirus DNA. The Centers for Disease Control and Prevention (CDC) can confirm the presence of MPXV and determine the clade (West African or Congo Basin clade) by MPXV species-specific RT-PCR. Commercial testing is likely to become available during 2022.

Monkeypox does not spread easily person-to-person, but transmission can occur through direct contact with lesions or bodily fluids, indirect contact through fomites (materials that were in contact with lesions or bodily fluids), and through exposure to large respiratory droplets from prolonged face-to-face contact.[6] Individuals with exposures that support the highest likelihood of transmission should follow the latest guidance for post-exposure

vaccine.[7] No commercially available vaccines exist; products are only available through request from the federal government by a public health authority. All individuals with a potential exposure to an infected person should be monitored for 21 days post-exposure for the development of symptoms.[7] Both vaccine acquisition for post-exposure and symptom monitoring should be coordinated with public health authorities.

Currently, 13 jurisdictions in the U.S. have mandated reporting of monkeypox explicitly. One additional jurisdiction has orthopox virus as explicitly reportable to public health authorities. The apparent changing epidemiology of the disease, the current reliance on the public health system for testing and access to vaccine, and the need for prompt public health response to identify cases for the purposes of reducing spread all support the need for a standardized case definition and national notifiability for MPXV infection.

III. Statement of the desired action(s) to be taken

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for **monkeypox virus infection**.
    A. Utilize standard sources (e.g., reporting*) for case ascertainment for monkeypox virus infection. Surveillance for monkeypox virus infection should use the recommended sources of data to the extent of coverage presented in Section V.

    B. Utilize standardized criteria for case ascertainment for monkeypox virus infection presented in Section VI and Table VI in Technical Supplement.

    C. Utilize standardized criteria for case classification for monkeypox virus infection presented in Section VII and Table VII in Technical Supplement.

2. Utilize standardized criteria for case ascertainment and classification (based on Sections VI and VII and Technical Supplement) for **monkeypox virus infection** and **add** monkeypox virus infection to the *Nationally Notifiable Condition List:*
    ☐ Immediately notifiable, extremely urgent (within 4 hours)
    ☒ Immediately notifiable, urgent (within 24 hours)
    ☐ Routinely notifiable
    ☐ No longer notifiable

3. CSTE recommends that all States and Territories enact laws (statute or rule/regulation as appropriate) to make this disease or condition reportable in their jurisdiction. Jurisdictions (e.g. States and Territories) conducting surveillance (according to these methods) should submit case notifications** to CDC.

4. Expectations for Message Mapping Guide (MMG) development for a newly notifiable condition: the National Notifiable Diseases Surveillance System (NNDSS) is transitioning to HL7-based messages for case notifications; the specifications for these messages are presented in MMGs. When CSTE recommends a new condition be made nationally notifiable, CDC must obtain Office of Management and Budget Paperwork Reduction Act (OMB PRA) approval prior to accepting case notifications for the new condition. Under anticipated timelines, notification using the Generic V2 MMG would support transmission of the basic demographic and epidemiologic information common to all cases and could begin with the new *MMWR* year following the CSTE annual conference. Input from CDC programs and CSTE would prioritize development of a disease-specific MMG for the new condition among other conditions waiting for MMGs.

5. CDC should publish data on monkeypox virus infection as appropriate (see Section IX). CSTE recommends the following case statuses be included in the CDC Print Criteria:
   - ☒Confirmed
   - ☒Probable
   - ☐Suspect
   - ☐Unknown

6. CSTE recommends that all jurisdictions (e.g. States, Localities, or Territories) with legal authority to conduct public health surveillance follow the recommended methods outlined in this standardized surveillance position statement.

**Reporting: process of a healthcare provider or other entity submitting a report (case information) of a condition under public health surveillance to local, state, or territorial public health.*
***Notification: process of a local or state public health authority submitting a report (case information) of a condition on the* Nationally Notifiable Conditions List *to CDC.*

IV. Goals of Surveillance

To provide information on the temporal, geographic, and demographic occurrence of infections due to MPXV, to describe risk factors for infection, and to facilitate prevention and control efforts.

