Laboratory Outreach Communication System (LOCS) Call

Monday, September 16, 2024, at 3:00 P.M. ET

- **Welcome**
  - Sean Courtney, CDC Division of Laboratory Systems
- **Mpox Update**
  - Nicolle Baird, CDC Division of High-Consequence Pathogens and Pathology
- **Oropouche virus: An Emerging Threat in the Americas/Updated Testing and Reporting Guidance and New Response Plan**
  - Aaron Brault, CDC Division of Vector-Borne Diseases

Thank you for joining, we'll begin the call momentarily.

About DLS

Vision

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

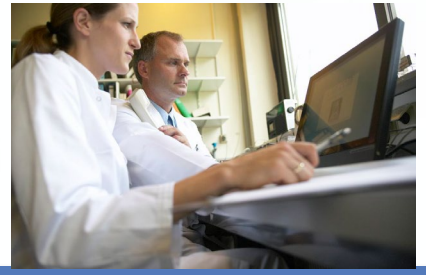
Four Goal Areas

Quality Laboratory Science

- Improve the quality and value of laboratory medicine 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

DLS ECHO Biosafety Program

- **Date:** September 24, 12:00 PM ET
- **Topic:** Operations: Emergency Response and Contingency Plans
- **Speakers:** Benjamin Fontes, MPH, CBSP from Yale University
- For questions, contact DLSbiosafety@cdc.gov

Scan QR code to register

www.cdc.gov/safelabs/resources-tools/echo-biosafety.html

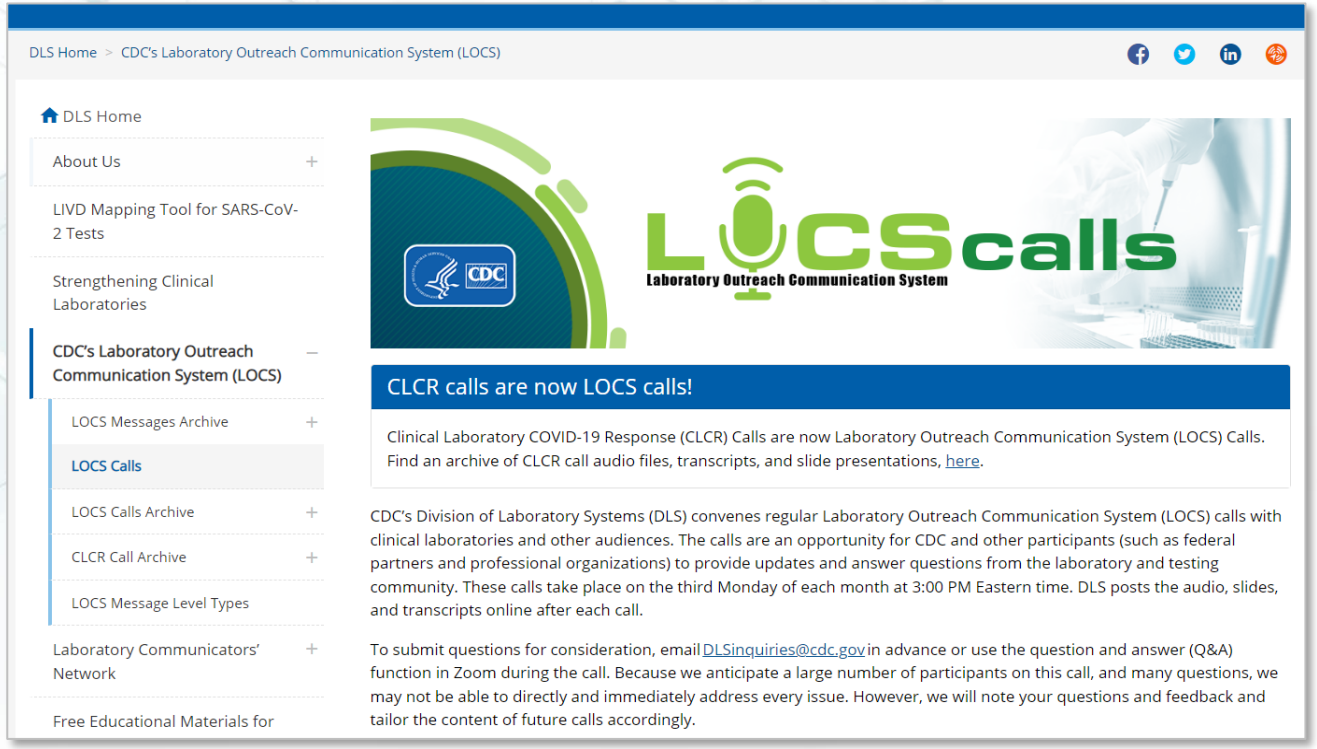
We Want to Hear From You!

Training and Workforce Development

Questions about education and training?

Contact LabTrainingNeeds@cdc.gov

LOCS Calls



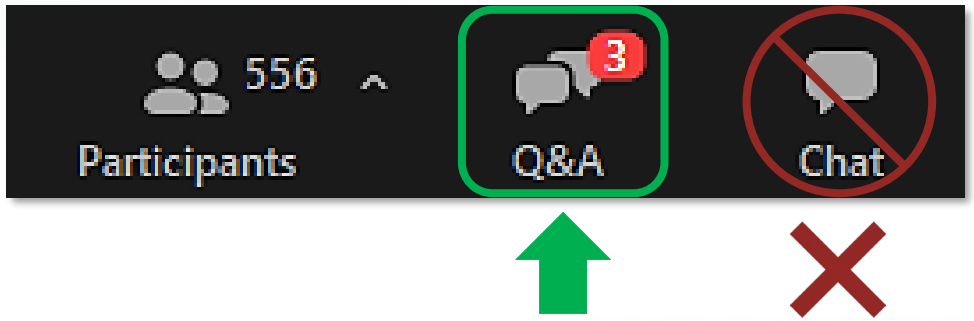
On this page, you can find:

- LOCS Call information
- Transcripts
- Slides
- Audio Recordings

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

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.

