Laboratory Outreach Communication System (LOCS) Call

Monday, August 15, 2022, at 3:00PM EDT

- **Welcome**
  - Sean Courtney, Division of Laboratory Systems, CDC
- **SARS-CoV-2 Variants Update**
  - Natalie Thornburg, Division of Viral Diseases, CDC
- **Monkeypox Update**
  - Christina Hutson, Monkeypox Response, CDC
- **Laboratory Developed Tests (LDTs) & CLIA Establishment Regulations**
  - Keith Scott, Centers for Medicare and Medicaid Services (CMS)
- **FDA Update**
  - Tim Stenzel, US Food and Drug Administration (FDA)

About DLS

Vision

Exemplary laboratory science and practice advance clinical care, public health, and health equity.

Mission

Improve public health, patient outcomes, and health equity by advancing clinical and public health laboratory quality and safety, data and biorepository science, and workforce competency.

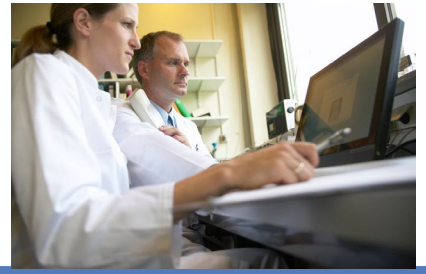
Four Goal Areas

Quality Laboratory Science

- Improve the quality and value of laboratory medicine and biorepository science for better health outcomes and public health surveillance

Highly Competent Laboratory Workforce

- Strengthen the laboratory workforce to support clinical and public health laboratory practice



Safe and Prepared Laboratories

- Enhance the safety and response capabilities of clinical and public health laboratories

Accessible and Usable Laboratory Data

- Increase access and use of laboratory data to support response, surveillance, and patient care

Materials for Validation of Laboratory-Developed Tests (LDTs)

- Laboratories can develop their own LDT:
  - Information For Laboratory Personnel: https://www.cdc.gov/poxvirus/monkeypox/lab-personnel/index.html
  - Test Procedure - Non-variola Orthopoxvirus Generic Real-Time PCR Test: https://www.cdc.gov/poxvirus/monkeypox/pdf/Non-variola-Orthopoxvirus-Generic-Real-Time-PCR-Test.pdf
  - Test Procedure: Monkeypox virus Generic Real-Time PCR Test: https://www.cdc.gov/poxvirus/monkeypox/pdf/PCR-Diagnostic-Protocol-508.pdf

- Genetic material can be used for validation studies, such as creating contrived specimens and used as positive controls:
  - NIST: https://www.nist.gov/programs-projects/mpxv-monkeypox-synthetic-dna-pcr-standards
  - BEI Resources: https://www.beiresources.org/

BEI Catalog #		
NR-2500	NR-27	NR-2324
NR-21738.1	NR-4928	NR-58622 Monkeypox Virus hMPXV/USA/MA001/2022

