

#### **Clinical Description**

Monkeypox is a severe acute illness caused by infection with the monkeypox virus, a species in the genus *Orthopoxvirus* and the family *Poxviridae*. Onset is usually sudden with initial symptoms of fever, headache, muscle aches, backache, swollen lymph nodes (lymphadenopathy), chills, and exhaustion. Shortly afterwards, a rash develops, usually starting on the face and spreading to other body parts. Lesions typically begin to form simultaneously and evolve together on any part of the body as they progress from small red bumps to larger pus-filled bumps to scabs before falling off. Clinically, the disease closely resembles smallpox, but lymphadenopathy is a more prominent feature in the early stage of monkeypox disease.

**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.

### **Laboratory Confirmation Criteria**

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

#### Epidemiologic Linkage (within 21 days of illness onset)

### Higher Risk Epidemiologic Linkages

- Contact, without the use of appropriate PPE<sup>‡</sup>, 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.* 

#### **Case Classification**

**Confirmed**: A case that meets confirmatory laboratory criteria.

**Probable:** A case that has 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\*\*\*.

Suspect: A case that meets clinical criteria AND epidemiologic criteria^ AND no evidence of a

negative test for either non-variola orthopoxvirus or MPXV.



\*\*\*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 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.

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.

#### **Additional Information**

For surveillance purposes, a new case of MPXV infection meets the following criteria:

- 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.



### **NBS Entry Guidelines for Laboratory Reports**

Required fields are noted by  $\rightarrow$  and **BOLD** and other preferred data entry fields by  $\Rightarrow$  and *italics*. Control + Click to see Patient Tab Lab Report Table

	tient Tab Lab Report Table			
Lab Report		NBS Field Name	Description/Instructions	
•	Or	der Information		
	<b>→</b>	Reporting Facility	Search for reporting facility or enter quick code. Select <b>original source of report</b> , not other public health entity sharing report. Note: If Facility is not found, search by other criteria (city, etc.) then enter a new Organization as needed.	
	⇒	Ordering Facility	Search for ordering facility, enter quick code or check "Same as Reporting Facility." Note: If Facility is not found, search by other criteria (city, etc.) then enter a new Organization as needed.	
	₽	Ordering Provider	Search for ordering provider or enter quick code. Note: If Provider is not found, search by other criteria (city, etc.) then enter a new Provider as needed.	
	<b>→</b>	Program Area	Enter or edit to <b>IDEAS – Infectious Disease</b> Note: Use the drop-down list for manual lab entry. An ELR will pre-populate based on the condition. Check and edit if incorrect using Transfer Ownership button.	
	<b>→</b>	Jurisdiction	Jurisdiction is automatically filled in based on the patient's zip code. Review and correct as needed. Select or edit "Jurisdiction" based on patient address if available, location of patient's provider, or location of reporting facility, in that order.	
	⇒	Lab Report Date	Enter date result was reported to provider if available.	
	<b>→</b>	Date Received by Public Health	"Date Received by Public Health" pre-populates with current date. Enter correct date - earliest date the lab report was received by a public health entity (local, regional or state).	
	⇒	Ordered Test	Refer to table below.	
		Accession Number	Enter unique ID assigned to specimen.	
	<b>→</b>	Specimen Source	Select Blood venous, other appropriate choice, or Other with description in Result Comments.	
		Specimen Site		
	<b>→</b>	Date Specimen Collected	Enter date specimen collected.	
		Patient Status at Specimen Collection		
		Pregnant		
		Weeks		
	Te	est Result(s)		
	<b>→</b>	Resulted Test and Result(s)	Refer to table below and use appropriate fields below.	
	<b>→</b>	Resulted Test	Refer to table below.	
	ጏ	Coded Result	Refer to table below.	
	⇒	Numeric Result	Refer to table below. Enter units in the 2 <sup>nd</sup> box.	
	⇒	Text Result	Refer to table below.	