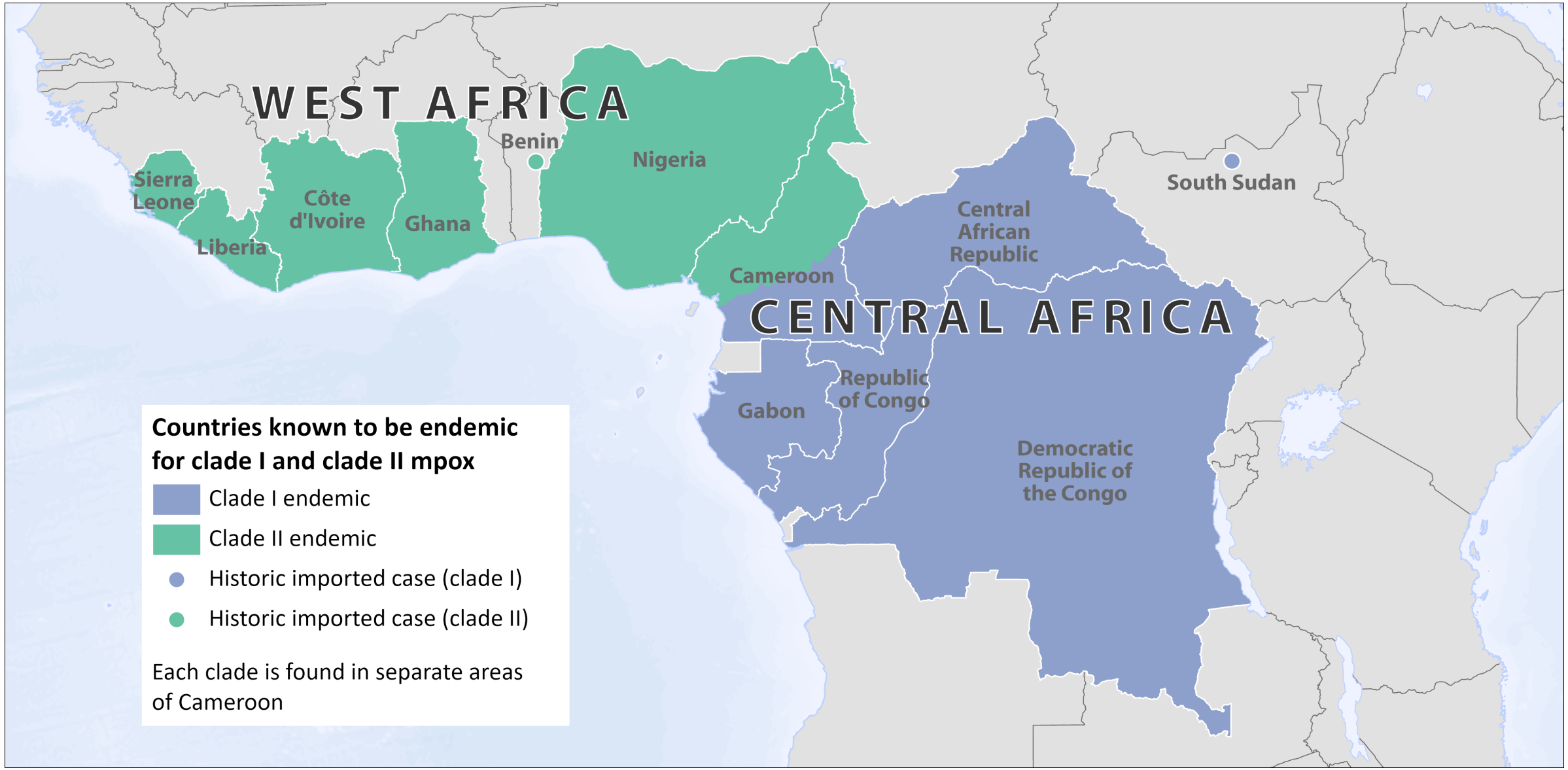
Mpox Update

September 2024

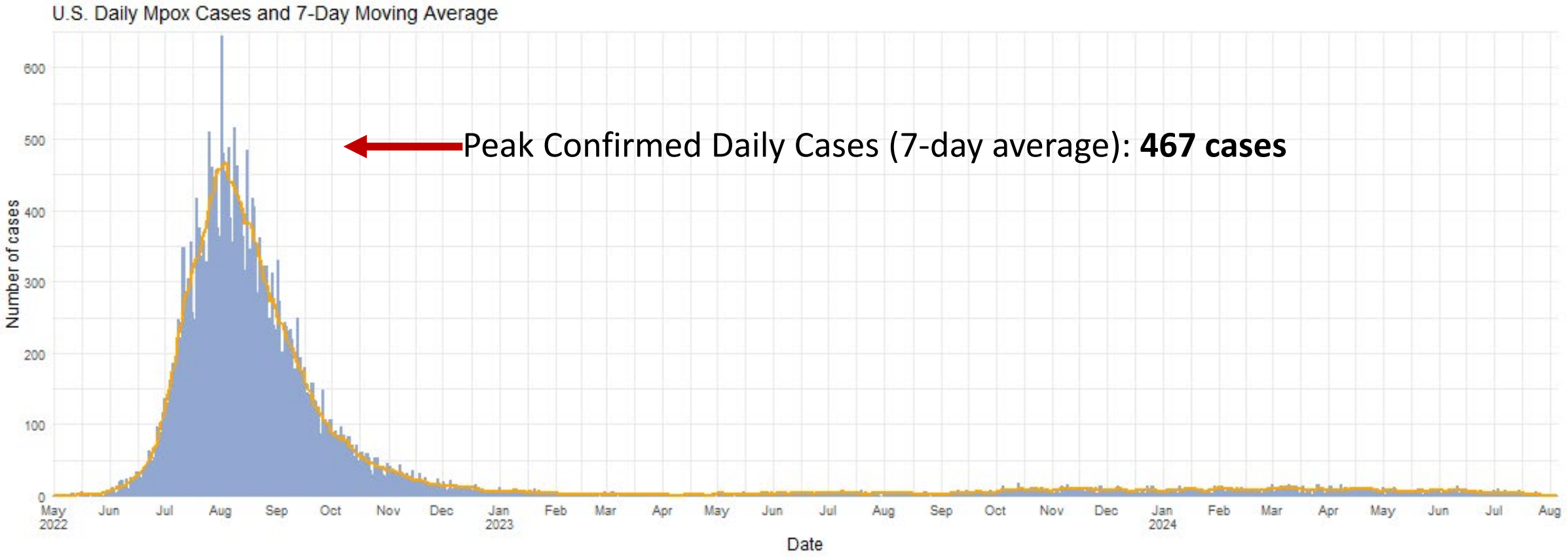
Nicolle Baird, PhD

CDC Division of High Consequence Pathogens and Pathology

MPXV Clades: Historical Geographic Distribution

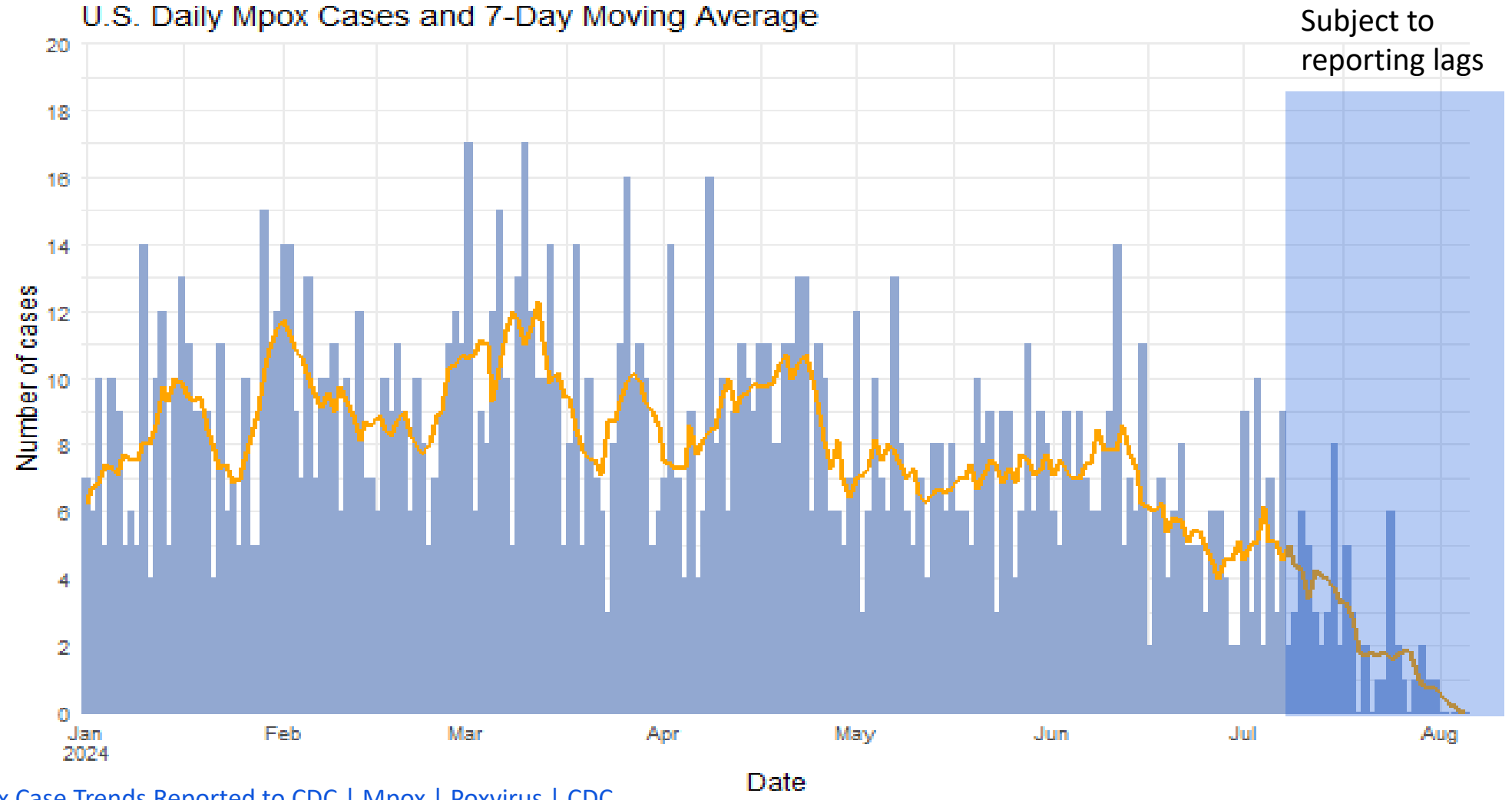


Mpox Clade II Epi-Curve and 7 Day Moving Average – United States, May 2022 to August 2024



[U.S. Mpox Case Trends Reported to CDC | Mpox | Poxvirus | CDC]

Mpox Clade II Epi-Curve and 7 Day Moving Average – United States, May 2022 to August 2024



The median moving 7-day avg daily cases for August is currently 4.85, compared to 7.14 daily cases for July.

The current total cases for the U.S. for 2024 are 1,983 cases, compared to 1,742 cases for 2023.