  - Other commercial sources

Public Comments Solicited for Proposed CLIA Rule

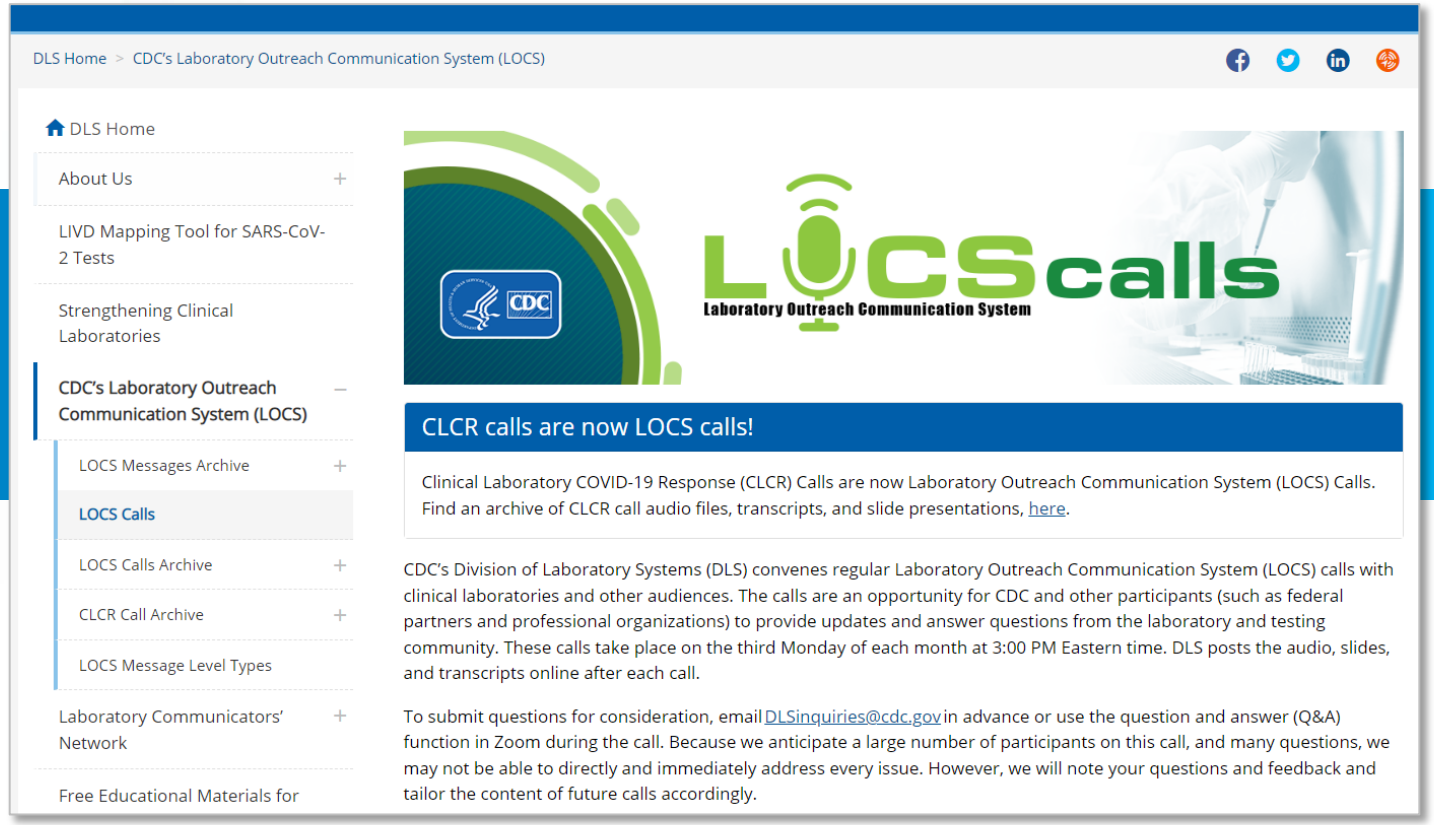
- CMS and CDC seek public comments regarding the proposed rule to update:
  - CLIA fees
  - Histocompatibility requirements
  - Personnel requirements
  - Alternative sanctions for Certificate of Waiver (CoW) laboratories

- The proposed rule affects all CLIA-certified laboratories
- Public comment period will be open until August 25, 2022
- Read the proposed rule and submit comments by visiting: https://www.federalregister.gov/

LOCS Calls

https://www.cdc.gov/locs/calls

Find LOCS Call information, transcripts, and audio recordings on this page



We Want to Hear From You!

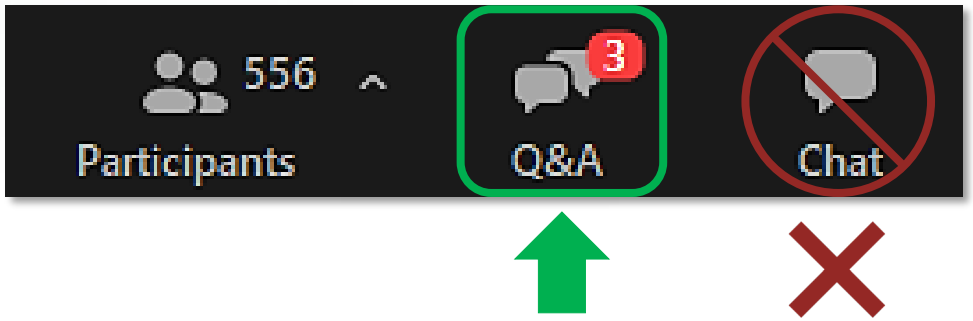
Training and Workforce Development

Questions about education and training?

Contact LabTrainingNeeds@cdc.gov

How to Ask a Question

- **Using the Zoom Webinar System**
  - Click the **Q&A button** in the Zoom webinar system
  - Type your question in the **Q&A box** and submit it
  - Please do not submit a question using the chat button



- For media questions, please contact CDC Media Relations at media@cdc.gov
- If you are a patient, please direct any questions to your healthcare provider

Slide decks may contain presentation material from panelists who are not affiliated with CDC. Presentation content from external panelists may not necessarily reflect CDC's official position on the topic(s) covered.