	NBS Field Name	Description/Instructions
⇧	Reference Range	If applicable, enter the reference range or cut-off value for normal results.
	Result status	
	Result comments	
If your choice for Resulted Test brings up additional fields (not listed in the Lab Report table), entering data in these fields is optional.		
Click on Add Test Result when the Test Result(s) section is completed and add additional lab results as needed.		
Administrative		
	Comments	
	If tal Cli ad	Result status Result comments  If your choice for Resulted Test bring table), entering data in these fields in the Click on Add Test Result when the Te additional lab results as needed.  Administrative

Ordered Test, Resulted Test and Test Results				
Description	⇒ Ordered Test	→ Resulted Test	→ Test Result(s)	
PCR for Orthopoxvirus	Orthopoxvirus DNA (Long search "ortho")	Orthopoxvirus DNA (Long search "ortho")	Detected, Not Detected, etc.	
PCR for Orthopoxvirus non- variola	Orthopoxvirus. non- variola DNA [Presence] in Specimen by NAA with probe detection (Long search "ortho")	Orthopoxvirus. non- variola DNA [Presence] in Specimen by NAA with probe detection (Long search "ortho")	Detected, Not Detected, etc.	
PCR for monkeypox virus	Monkeypox virus DNA [Presence] in Specimen by NAA with probe detection (long search "monkey"	Monkeypox virus DNA [Presence] in Specimen by NAA with probe detection (long search "monkey"	Detected, Not Detected, etc.	
Viral Culture	Culture, viral (short search "viral")	Microorganism Identified (short search "microorganism")	Organism: Select genus and species of organism isolate If no isolate, search for "growth" and select "No growth"	
Electron microscopy	Virus, electron microscopic exam (short search "virus, elec")	Virus, electron microscopy (short search "virus, elec")	Text Result: Describe findings	
Tests for possible alt	ernative diagnosis			
PCR for Varicella Zoster Virus (VZV)	Varicella zoster virus (VZV) PCR (DNA or RNA) (short search "varicella")	Varicella-Zoster Virus (VZV) DNA (short search VZV)	Coded Result: "detected" or "not detected"	
PCR for HSV	Herpes Simplex virus (HSV), PCR (DNA or RNA) (short search "HSV")	Herpes simplex virus (HSV) DNA (short search HSV)	Coded Result: "detected" or "not detected"	
PCR for Enterovirus	Enterovirus PCR (DNA or RNA) (short search "enterovirus")	Enterovirus, RNA (short search "enterovirus")	Coded Result: "detected" or "not detected"	



DFA for VZV	Virus Direct Detection, by DFA (short search "DFA")	Varicella-Zoster Virus (VZV) antigen (short search "varicella")	Coded Result: "detected" or "not detected" and if known, enter titer in Numeric Result:
DFA for HSV	Virus Direct Detection, by DFA (short search "DFA")	Herpes simplex virus (HSV) antigen (short search "HSV")	Coded Result: "detected" or "not detected" and if known, enter titer in Numeric Result:

### NBS Entry Guidelines for Investigation

Required fields are noted by  $\rightarrow$  and **BOLD** and other preferred data entry fields by  $\Rightarrow$  and *italics*. Control + Click to see <u>Patient Tab Investigation</u>

Investi- gation	NBS Field Name		Description/Instructions	
		Investigat	tion Information	
	<b>→</b>	Jurisdiction	Jurisdiction is automatically filled in based on the patient's zip code. Review and correct as needed. Select or edit "Jurisdiction" based on patient address if available, location of patient's provider, or location of reporting facility, in that order.	
	<b>→</b>	Program Area	IDEAS – Infectious Disease - Will default based on condition.	
	<b>→</b>	Investigation Start Date	Enter Date Investigation began or if no follow up was done, enter the date the report was received.	
	<b>→</b>	Investigation Status	Defaults to "Open." Change to "Closed" when investigation and data entry are completed.	
	<b>→</b>	Shared Indicator	Select "Yes".	
		State Case ID	Enter number assigned for CDC tracking.	
	₽	Investigator	Search or enter quick code to enter the name of the person who completed the investigation or the person who could answer NBS data entry inquiries.	
	⇒	Date Assigned to Investigation	Enter date investigation assigned to investigator.	
	Reporting Information			
	<b>→</b>	Date of Report	Enter the earliest date first reported to public health. Date will auto-populate when investigation is created from a lab report, but may be edited if the report was received earlier from another provider.	
	⇒	Earliest Date Reported to County	Enter earliest date information was reported to county health department. If the regional office is acting as the local health department, record the date received by the regional office.	