U.S. Mpox Case Trends Reported to CDC | Mpox | Poxvirus | CDC

Clade I MPXV

Ongoing Mpox Cases & Deaths– Democratic Republic of the Congo

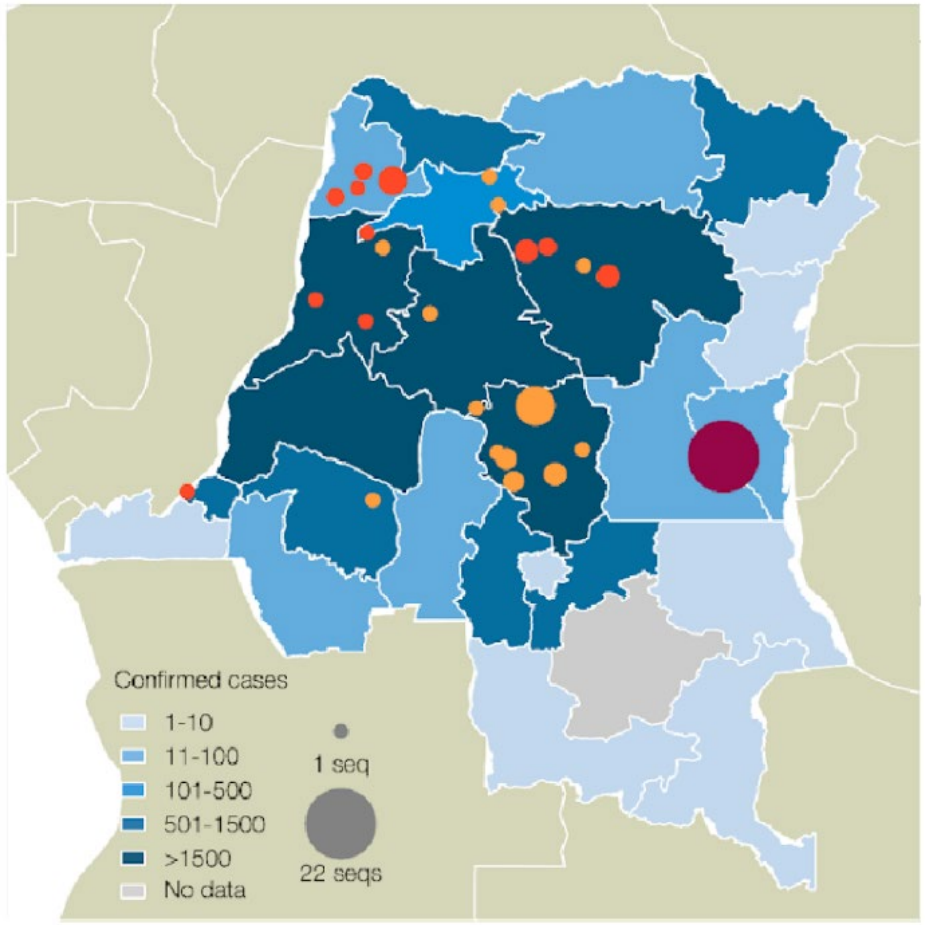
	Cases		Suspected Deaths
Year	Suspected	Confirmed	
2021	2,497	N/A	68
2022	5,697	N/A	234
2023	14,626	N/A	654

- **Suspected cases ≠ mpox**
  - Varicella zoster virus
  - Measles
  - Other rash illnesses
- **Confirmed are not necessarily a proportion of suspected cases**

***Most cases are based on clinical suspicion; only a fraction of cases are laboratory-confirmed**

§ Preliminary data and subject to change. Note case numbers reported in previous epi weeks may increase or decrease in the current week's data. This can result in changes in the cumulative number of cases reported. Additional investigation is underway.

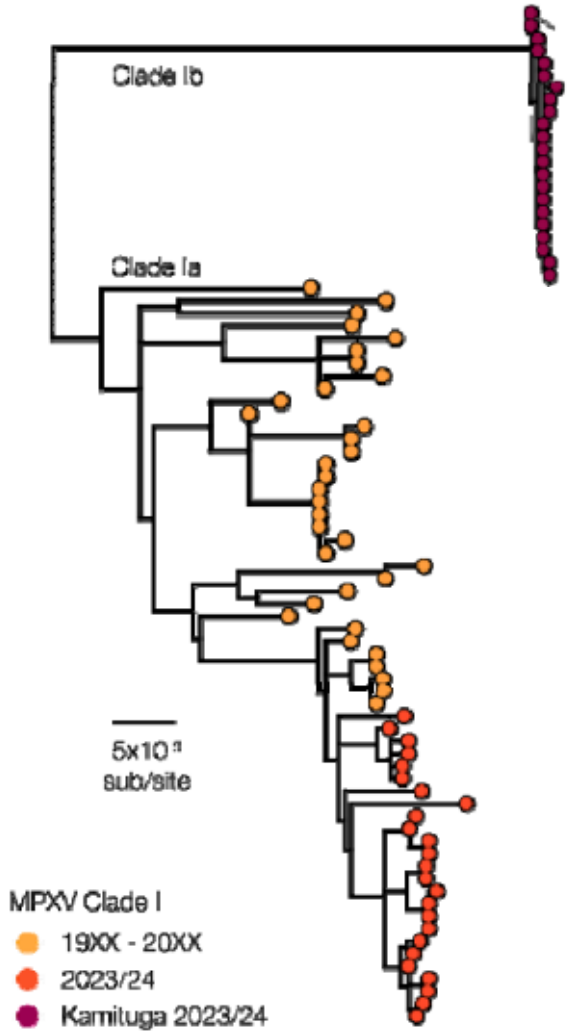
DRC MPXV Sequence Summary To Date



- **Data are limited**
  - 59 sequences from the past year
  - 173 whole genome clade I sequences available (since 1970s)
- **In many areas, transmission is reported to be dominated by zoonotic spillover with limited human-to-human spread (within households or close contacts)**
- **Outbreak in Kamituga mining region of South Kivu (maroon dot)**
  - Enrichment of APOBEC3 signature mutations suggestive that human-to-human spread has occurred
  - High prevalence in sex workers, suggestive of sexual transmission

Vakaniaki, et al. "Sustained Human Outbreak of a New MPXV Clade I Lineage in the Eastern Democratic Republic of the Congo." *Nature Medicine* (2024).
Masirika, et al. "Ongoing mpox outbreak in Kamituga, South Kivu province, associated with monkeypox virus of a novel Clade I sub-lineage, Democratic Republic of the Congo, 2024." *Eurosurveillance* 29.11 (2024): 2400106.