V. Methods for Surveillance: Surveillance for monkeypox virus infection should use the recommended sources of data and the extent of coverage listed in Table V.

Surveillance for MPXV infection will initially rely on reporting individuals with symptoms consistent with monkeypox, especially among those with a known exposure or other known epidemiologic risk factor. These individuals will have testing coordinated through public health authorities.

As laboratories outside of the public health system implement testing for orthopoxvirus and/or MPXV, laboratory reporting may become a more common source of initial reports. Healthcare providers and facilities who diagnose or become aware of monkeypox cases should report them to public health authorities.

Table V. Recommended sources of data and extent of coverage for ascertainment of cases of monkeypox virus infection.

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities (e.g., hospitals, veterinarians, pharmacies, poison centers), specify: hospitals, veterinarians and veterinary laboratories	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Data from electronic medical records	X	
Telephone survey		
School-based survey		
Other, specify: N/A		

VI. Criteria for case ascertainment

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition.

Monkeypox is described in the literature as usually beginning with a febrile prodrome and including lymphadenopathy. The characteristic rash lesions historically described as associated with MPXV infection typically begin to develop simultaneously, within 5 days of symptom onset, and evolve together on any given part of the body. The evolution of rash lesions progresses through four stages—macular, papular, vesicular, to pustular—before scabbing over and resolving. The typical rash lesions are well circumscribed, deep seated, and often develop umbilication. Rash lesions can occur on palmar and plantar surfaces; when a disseminated rash occurs, it is often centrifugal (with more lesions occurring on extremities, face). Rash lesions are often reported as painful, but can also be pruritic, especially once a scab or crust has formed as they resolve. In addition to the febrile prodromal symptoms (fever, chills, headache, and myalgia), lymphadenopathy, and rash lesions, other symptoms that may occur include sore throat (which may be associated with oral lesions), cough, and significant fatigue. Complications of MPXV infection can include pneumonitis, encephalitis, sight-threatening keratitis, and secondary bacterial infections.

Emerging data from the 2022 outbreak indicate that people infected with MPXV many not always present with, or recognize, a prodromal period. Additionally, the presentation of rash lesions has been reported to be highly variable; rash lesions may be highly localized and involve only a few lesions or be more generalized. The rash lesions may occur on skin or mucous membranes and in recent cases where exposure to the virus has occurred during sexual contact, the initial lesions have been more commonly seen in the genital, anal, perianal, or oral areas. Proctitis has been reported in multiple cases.

Rash lesions caused by MPXV infection can be confused with other diseases that are more commonly encountered in clinical practice (e.g., syphilis, herpes, and varicella zoster; co-infections have been documented). Individuals suspected of having MPXV infection should also receive diagnostic work-up for other, more common infections, as indicated by the clinical presentation. Laboratory evidence of MPXV infection does not eliminate the possibility of a co-infection; similarly, diagnosis of an alternative etiology does not, in and of itself, exclude the possibility of MPXV infection.

MPXV infection in individuals that meet epidemiologic criteria who develop a febrile illness, lymphadenopathy, and other non-specific signs and symptoms can be considered unlikely if a rash does not develop within 5 days of symptom onset.

Report any illness to public health authorities that meets criteria below.

A1. Clinical Criteria for Reporting

A person presenting with new onset of:

- clinically compatible rash lesions*; OR
- lymphadenopathy or fever**

** When access to testing is being triaged through the public health authority, the presence of clinically compatible rash lesions alone is sufficient to report, even in the absence of an epidemiologic linkage criterion. Once testing is available without public health pre-approval, the presence of clinically compatible rash lesions should be combined with either a higher or lower epidemiologic linkage criterion for reporting.*

***A person presenting with lymphadenopathy or fever without any clinically compatible rash lesions must meet a higher risk epidemiologic risk criterion for reporting.*

A2. Laboratory Criteria for Reporting

- Detection of MPXV or orthopoxvirus nucleic acid by molecular testing in a clinical specimen; OR
- Detection of presence of orthopoxvirus by immunohistochemistry in tissue; OR
- Detection of MPXV or orthopoxvirus by genomic sequencing in a clinical specimen; OR

- Detection of anti-orthopoxvirus IgM antibody using a validated assay on a serum sample drawn 4-56 days after rash onset with no recent history (last 60 days) of vaccination***.