9	Piolikeypox		
Investi- gation	NBS Fi	eld Name	Description/Instructions
	₽	Earliest Date Reported to State	Enter earliest date information was reported to the state health department (regional or central office). The ELR date created should be listed if it is the earliest report date.
	Ŷ	Reporting Source Type	Select type of "Reporting Source" for original reporting entity such as laboratory, hospital, or private physician. For cases identified by a health department during an investigation, select "other state and local agencies." If none of the categories apply, note source in comments.
	Ŷ	Reporting Organization	"Reporting Organization" auto populates if investigation is created from a lab report. Conduct search for "Reporting Source" as needed.  Note: If not found, search by city, etc. and then enter new Organization as needed.
	₽	Reporting Provider	Search for reporting provider if known.  Note: If not found, search by city, etc. and then enter new Provider as needed.
		Reporting County	Select county where the reporting source is located
			Clinical
	₽	Physician	Search for "Physician" if known. Note: If not found, search by city, etc. and then enter new Provider as needed.
		Epid	lemiologic
		Is this patient associated with a day care facility?	Select Yes, No, or Unknown.
		Is this patient a food handler?	Select Yes, No, or Unknown.
	₽	Is this case part of an outbreak?	If applicable, select "Yes" and select the corresponding "Outbreak Name." Contact the NEDSS Project Office to have an outbreak name entered.
	⇒	Outbreak Name	Select outbreak name from drop-down list.
		Case C	Classification
	₽	Where was the disease acquired?	Indicate where disease was acquired; if patient became ill while traveling, designate appropriately.
	⇒	Imported Country	Indicate country where patient became ill.
	⇒	Imported State	Indicate state where patient became ill.
	⇒	Imported City	Indicate city where patient became ill.
	⇒	Imported County	Indicate county where patient became ill.
	⇒	Country of Usual Residence	Indicate country where usually resides.
	⇔	Country of Exposure	Indicate country where patient was exposed.
	⇒	State or Province of Exposure	Indicate state where patient was exposed.
	⇒	City of Exposure	Indicate city where patient was exposed.
Monkeynox			6 of 14



9	Нопксурох			
Investi- gation	NBS Fi	eld Name	Description/Instruction	ons
	⇔	County of Exposure	Indicate county where pa	atient was exposed.
		Binational Reporting Criteria		
		Transmission Mode	Select from	
		Detection Method		
	↑	Confirmation Method	Select method used to determine case status. Select lab confirmed, clinical diagnosis, or epilinked.	Laboratory confirmed – laboratory criteria required for case status selected was met; if NBS lab report not entered, enter lab information into comments. Epidemiologically linked – case status selected is based on epidemiological linkage; indicate name and case number of epi-link in appropriate fields or comments. Clinical Diagnosis – case status selected is based on clinical diagnosis as evidenced by diagnosis reported by physician or health care provider.
	<b>→</b>	Confirmation Date	were met.	
	<b>→</b>	Case Status	Select Confirmed, Probat Case according to the ca Epi Case Criteria Guide	
	<b>→</b>	MMWR Week	Auto-populates based on the beginning of the year edited to the previous ye should be edited to the la or 53) of the preceding N	r if the MMWR Year is ear, the MMWR week ast MMWR week (52



	Tionkeypox			
Investi- gation	NBS Fi	eld Name	Description/Instructions	
	<b>→</b>	MMWR Year	Auto-populates based on data entry date. This does not need to be edited. However, at the beginning of the year, the MMWR week and year should be edited as needed to either the last MMWR week of the preceding calendar year or the first MMWR week of the following year so the MMWR year reflects the year in which the case occurred.	
		Immediate National Notifiable Condition		
		Notification Comments to CDC		
			al Comments	
·		General Comments		
		Vaccina	ation History	
	₽	Did patient ever receive a vaccine against smallpox?	Select Yes, No, or Unknown.	
	₽	Reason for Vaccination Dose 1	Select from Post-exposure, Pre-exposure, Routine Pre-exposure, or Unknown.	
	₽	Reason for Vaccination Dose 2	Select from Post-exposure, Pre-exposure, Routine Pre-exposure, or Unknown.	
	₽	Reason for Vaccination Dose 3	Select from Post-exposure, Pre-exposure, Routine Pre-exposure, or Unknown.	
		Ris	k Factors	
	⇧	Sexual Orientation	Select from Bisexual, Lesbian or Gay, Other, Prefer not to answer, or Straight.	
	₽	Other Sexual Orientation	Free text.	
	⇧	Did the patient engage in sex and/or close intimate contact?	Select Yes, No, or Unknown.	
	⇧	Male	Select Yes, No, or Unknown.	
	Ŷ	If had sex with men, how many?	Enter total.	
	Ŷ	If unable to specify number above: Range of Male Partners	Select from 1, 2-4, 5-9, 10+, or Refused to answer.	
	⇧	Female	Select Yes, No, or Unknown.	
	Ŷ	If had sex with women, how many?	Enter total.	
	⇧	If unable to specify number above: Range of Female Partners	Select from 1, 2-4, 5-9, 10+, or Refused to answer.	
	⇧	Transgender Female	Select Yes, No, or Unknown.	
	⇧	If had sex with transgender female partners, how many?	Enter total.	