DRC South Kivu Outbreak 2024



- **MPXVs from Kamituga (South Kivu) are genetically distinct, sub-clade Ib**
- **MPXV from South Kivu contain a deletion that impacts CDC-developed clade I specific PCR assay.**
  - Viruses with the deletion cannot be detected by the PCR assay
  - CDC NVO test can detect clades and sub-clades (including Ib)
- **2015 CDC publication showed 2011/2012 cases from Kivu were genetically divergent based on partial genome sequencing**
  - **1b has been evolving prior to current outbreak**

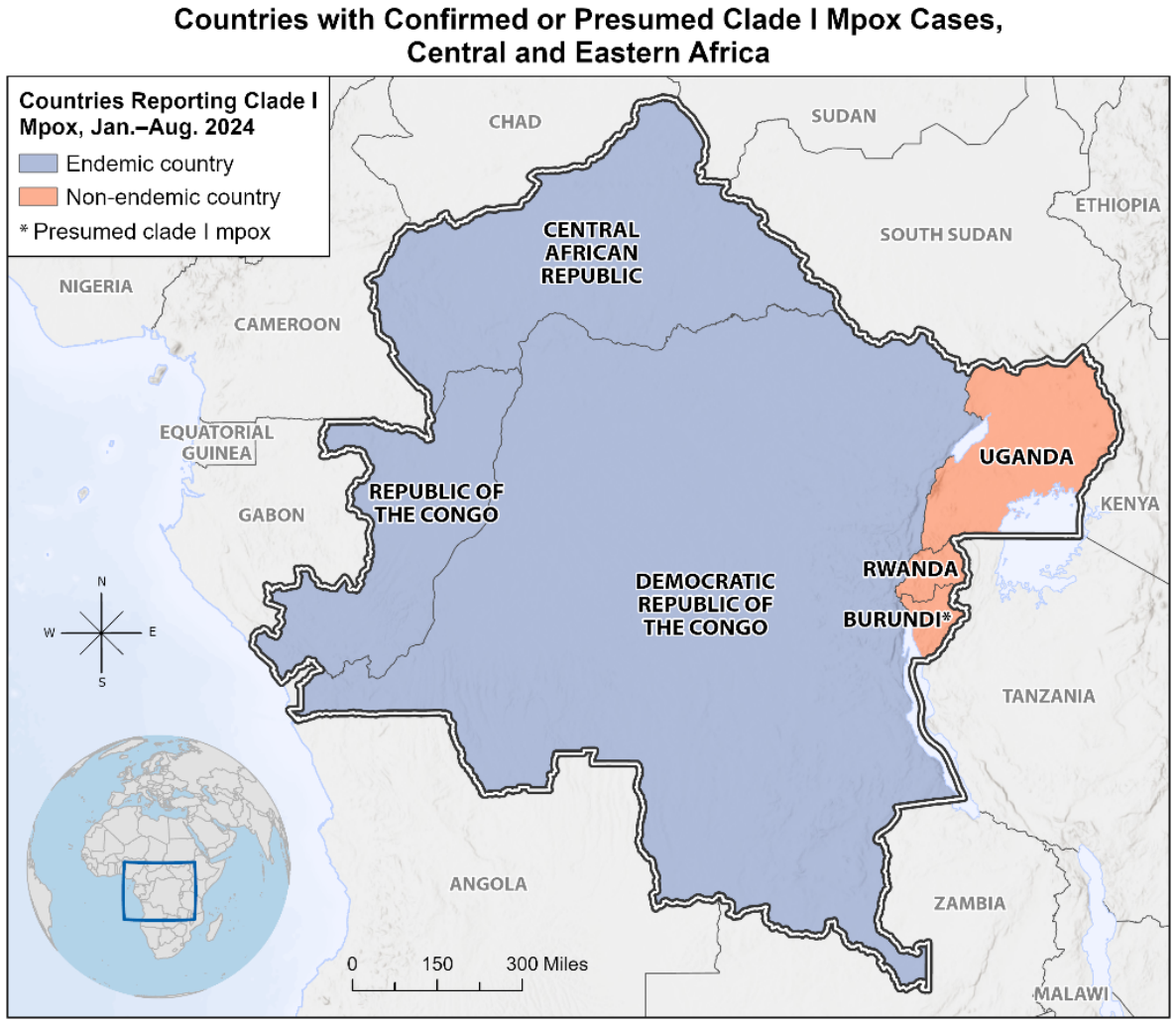
Vakaniaki, et al. "Sustained Human Outbreak of a New MPXV Clade I Lineage in the Eastern Democratic Republic of the Congo." *Nature Medicine* (2024).
Masirika, et al. "Ongoing mpox outbreak in Kamituga, South Kivu province, associated with monkeypox virus of a novel Clade I sub-lineage, Democratic Republic of the Congo, 2024." *Eurosurveillance* 29.11 (2024): 2400106.