****Recent administration of ACAM2000 and Jynneos needs to be considered when interpreting an antibody titer. RABORAL V-RG is an oral rabies vaccine product for wildlife, is a recombinant vaccinia virus, and could lead to an antibody response in an individual exposed to the liquid vaccine; this is expected to be an extremely rare occurrence.*

A3. Epidemiologic Linkage Criteria for Reporting^

Epidemiologic risk factors within 21 days of illness onset:

- Higher Risk Epidemiologic Linkages
  - Contact, without the use of appropriate PPE‡, with a person or animal with a suspected or known orthopoxvirus or MPXV infection; OR
  - Contact, without the use of appropriate PPE‡ or Biosafety Level protocols‡, with laboratory specimens or other items that could serve as fomites that have been in contact with a person or animal with a suspected or known orthopoxvirus or MPXV infection; OR
  - Member of an exposed cohort as defined by public health authorities experiencing an outbreak (e.g., participated in activities associated with risk of transmission in a setting where multiple cases occurred).
- Lower Risk Epidemiologic Linkages
  - Member of a cohort as defined by public health authorities experiencing monkeypox activity; OR
  - Contact with a dead or live wild or exotic pet animal of an African species, or used or consumed a product derived from such an animal (e.g., game meat, powders, etc.); OR
  - Residence in or travel to a country where monkeypox is endemic.

^Epidemiologic linkage criteria must be paired with clinical criteria to trigger a report to public health.
‡The language "without the use of appropriate PPE or Biosafety Level protocols" includes breaches in the recommended PPE and deviations from appropriate BSL protocols.

A4. Vital Records Criteria for Reporting

A person whose death certificate lists monkeypox as a cause of death or a significant condition contributing to death.

A5. Other Criteria for Reporting

Diagnosis of an animal with MPXV infection by a veterinarian or a veterinary diagnostic laboratory.

B. Disease-specific data elements to be included in the initial report

Epidemiologic risk factors within 21 days of illness onset:

- Contact, without the use of appropriate PPE‡ with a person or animal with a suspected or known orthopoxvirus or MPXV infection; OR
- Contact, without the use of appropriate PPE‡ or Biosafety Level protocols‡, with laboratory specimens or other items that could serve as fomites that have been in contact with a person or animal with a suspected or known orthopoxvirus or MPXV infection; OR
- Member of an exposed cohort as defined by public health authorities experiencing an outbreak (e.g., participated in activities associated with risk of transmission in a setting where multiple cases occurred); OR
- Member of a cohort as defined by public health authorities experiencing monkeypox activity; OR
- Contact with a dead or live wild or exotic pet animal of an African species, or used or consumed a product derived from such an animal (e.g., game meat, powders, etc.); OR
- Residence in or travel to a country where monkeypox is endemic.

Occupation
Pregnancy Status
MPXV Clade (if available)

‡The language "without the use of appropriate PPE or Biosafety Level protocols" includes breaches in the recommended PPE and deviations from appropriate BSL protocols.

VII. Case Definition for Case Classification

A. Narrative: Description of criteria to determine how a case should be classified.

A1. Clinical Criteria

A person presenting with new onset of:

- clinically compatible rash lesions*; OR
- lymphadenopathy or fever**

**The presence of clinically compatible rash lesions should be combined with either a higher or lower epidemiologic linkage criterion for case classification.*

***A person presenting with lymphadenopathy or fever without any clinically compatible rash lesions must meet a higher risk epidemiologic risk criterion for case classification.*

A2. Laboratory Criteria

Confirmatory laboratory evidence:

- Detection of MPXV nucleic acid by molecular testing in a clinical specimen; OR
- Detection of MPXV by genomic sequencing in a clinical specimen.