SARS-CoV-2 Variants Update

Natalie Thornburg
Division of Viral Diseases, CDC

MONKEYPOX

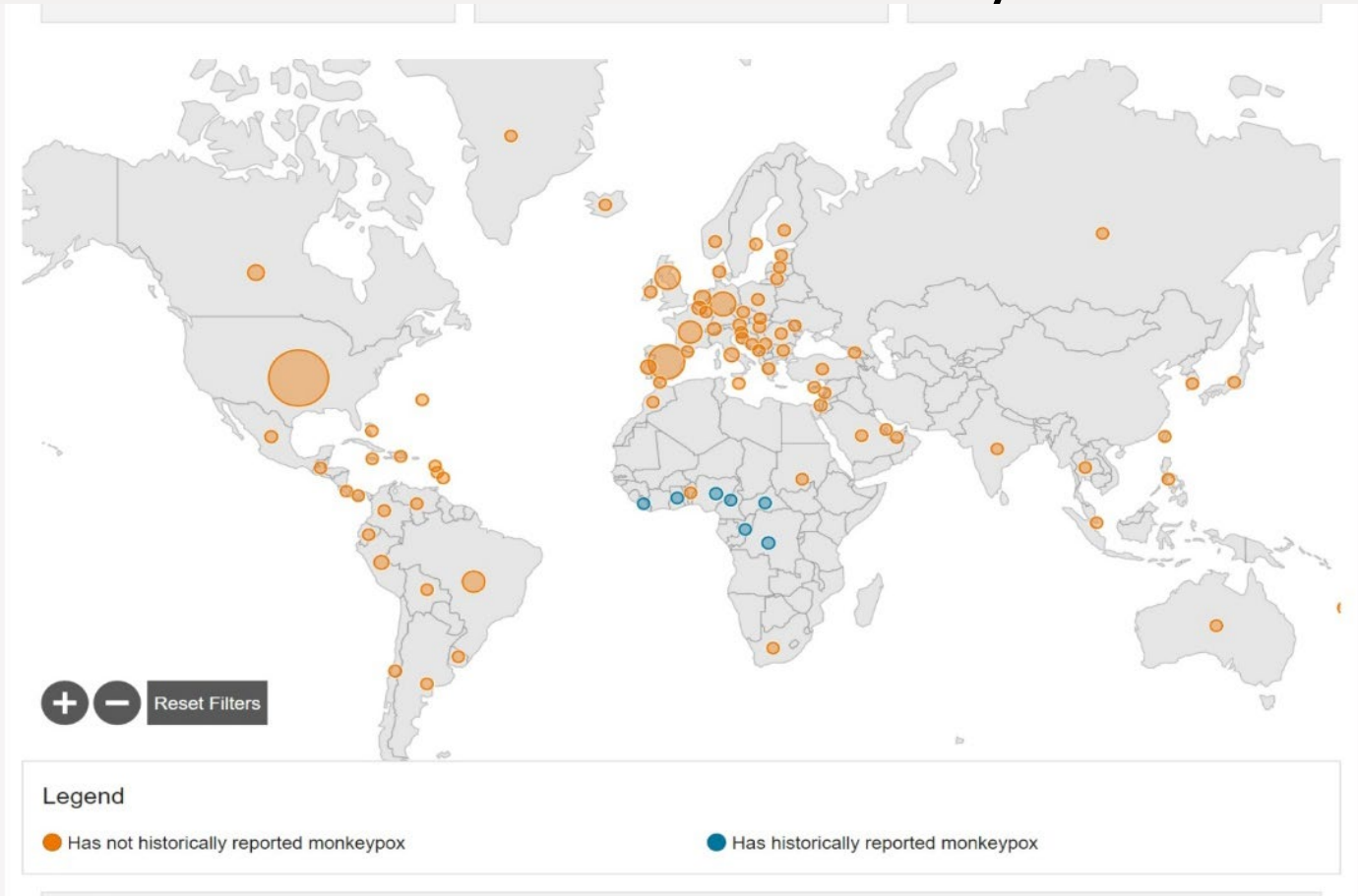
Monkeypox Outbreak Update

August 15, 2022

Christina L. Hutson, Ph.D.