Clade Ib suggestive of decreased virulence

- **Target of CDC clade I test (C3) is not found in clade II**
  - CDC clade I test will not detect clade Ib isolates
  - Non-variola orthopoxvirus (DNA polymerase) test is not impacted
- **Swapping complement control protein (C3) between the clades –**
  - **Delete from clade I and compare to wild-type clade I**
    - **100% mortality in wildtype, 0% in C3-deletion virus (small animal study)**
  - Hudson PN, Self J, Weiss S, Braden Z, Xiao Y, Girgis NM, Emerson G, Hughes C, Sammons SA, Isaacs SN, Damon IK, Olson VA. (2012) Elucidating the role of the complement control protein in monkeypox pathogenicity. *PLoS One, 7*(4):e35086. doi: 10.1371/journal.pone.0035086. Epub 2012 Apr 9. PMID: 22496894; PMCID: PMC3322148.
- **Case-fatality rate in South Kivu has consistently stayed below 1%**
  - Likely multi-factorial but gene deletion may contribute

Clade I Cases Detected Outside of DRC

- Central African Republic and Republic of the Congo are endemic for clade I
- Uganda, Rwanda, Burundi are non-endemic
- Health Alert Network
- Travel Health Notices
- CDC supporting DRC and neighboring countries

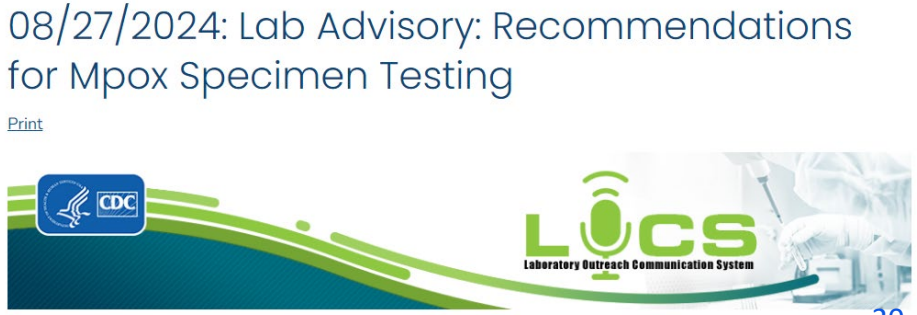


Clade I MPXV Surveillance in the U.S.

GOAL: To Identify if Clade I MPXV is Circulating in the U.S.

- **Patient care and IPC does not change based on the mpox clade**
  - Early cases: rigorous case investigation and contact tracing
- **CDC testing: CDC continues to solicit all mpox specimens from labs using the CDC 510(k) cleared non-variola orthopoxvirus (NVO) test to be forwarded on to CDC after initial diagnosis – clade specific PCR testing, sequencing to look for mutations**
- **Support laboratories that are able and willing to bring up clade-specific testing**
- **CDC collaborates with laboratories who perform testing that can flag a high likelihood of clade I**
  - Laboratories that sequence virus
  - Laboratories perform clade II testing & NVO test multiplex: positive NVO/negative clade II = high suspicion for clade I

09/02/2022: Lab Alert: MPXV TNF Receptor Gene Deletion May Lead to False Negative Results with Some MPXV Specific LDTs (cdc.gov)



Testing Algorithm Considerations

- **Non-variola orthopoxvirus (NVO) test utilized as primary test**
- **Accurate test is most critical: PCR targeting viral essential gene not impacted by mutations**
    - Not missing mpox cases is most important
    - Isolation, clinical care etc. can be started while waiting on clade identification (e.g. if NVO positive and clade I epi criteria)
    - Start with OPXV (e.g. NVO) generic test that targets a viral essential gene, follow-up with additional clade PCR testing or sequencing if needed.
- Mpox Triplex Test: NVO, Clade Ia, Clade II
    - NVO positive, Clade Ia and II negative: Sequence
- Clade Ib PCR test(s) are being developed

Disclosures

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

Oropouche virus: An emerging threat in the Americas/ Updated Testing and Reporting Guidance and New Response Plan

Aaron C. Brault, PhD

Lead for Oropouche Laboratory Task Force
CDC 2024 Dengue Oropouche Emergency Response
abrault@cdc.gov

September 16, 2024

Oropouche virus (OROV)