Presumptive laboratory evidence:

- Detection of orthopoxvirus nucleic acid by molecular testing in a clinical specimen AND no laboratory evidence of infection with another non-variola orthopox virus; OR
- Detection of presence of orthopoxvirus by immunohistochemistry in tissue; OR
- Detection of orthopoxvirus by genomic sequencing in a clinical specimen; OR
- Detection of anti-orthopoxvirus IgM antibody using a validated assay on a serum sample drawn 4-56 days after rash onset, with no recent history (last 60 days) of vaccination***.

Supportive laboratory evidence:
N/A

****Recent administration of ACAM2000 and Jynneos needs to be considered when interpreting an antibody titer. RABORAL V-RG is an oral rabies vaccine product for wildlife, is a recombinant vaccinia virus, and could lead to an antibody response in an individual exposed to the liquid vaccine; this is expected to be an extremely rare occurrence.*

Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.

A3. Epidemiologic Linkage

Epidemiologic risk factors within 21 days of illness onset:

- Higher Risk Epidemiologic Linkages
  - Contact, without the use of appropriate PPE‡, with a person or animal with a known orthopoxvirus or MPXV infection; OR
  - Contact, without the use of appropriate PPE‡ or Biosafety Level protocols‡, with laboratory specimens or other items that could serve as fomites that have been in contact with a person or animal with a known orthopoxvirus or MPXV infection; OR
  - Member of an exposed cohort as defined by public health authorities experiencing an outbreak (e.g., participated in activities associated with risk of transmission in a setting where multiple cases occurred).
- Lower Risk Epidemiologic Linkages
  - Member of a cohort as defined by public health authorities experiencing monkeypox activity; OR

- Contact with a dead or live wild or exotic pet animal of an African species, or used or consumed a product derived from such an animal (e.g., game meat, powders, etc.); OR
- Residence in or travel to a country where monkeypox is endemic.

‡*The language "without the use of appropriate PPE or Biosafety Level protocols" includes breaches in the recommended PPE and deviations from appropriate BSL protocols.*

A4. Case Classifications

Confirmed:
- Meets confirmatory laboratory criteria

Probable:
- Meets presumptive laboratory criteria

Suspect:
- Meets clinical criteria AND epidemiologic criteria^ AND no evidence of a negative test for either non-variola orthopoxvirus or MPXV

^*The presence of clinically compatible rash lesions should be combined with either a higher or lower epidemiologic linkage criterion for case classification. A person presenting with lymphadenopathy or fever without any clinically compatible rash lesions must meet a higher risk epidemiologic risk criterion for case classification.*

B. Criteria to distinguish a new case of this disease or condition from reports or notifications which should not be enumerated as a new case for surveillance

For surveillance purposes, a new case of MPXV infection meets the following criteria:
1. Healthy tissue has replaced the site of all previous lesions after they have scabbed and fallen off; AND
2. New lesions are present which have tested positive for orthopoxvirus or MPXV DNA by molecular methods or genomic sequencing.

VIII. Period of Surveillance

Surveillance should be routine and ongoing.

IX. Data sharing/release and print criteria

CSTE recommends the following case statuses* be included in the 'case' count released outside of the public health agency:

☒Confirmed
☒Probable
☐Suspect
☐Unknown

* Which case statuses are included in the case counts constitute the "print criteria."

Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.

Production of national data summaries and national data re-release for non-NNCs:

- Prior to release of national data summaries CDC should follow the CDC/ATSDR Policy on Releasing & Sharing Data, issued on April 16, 2003 and referenced in 11-SI-01 and custodians of such data should consult the CDC-CSTE Intergovernmental Data Release Guidelines Working Group report (www.cste2.org/webpdfs/drgwgreport.pdf) which contains data release guidelines and procedures for CDC programs re-releasing state, local, or territorial-provided data.
- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

X. Revision History

N/A. This is the first standardized surveillance position statement for MPXV infection.