MONKEYPOX

Case Count: 35, 492 August 12, 2022
83 countries historically have not reported MPXV

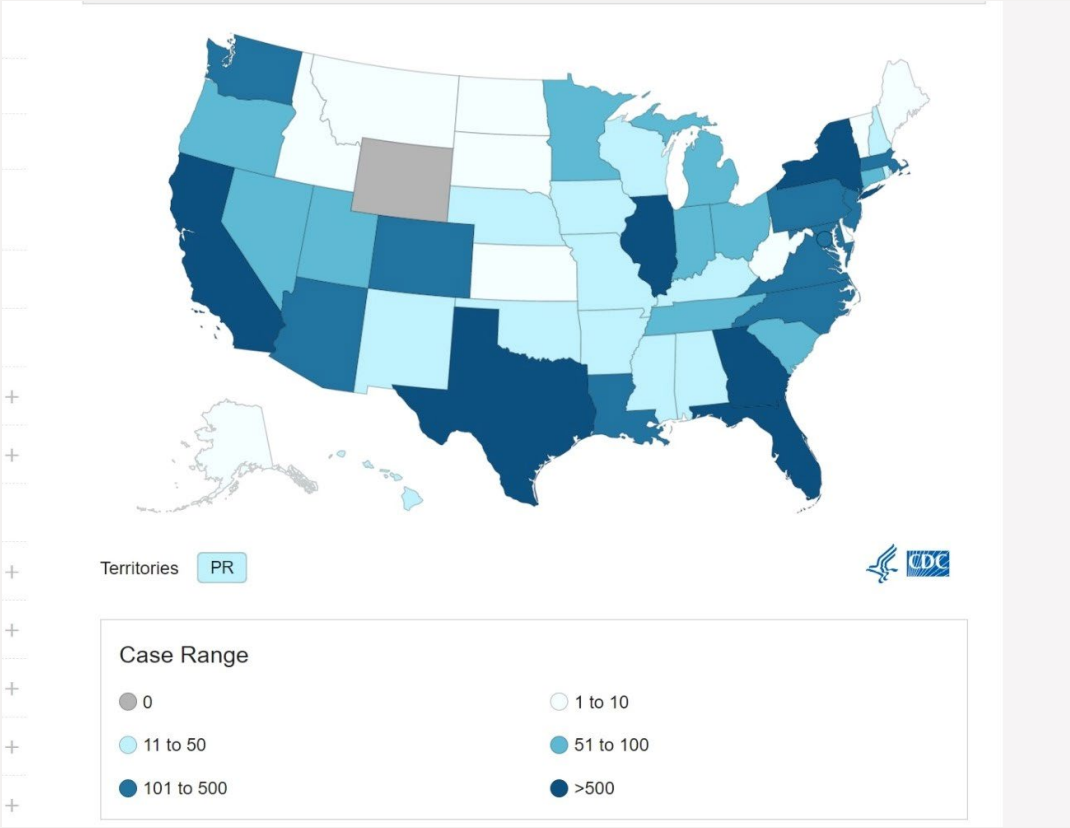


COUNTRY	COUNT
United States	11,176
Spain	5719
Germany	3102
United Kingdom	3017
France	2673
Brazil	2458
Canada	1059
Netherlands	1025

Source: [2022 Monkeypox Outbreak Global Map | Monkeypox | Poxvirus | CDC]

MONKEYPOX

Case Count: August 12, 2022: 11, 177



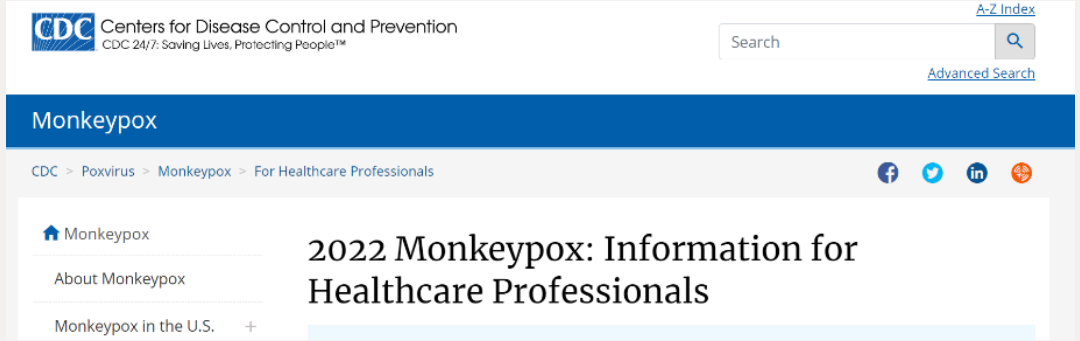
STATE	COUNT
New York	2,295
California	1,945
Florida	1,085
Georgia	851
Texas	815
Illinois	771
District of Columbia	328