	<b>/</b> Г -		
Investi- gation	NBS Fi	eld Name	Description/Instructions
	Ŷ	If unable to specify a number above: Range of Transgender Female Partners	Select from 1, 2-4, 5-9, 10+, or Refused to answer.
	⇒	Transgender Male	Select Yes, No, or Unknown.
	↔	If had sex with transgender male partners, how many?	Enter total.
	Ŷ	If unable to specify number above: Range of Transgender Male Partners	Select from 1, 2-4, 5-9, 10+, or Refused to answer.
	⇒	Other Gender Identity	Select Yes, No, or Unknown.
	Ŷ	If had sex with persons of other gender identity, how many?	Enter total.
	⇔	If unable to specify number above: Range of Other Partners	Select from 1, 2-4, 5-9, 10+, or Refused to answer.
	↔	If the patient engaged in sex in three weeks before symptom onset, did patient engage in group sex?	Select Yes, No, or Unknown.
	↔	If patient engaged in group sex, specify the date of attendance, name, and location of the event.	Free text.
	Ŷ	Is this case epidemiologically linked to another confirmed or probable case?	Select Yes, No, or Unknown.
	₽	Case ID of epi-linked case 1-3	If yes, enter case ID (i.e., CASTX01).
	û	Contact Type	Select from Face-to-face contact, not including intimate contact (within 6 feet without mask), Health care worker, Identified air contact, Indirect contact (e.g., shared sexual partners), Other, Provide care to case – home setting, Sexual or intimate contact, Shared bathrooms (toilets, sinks, showers), Shared food, utensils, or dishes, Shared towels, bedding, or clothing, or Shared transportations.
	⇒	Other Contact Type	Free text.
		If shared transportation, specify the type of shared transportation	Free text.
		Trav	vel History
	↔	Did patient travel during 3 weeks before first symptom appeared?	Select Yes, No, or Unknown.



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Investi- gation	NBS Fie	eld Name	Description/Instructions	
	Ŷ	Was the travel domestic or international?	Select from Domestic or International.	
	⇧	Country	Select from drop down menu.	
	⇧	State	Select from drop down menu.	
	⇒	City	Free text.	
	⇒	Arrival Date to Destination		
	₽	Departure Date from Destination		
	₽	Reason for Travel	Select from Airline/ship crew, Business, Military, Missionary, and Other	
	⇒	Other Reason for Travel	Free text.	
	₽	Mode of Travel	Select from Aircraft, Automobile, Airbus, Passenger Vessel, or Railway train	
	⇒	Flight Number		
	₽	Seat Number		
	₽	Any additional comments on travel?		
	Ŷ	Intimate or Sexual Contact on Trip	Select Yes, No, or Unknown.	
	Click on Add when the Travel History entry is completed and add additional trips as needed.			
		Ex	posures	
	⇧	Is this individual a health care worker who was exposed at work?	Select Yes, No, or Unknown.	
	<b>₽</b>	Suspect Location of Exposure	Select from Air travel contact, Domestic, International, Other, and Unknown.	
	Ŷ	Other Suspect Location of Exposure:	Free text.	
	Ŷ	What was the likely source of exposure?	Free text.	
	<b>U</b>	Please provide any additional details on the location of exposure (e.g., health care setting, etc)	Free text.	
	⇧	Number of Contacts this Case May Have Exposed (named or anonymous)	Enter total.	
	₽	Did the patient attend any large public or private events?	Select Yes, No, or Unknown.	
	⇧	If attended event, specify date of attendance, name, and location of event(s)	Free text.	
	Laboratory Information			