XI. References

1. CDC. Monkeypox Virus Infection in the United States and Other Non-endemic Countries—2022. Health Advisory: CDCHAN-00466. May 20, 2022. https://emergency.cdc.gov/han/2022/han00466.asp
2. WHO. Multi-country monkeypox outbreak: situation update. Disease Outbreak News. June 4, 2022. https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON390
3. Petersen, et al. Human Monkeypox: Epidemiologic and Clinical Characteristics, Diagnosis, and Prevention. Infect Dis Clin N Am 33 (2019) 1027–1043. https://doi.org/10.1016/j.idc.2019.03.001
4. CDC. Update: multistate outbreak of monkeypox---Illinois, Indiana, Kansas, Missouri, Ohio, and Wisconsin, 2003. MMWR 2003;52 (27):642-646. https://www.cdc.gov/mmwr/preview/mmwrhtml/mm5227a5.htm
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7. CDC. Monitoring People Who Have Been Exposed. https://www.cdc.gov/poxvirus/monkeypox/clinicians/monitoring.html. Page accessed June 12, 2022.

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Council of State and Territorial Epidemiologists

Technical Supplement

Table VI. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Monkeypox Virus Infection			
Clinical Criteria for Reporting				
New onset of a clinically compatible rash lesions*			N	
New onset of lymphadenopathy or fever				N
Laboratory Criteria for Reporting				
Detection of MPXV nucleic acid by molecular testing in a clinical specimen	S			
Detection of orthopoxvirus nucleic acid by molecular testing in a clinical specimen	S			
Detection of presence of orthopoxvirus by immunohistochemistry in tissue	S			
Detection of MPXV by genomic sequencing in a clinical specimen	S			
Detection of orthopoxvirus by genomic sequencing in a clinical specimen	S			
Detection of anti-orthopoxvirus IgM antibody using a validated assay on a serum sample drawn 4-56 days after rash onset		N		
Absence of receipt of vaccination** in the 60 days prior to specimen collection		N		
Epidemiological Linkage Criteria for Reporting				
Higher Risk Epidemiologic Linkages				
Contact, without the use of appropriate PPE‡, with a person or animal with a suspected or known orthopoxvirus or MPXV infection within 21 days of illness onset			O	O
Contact, without the use of appropriate PPE‡ or Biosafety Level protocols‡, with laboratory specimens or other items that could serve as fomites that have been in contact with a person or animal with a suspected or known orthopoxvirus or MPXV infection within 21 days of illness onset			O	O
Member of an exposed cohort as defined by public health authorities experiencing an outbreak (e.g., participated in activities associated with risk of transmission in a setting where multiple cases occurred) within 21 days of illness onset			O	O
Lower Risk Epidemiologic Linkages				
Member of a cohort as defined by public health authorities experiencing monkeypox activity within 21 days of illness onset			O	
Contact with a dead or live wild or exotic pet animal of an African species, or used or consumed a product derived from such an animal (e.g., game meat, powders, etc.) within 21 days of illness onset			O	
Residence in or travel to a country where monkeypox is endemic within 21 days of illness onset			O	
Vital Records Criteria for Reporting				
A person whose death certificate lists monkeypox as a cause of death or a significant condition contributing to death.	S			
Other Criteria for Reporting				
Diagnosis of an animal with MPXV infection by a veterinarian or a veterinary diagnostic laboratory.	S			

Notes:

S = This criterion alone is SUFFICIENT to report a case.

N = All "N" criteria in the same column are NECESSARY to report a case.

O = At least one of these "O" (ONE OR MORE) criteria in **each category** (categories=clinical criteria, laboratory criteria, epidemiological criteria, vital records criteria, and other criteria for reporting) **in the same column**—in conjunction with all "N" criteria in the same column—is required to report a case.