Source: 2022 U.S. Map & Case Count | Monkeypox | Poxvirus | CDC

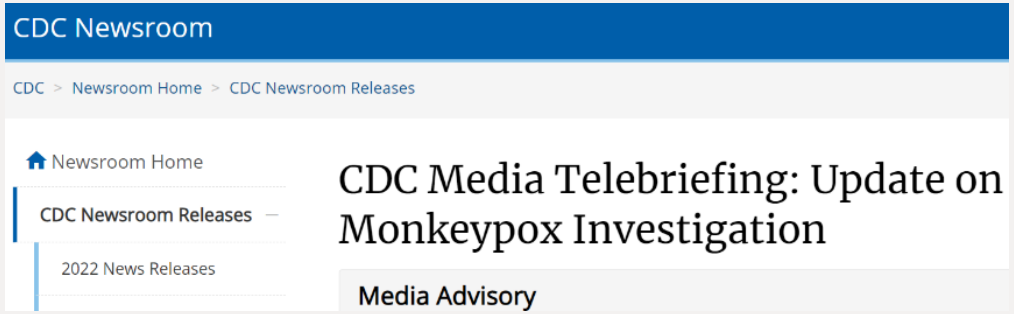
MONKEYPOX

What is CDC Doing?

- Providing advice to state and local health departments
- Supporting diagnostic testing at Laboratory Response Network labs, 5 commercial labs and CDC
- Providing frontline healthcare providers and public health officials with information on symptoms and how to manage illness



- Keeping public, clinicians, and laboratorians informed with updated information on CDC website, social media, and via media briefings
- Working closely with community partners and raising awareness with multiple partners in LGBTQIA+ community
- Seeking public health partners' feedback
- Consulting with other countries



MONKEYPOX

Clinical Illness: 'Classic'

- **Incubation period:** 5–13 days on average (range 4–17 days)
- **Prodrome:** fever, malaise, he
  that may be generalized or lo
  armpit)
- **Rash: appears shortly *after***
  - Typically lesions develop simultar
  - Four stages – macular, papular, v
  - Well-circumscribed, deep seated
  - When disseminated tend to be ce
  - Can involve palms and soles
- **Illness duration is typically**

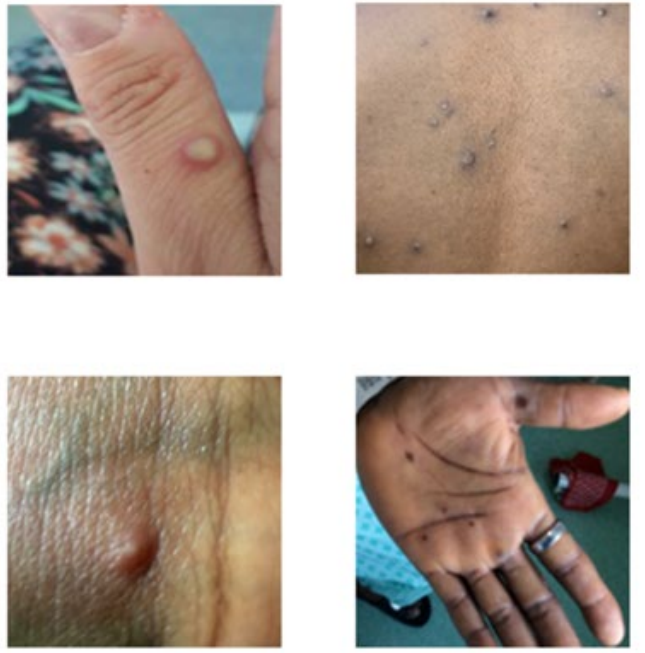
Symptoms of monkeypox can include:

- Fever
- Headache
- Muscle aches and backache
- Swollen lymph nodes
- Chills
- Exhaustion
- A rash that can look like pimples or blisters that appears on the face, inside the mouth, and on other parts of the body, like the hands, feet, chest, genitals, or anus.
  - The rash goes through different stages before healing completely. The illness typically lasts 2-4 weeks.

Sometimes, people get a rash first, followed by other symptoms. Others only experience a rash.