	Honkeypox		
Investi- gation	NBS Fi	eld Name	Description/Instructions
	⇧	Rectal Bleeding	Select Yes, No, or Unknown.
	⇧	Pus or Blood on Stools	Select Yes, No, or Unknown.
	⇧	Proctitis	Select Yes, No, or Unknown.
	⇧	Tenesmus/Urgency to Defecate	Select Yes, No, or Unknown.
	⇧	Headache	Select Yes, No, or Unknown.
	⇧	Malaise	Select Yes, No, or Unknown.
	介	Conjunctivitis	Select Yes, No, or Unknown.
	⇧	Abdominal Pain	Select Yes, No, or Unknown.
	⇧	Vomiting	Select Yes, No, or Unknown.
	⇧	Nausea	Select Yes, No, or Unknown.
	⇧	Myalgia	Select Yes, No, or Unknown.
	⇧	Chills	Select Yes, No, or Unknown.
	Ŷ	Any evidence of ocular involvement (ocular lesions, keratitis, conjunctivitis, eyelid lesions)?	Select Yes, No, or Unknown.
	<b>→</b>	Diagnosis Date	"Diagnosis Date" is required if onset date is unknown. Enter Diagnosis Date as evidence by:  ◆ Date of physician diagnosis, or  ◆ Date a condition specific positive laboratory result, or  ◆ Date identified as a symptomatic contact of another case.
	<b>→</b>	Illness Onset Date	Enter "Illness Onset Date."  Note: Leave blank if onset date is unknown or patient is asymptomatic.
		Illness End Date	Enter or select date.
		Illness Duration	Enter value.
		Illness Duration Units	Select from drop-down list.
		Age at Onset	Enter number and unit. Default is years. Use days if $< 1$ month, months for $\geq 1$ month and $< 1$ year, and years for $\geq 1$ year.
		Age at Onset Units	Use the drop-down list next to age to select, days, months, etc.
		Medi	cal History
	î	What is the individual's HIV status?	Select from HIV negative, HIV positive, or Unknown.
		If HIV positive, was the individual's viral load undetectable when it was last checked?	Select Yes, No, or Unknown.



	Tionkeypox			
Investi- gation	NBS Fi	eld Name	Description/Instructions	
	⇧	Is the individual currently receiving HIV pre-exposure prophylaxis?	Select Yes, No, or Unknown.	
	⇧	Any immunocompromising conditions (excluding HIV) or immunosuppressive medications?	Select Yes, No, or Unknown.	
	⇧	If immunocompromised, specify condition or treatment	Free text.	
	⇧	Has this individual been diagnosed with any other acute infections during this current illness?	Select Yes, No, or Unknown.	
	⇒	Specify the infections	Free text.	
	⇧	Was the patient hospitalized for this illness?	Select Yes, No, or Unknown.	
	Û	Reason for Hospitalization	Select from Breathing problems NOT requiring mechanical ventilation, Breathing problems requiring mechanical ventilation, Disseminated disease, Exacerbation of underlying condition, Other, Pain control, or Treatment for secondary infection.	
	⇧	Other Reason for Hospitalization	Free text.	
	Ŷ	Hospital	If hospitalized, search for "Hospital" and enter "Admission Date" and "Discharge Date." Capture all hospitals, dates, and durations of stay utilizing available fields and, as needed, the comments field. Note: If hospital is not found, search by city, etc. and then enter new Organization as needed.	
	↔	Most Recent Admission Date	If patient hospitalized, enter $1^{\text{st}}$ admission date.	
	Û	Most Recent Discharge Date	If patient hospitalized, enter 1 <sup>st</sup> discharge/transfer date.	
	⇧	Total Duration of Stay in the Hospital (in days)	Calculate duration of stay as discharge- admission date for listed hospital stay. If admission date is same as discharge date, enter 1.	
		Is the patient pregnant?		
		Due Date		
		Currently breast feeding?		
General Comments				



Investi- gation	NBS Field Name		Description/Instructions
		General Comments	

### NBS Entry Guidelines for Notification

Notifications are required for confirmed and probable cases.