** When access to testing is being triaged through the public health authority, the presence of clinically compatible rash lesions alone is sufficient to report, even in the absence of an epidemiologic linkage criterion. Once testing is available without public health pre-approval, the presence of clinically compatible rash lesions should be combined with either a higher or lower epidemiologic linkage criterion for reporting.*

***Recent administration of ACAM2000 and Jynneos needs to be considered when interpreting an antibody titer. RABORAL V-RG is an oral rabies vaccine product for wildlife, is a recombinant vaccinia virus, and could lead to an antibody response in an individual exposed to the liquid vaccine; this is expected to be an extremely rare occurrence.*

‡ The language "without the use of appropriate PPE or Biosafety Level protocols" includes breaches in the recommended PPE and deviations from appropriate BSL protocols.

Table VII. Classification Table: Criteria for defining a case of Monkeypox Virus Infection.

Criterion	Suspect		Probable			Confirmed
Clinical Evidence						
New onset of a clinically compatible rash lesions	N					
New onset of lymphadenopathy or fever		N				
Laboratory Evidence						
Detection of MPXV nucleic acid by molecular testing in a clinical specimen						S
Detection of MPXV by genomic sequencing in a clinical specimen						S
Detection of orthopoxvirus nucleic acid by molecular testing in a clinical specimen			N			
No laboratory evidence of infection with another non-variola orthopoxvirus			N			
Detection of presence of orthopoxvirus by immunohistochemistry in tissue				S		
Detection of orthopoxvirus by genomic sequencing in a clinical specimen				S		
Detection of anti-orthopoxvirus IgM antibody using a validated assay on a serum sample drawn 4-56 days after rash onset					N	
Absence of receipt of vaccination* in the 60 days prior to specimen collection					N	
No evidence of a negative test for either non-variola orthopoxvirus or MPXV	N	N				
Epidemiological Linkage Evidence						
Higher Risk Epidemiologic Linkages						
Contact, without the use of appropriate PPE‡, with a person or animal with a suspected or known orthopoxvirus or MPXV infection within 21 days of illness onset	O	O				
Contact, without the use of appropriate PPE‡ or Biosafety Level protocols‡, with laboratory specimens or other items that could serve as fomites that have been in contact with a person or animal with a suspected or known orthopoxvirus or MPXV infection within 21 days of illness onset	O	O				
Member of an exposed cohort as defined by public health authorities experiencing an outbreak (e.g., participated in activities associated with risk of transmission in a setting where multiple cases occurred) within 21 days of illness onset	O	O				
Lower Risk Epidemiologic Linkages						
Member of a cohort as defined by public health authorities experiencing monkeypox activity within 21 days of illness onset	O					
Contact with a dead or live wild or exotic pet animal of an African species, or used or consumed a product derived from such an animal (e.g., game meat, powders, etc.) within 21 days of illness onset	O					
Residence in or travel to a country where monkeypox is endemic within 21 days of illness onset	O					
Criteria to distinguish a new case:						
Healthy tissue has replaced the site of all previous lesions after they have scabbed and fallen off			N	N	N	N
New lesions are present which have tested positive for orthopoxvirus or MPXV DNA by molecular methods or genomic sequencing			N	N	N	N

Notes:
S = This criterion alone is SUFFICIENT to classify a case.
N = All "N" criteria in the same column are NECESSARY to classify a case.
O = At least one of these "O" (ONE OR MORE) criteria in **each category** (categories=clinical evidence, laboratory evidence, and epidemiologic evidence) **in the same column**—in conjunction with all "N" criteria in the same column—is required to classify a case.

**Recent administration of ACAM2000 and Jynneos needs to be considered when interpreting an antibody titer. RABORAL V-RG is an oral rabies vaccine product for wildlife, is a recombinant vaccinia virus, and could lead to an antibody response in an individual exposed to the liquid vaccine; this is expected to be an extremely rare occurrence.*

‡ The language "without the use of appropriate PPE or Biosafety Level protocols" includes breaches in the recommended PPE and deviations from appropriate BSL protocols.