Examples of Monkeypox Rashes

Photo Credit: NHS England High Consequence Infectious Diseases Network



MONKEYPOX

Clinical Illness: '2022 Lesions'

- Pattern: **scattered or localized** to a body site rather than diffuse
- **Rash often starts in mucosal areas** (e.g., genital, perianal, oral mucosa) and may not develop simultaneously in all body areas
  - **Proctitis**: anorectal pain, tenesmus, and rectal bleeding; associated with visible perianal vesicular, pustular, or ulcerative skin lesions and proctitis
  - **Oropharyngitis**: complicated by tonsillar swelling, abscess, dysphagia
- "Prodromal" symptoms can be absent or follow rash onset

Clinical Illness: '2022 Lesions'

Characteristic	(N = 528)
No. of skin lesions — no. (%)	
<5	207 (39)
5–10	131 (25)
11–20	112 (21)
>20	56 (11)
No lesions or missing data	22 (4)
Mucosal lesions present — no. (%)	217 (41)
Site of mucosal lesions — no./total no. (%)	
Anogenital only	148/217 (68)
Oropharyngeal only	50/217 (23)
Anogenital and oral	16/217 (7)
Nasal and eye	3/217 (1)

Source: Thornhill 2022, N Engl J Med

Testing for Suspect MPX Cases

- US Laboratory Response Network (LRN) labs (10,000 tests/week)
  - LRN labs (located within the state public health labs) perform CDC's FDA cleared non-variola Orthopoxvirus (NVO)-specific PCR test
  - Send samples to CDC for MPX-specific PCR and sequencing
- Commercial laboratory testing is now available (70,000 additional tests/week)
  - 40,000 testing capacity per week using CDC NVO test
  - 30,000 tests of commercial MPOX-specific laboratory test
- Current testing capacity is at least 80,000 tests per week

Testing for Suspect MPX Cases

- Specimen type
  - Commercial and LRN labs-accepted specimen type is lesion material
  - Swab of lesion from any part of the body is acceptable
    - Does not need to be deroofed or lanced
  - CDC is evaluating other specimen types through a research protocol
- Specifics on the acceptable lesion specimen type accepted within the LRN and commercial laboratories may vary (e.g., dry swab or swab in VTM or UTM)
  - This is based on the laboratory's CLIA approval
- Clinicians should initiate diagnostic testing for any suspect monkeypox patient
  - Based on clinical presentation and/or epidemiologic criteria
  - Other differentials should also be considered if there are no known monkeypox epi links or risk factors

Vaccines

- Two vaccines licensed by the U.S. Food and Drug Administration (FDA) are available for preventing monkeypox infection – JYNNEOS (also known as Imvamune or Imvanex) and ACAM2000.
- In the United States, there is currently a limited supply of JYNNEOS, although more is expected in coming weeks and months.
- There is an ample supply of ACAM2000. However, this vaccine should not be used in people who have some health conditions, including a weakened immune system, skin conditions like atopic dermatitis/eczema, or pregnancy.
- No data are available yet on the effectiveness of these vaccines in the current outbreak.
- People are considered fully vaccinated about 2 weeks after their second shot of JYNNEOS and 4 weeks after receiving ACAM2000.
  - People who get vaccinated should continue to take steps to protect themselves from infection by avoiding close, skin-to-skin contact, including intimate contact, with someone who has monkeypox.

Tecovirimat

- Tecovirimat is an antiviral medication developed to treat smallpox
  - Also known as TPOXX or ST-246
- Oral capsule and IV formulations approved by FDA in July 2018 and May 2022, respectively
- Available from the Strategic National Stockpile as an oral capsule formulation or an intravenous vial
- Indication
  - Tecovirimat is indicated for the treatment of human smallpox disease in adults and pediatric patients weighing at least 3 kg
  - CDC-held Expanded Access Investigational New Drug (EA IND) Protocol allows use of Tecovirimat for Non-Variola Orthopoxvirus Infection (e.g., monkeypox)

https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/208627s000lbl.pdf

Revised Tecovirimat EA-IND

- Reduced number of case report forms from 6 forms (17 pages) to 2 forms (6 pages)
- Changed all patient assessments to virtual (via telemedicine) or in-person
- Reduced required assessment and follow-up visit to 3 time points that could be done via telemedicine visits
  - Patients would be assessed prior to treatment, once during the 14-day therapy, and once after completion of treatment

MONKEYPOX

Research Efforts *

- Specimens for detection prior to rash onset
  - Blood, throat swabs, rectal swabs
- Prevalence of monkeypox prior to first confirmed case
  - Serologic retrospective studies
- Prevalence of undetected monkeypox within higher risk populations
  - Serologic prospective studies
  - PCR testing of banked specimens
- Transmission dynamics during this outbreak
  - Household transmission studies
- Transmission to animals
  - Domestic animals
  - Escape to wildlife
- Wastewater detection
  - CDC efforts
  - California
- Sequence monitoring
  - Testing sensitivity of isolates with changes in the TPOXX target

MONKEYPOX

Conclusions

- Largest monkeypox outbreak outside African continent currently ongoing
  - >35,000 cases in 90 countries
  - High transmission between men who have sex with men (MSM)
- Multiple medical countermeasures developed through US Smallpox Research Agenda are beneficial for detection and treatment of monkeypox
  - FDA cleared diagnostic assay within Laboratory Response Network
    - Expansion to commercial laboratories
  - Two anti-viral therapies (TPOXX® and Tembexa®) approved by US Food and Drug Administration
  - Smallpox and monkeypox vaccine [IMVAMUNE® (JYNNEOS ®)] approved by US Food and Drug Administration

MONKEYPOX

Questions?

Laboratory Developed Tests (LDTs) & CLIA Establishment Regulations

Keith A. Scott, MLS(ASCP)CM
Laboratory Consultant, CLIA Program
Division of Clinical Laboratory Improvement & Quality
Southern Operations Branch, Dallas Location

Laboratory Developed Test

A laboratory developed test (LDT) is a type of in vitro diagnostic test that is designed, manufactured and used within a single laboratory.

§493.1253 Standard: Establishment and verification of performance specifications

(b)(2) Establishment of performance specifications. Each laboratory that modifies an FDA-cleared or approved test system, or introduces a test system not subject to FDA clearance or approval (including methods developed in-house and standardized methods such as textbook procedures), or uses a test system in which performance specifications are not provided by the manufacturer must, before reporting patient test results, establish for each test system the performance specifications for the following performance characteristics, as applicable:

§493.1253 Standard: Establishment and verification of performance specifications

(b)(2)(i) Accuracy

Interpretive Guidelines

The laboratory is responsible for establishing that the method produces correct results.

§493.1253 Standard: Establishment and verification of performance specifications

(b)(2)(ii) Precision

Interpretive Guidelines

The laboratory is responsible for establishing the precision of each test system by assessing day-to-day, run-to-run, and within-run variation, as well as operator variance.

§493.1253 Standard: Establishment and verification of performance specifications

(b)(2)(iii) Analytical sensitivity.

Interpretive Guidelines

The laboratory is responsible for determining the lowest concentration or amount of the analyte or substance that can be measured or distinguished from a blank, i.e., minimum detection limits or how much of the analyte must be present to be measured.

§493.1253 Standard: Establishment and verification of performance specifications

(b)(2)(iv) Analytical specificity to include interfering substances.

Interpretive Guidelines

The laboratory must determine the extent to which the method measures the analyte for which it is reporting results.

The laboratory must document information regarding interfering substances from product information, literature, or its own testing.

§493.1253 Standard: Establishment and verification of performance specifications

(b)(2)(v) Reportable range of test results for the test system.

Interpretive Guidelines

The laboratory is responsible for establishing the upper and lower limits of the test system.

§493.1253 Standard: Establishment and verification of performance specifications

(b)(2)(vi) Reference intervals (normal values).

Interpretive Guidelines

The laboratory must establish a reference range that is appropriate for the laboratory's patient population (i.e., a normal range that reflects the type of specimen and demographic variables such as age and sex, as applicable).

§493.1253 Standard: Establishment and verification of performance specifications

(b)(2)(vii) Any other performance characteristic required for test performance.

Questions?

FDA Update

Tim Stenzel
US Food and Drug Administration (FDA)

U.S. Food and Drug Administration

- **COVID-19 Emergency Use Authorization (EUA) Information for Medical Devices**
  https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations-medical-devices
- **COVID-19 In Vitro Diagnostic EUAs**
  https://www.fda.gov/medical-devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/vitro-diagnostics-euas
- **COVID-19 Frequently Asked Questions**
  https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-frequently-asked-questions
- **COVID-19 Updates**
  https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization#2019-ncov
- **FDA Townhall Meetings**
  https://www.fda.gov/medical-devices/workshops-conferences-medical-devices/virtual-town-hall-series-immediately-effect-guidance-coronavirus-covid-19-diagnostic-tests-06032020
- **Independent Evaluations of COVID-19 Serological Tests**
  https://open.fda.gov/apis/device/covid19serology/

U.S. Food and Drug Administration

- **COVID-19 Diagnostic Development**
  CDRH-EUA-Templates@fda.hhs.gov

- **Spot Shortages of Testing Supplies: 24-Hour Support Available**
  1. Call 1-888-INFO-FDA (1-888-463-6332)
  2. Then press star (*)

- **FDA MedWatch**
  https://www.fda.gov/safety/medwatch-fda-safety-information-and-adverse-event-reporting-program

Next Scheduled Call

Monday, September 19

@ 3:00 PM to 4:00 PM EDT

CDC Social Media

https://www.facebook.com/CDC

https://twitter.com/cdcgov

https://www.instagram.com/cdcgov

https://www.linkedin.com/company/cdc

Thank You For Your Time!

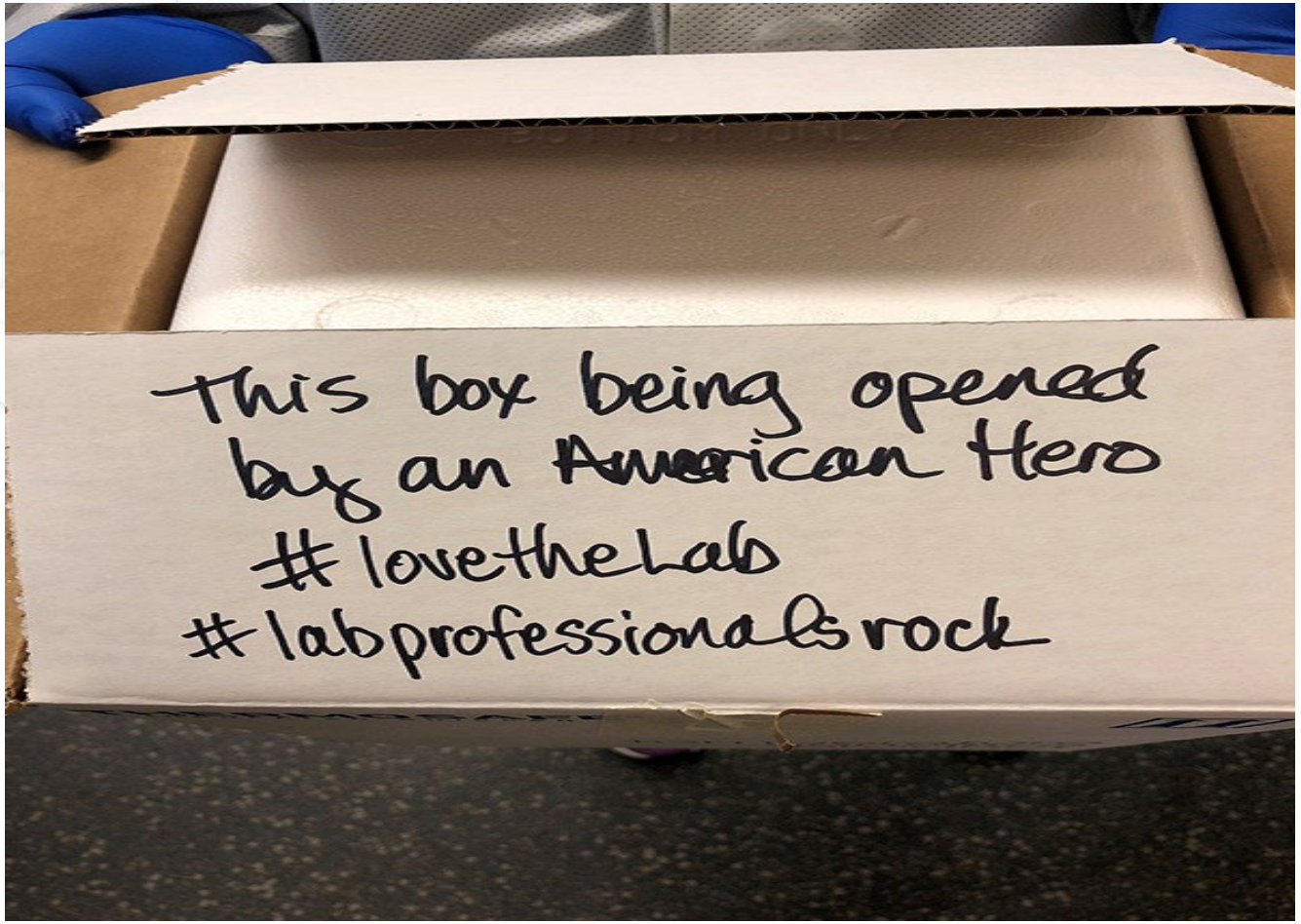


Photo submitted by the Microbiology Laboratory at The University of Pittsburgh Medical Center

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Images used in accordance with fair use terms under the federal copyright law, not for distribution.

Use of trade names is for identification only and does not imply endorsement by U.S. Centers for Disease Control and Prevention.

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of Centers for Disease Control and Prevention.