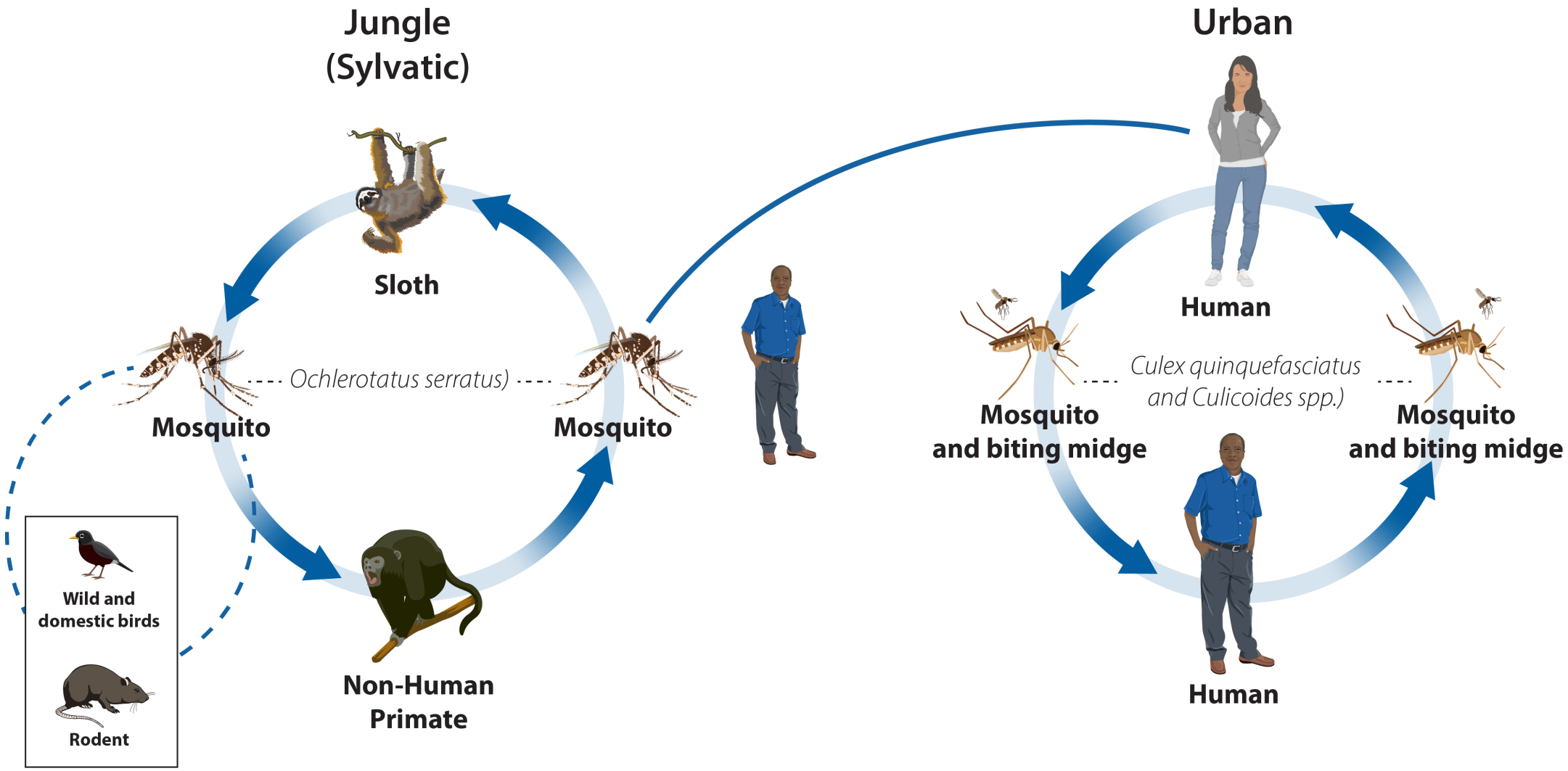
An emerging arbovirus in the Americas

- **Belongs to Simbu serogroup, genus *Orthobunyavirus*, *Peribunyaviridae* family**
- **First detected in Trinidad and Tobago in 1955 and endemic in Amazon basin**
- **Previous outbreaks detected Bolivia, Brazil, Colombia, Ecuador, French Guiana, Panama, and Peru; one child in Haiti found to be infected in 2014**
- **As of August 1, 2024, >8,000 confirmed OROV disease cases have reported in the Americas, including in non-endemic areas**
- **In the United States and Europe, travel-associated cases (n=30) have been identified in travelers returning from Cuba (n=29) and Brazil (n=1)**

https://www.paho.org/en/documents/epidemiological-alert-oropouche-region-americas-1-august-2024

https://www.ecdc.europa.eu/en/publications-data/threat-assessment-brief-oropouche-virus-disease-cases-imported-european-union

Oropouche Virus (OROV)



OROV infection

Clinical illness similar to other arboviral pathogens in the Americas

- **Most (~60%) people become symptomatic; incubation period about 3-10 days**
- **Initial clinical presentation similar to infections caused by dengue, Zika, and chikungunya viruses**
  - Acute onset of fever, chills, headache, myalgia, and arthralgia
  - Other symptoms can include retroorbital pain, photophobia, vomiting, diarrhea, fatigue, maculopapular rash, conjunctival injection, and abdominal pain
- **Clinical laboratory findings can include lymphopenia and leukopenia, and slightly elevated liver enzymes**
- **Initial symptoms resolve after few days, but high proportion (~70%) experience recurrent symptoms within days to weeks after resolution of initial illness**

OROV infection

Typically mild illness, but severe manifestations are possible

- **Hemorrhagic manifestations (e.g., epistaxis, gingival bleeding, melena, menorrhagia, petechiae)**
- **Neuroinvasive disease (e.g., meningitis, meningoencephalitis)**
  - Clinical symptoms: Intense occipital pain, dizziness, confusion, lethargy, photophobia, nausea, vomiting, nuchal rigidity, nystagmus
  - Clinical laboratory findings: pleocytosis and elevated protein in CSF
- **Brazil recently reported two deaths in otherwise healthy, non-pregnant women**

OROV infection in pregnancy
Limited data indicate vertical transmission

- **Based on limited data from Brazil, vertical transmission of Oropouche virus is possible**
  - Several pregnant people with evidence of vertical transmission to their fetus associated with fetal death or congenital abnormalities, including microcephaly
  - Pregnant persons all had symptoms of consistent with Oropouche virus disease during pregnancy and most had positive test results of recent Oropouche virus infection
  - Tissues from still births and one infant born with microcephaly have tested positive by RT-PCR for Oropouche viral RNA
- **Currently, it is not known how frequent vertical transmission occurs during pregnancy and if timing of Oropouche during pregnancy increases risk of adverse outcome**

Suspect case definition

Patient with travel within two weeks of *initial* symptom onset (as patients may experience recurrent symptoms) to an area with documented or suspected Oropouche virus circulation* and the following:

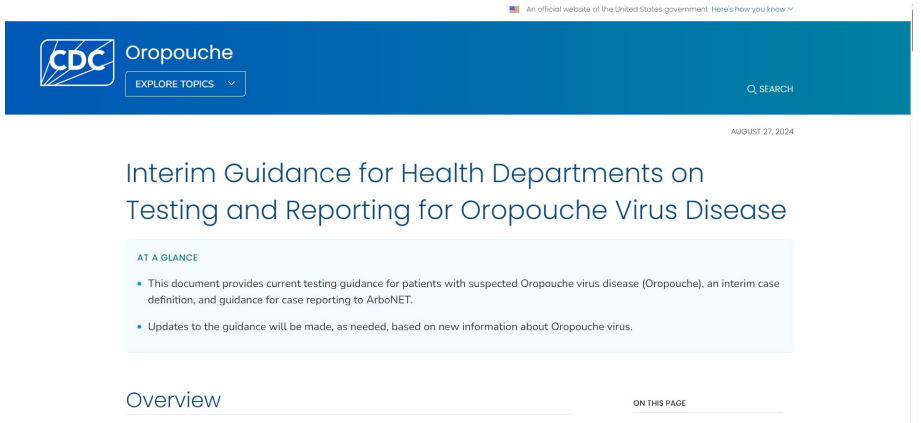
- **Abrupt onset of reported fever, headache, and one or more of the following: myalgia, arthralgia, photophobia, retroorbital/eye pain, or signs and symptoms of neuroinvasive disease (e.g., stiff neck, altered mental status, seizures, limb weakness, or cerebrospinal fluid pleocytosis); AND**
- **No respiratory symptoms (e.g., cough, rhinorrhea, shortness of breath); AND**
- **Tested negative for other possible diseases, in particular dengue†.**

***If concern exists for local transmission in a non-endemic area, consider if the patient had contact with a person with confirmed Oropouche virus infection, lives in an area where travel-related cases have been identified, or has known vector exposure (e.g., mosquitoes or biting midges).**

†If strong suspicion of Oropouche virus disease exists based on the patient's clinical features and history of travel to an area with virus circulation, do not wait on negative testing before sending specimens to CDC.

Updated Interim Guidance for Health Departments on Testing and Reporting for Oropouche Virus Disease

- **Revised suspect case definition**
  - Removed “No respiratory symptoms (e.g., cough, rhinorrhea, shortness of breath)” and added “Absence of a more likely clinical explanation”
    - ~14% of U.S. travel-associated cases reported cough or sore throat
- **Added anticipated CLIA-validated RT-PCR**
  - Removed surveillance testing
  - Simplified specimen submission process
  - Revised testing algorithm



Laboratory diagnosis of OROV infection

Typically relies on testing serum; CSF can be tested in neuroinvasive disease

- **Clinical diagnostic testing using plaque reduction neutralization test (PRNT) currently available at CDC and few state health departments; as of September 10-molecular testing available for acute serum/CSF specimens**

- **Surveillance testing using RT-PCR is currently available at CDC**
  - Results only for surveillance, not clinical management*
  - Shared with health departments for awareness and public health action

*results not to be shared with patient or clinical care team

Testing algorithm

Day of specimen collection post symptom onset	Assay
0–7	RT-PCR
6–7	PRNT, if RT-PCR is negative
>7	PRNT

^If a patient is immunocompromised from an underlying illness or medication or has another condition that might impact their immune response, RT-PCR can be conducted on samples collected after the first week of illness. Please indicate if a patient is considered immunocompromised in CSTOR or on the 50.34 Specimen Submission Form.

Image from phil.cdc.gov

- For most nonpregnant patients a single PRNT positive result is adequate to diagnose
- Paired specimens still preferred for pregnant patients

Reporting cases to ArboNET

- Added two new event (condition) codes*
  - 50290: Oropouche virus disease, non-congenital
  - 50291: Oropouche virus disease, congenital

*jurisdictions should continue to use condition code 10072 (Other arboviral disease, not otherwise specified) while transitioning their systems

OROV disease
No vaccine or specific treatment

- **No specific antiviral treatment is available for OROV disease**
- **Treatment for symptoms include rest, fluids, and use of analgesics and antipyretics**
  - Acetaminophen is the preferred first-line treatment for fever and joint pain in travelers returning from or people living in dengue-endemic areas
  - Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDS) should not be used to reduce the risk of hemorrhage
- **Patients who develop more severe symptoms should be hospitalized for observation and supportive treatment**

Guidance and resources from CDC

Updated Travel Health Notices

Pregnant people should reconsider non-essential travel to Cuba and take precautions to prevent bites in other areas where OROV may be circulating

Oropouche in Cuba

- Level 4 - Avoid All Travel
- Level 3 - Reconsider Nonessential Travel
- **Level 2 - Practice Enhanced Precautions**
- Level 1 - Practice Usual Precautions

Key points

- **There is an outbreak of Oropouche in Cuba (see map).**
  - **A Level 1 Travel Health Notice has been issued for Oropouche in South America.**
- Multiple cases of Oropouche have recently been reported in U.S. and European travelers returning from travel to Cuba indicating there is ongoing risk.
- Oropouche is spread by the bite of infected midges (small flies) and mosquitoes.
- All travelers to Cuba should take steps to prevent bug bites during travel to protect themselves from infection.
- **Pregnant people** should **reconsider non-essential travel** to Cuba. If travel is unavoidable, these travelers should **strictly** follow Oropouche prevention recommendations.
- Illness can occur in people of any age and is often mistaken for dengue.

Map: Areas in Cuba with reported cases of Oropouche (see larger map)

Current Situation

- On August 1, 2024, the Pan American Health Organization (PAHO) issued an epidemiological alert about Oropouche cases, including deaths, in the Americas. There were also concerns about an

What is Oropouche?

Oropouche is a disease caused by Oropouche virus. It is spread through the bites of infected midges (small flies) and mosquitoes.

Symptoms of Oropouche include headache, fever, muscle aches, stiff joints, nausea, vomiting, chills, or sensitivity to light. Severe

Oropouche in South America

- Level 4 - Avoid All Travel
- Level 3 - Reconsider Nonessential Travel
- Level 2 - Practice Enhanced Precautions
- **Level 1 - Practice Usual Precautions**

Key points

- **Parts of Bolivia, Brazil, Colombia, and Peru (see map) are reporting cases of Oropouche, although the case numbers are declining.**
  - **A Level 2 Travel Health Notice has been issued for Oropouche in Cuba.**
- Oropouche is spread by the bite of infected midges (small flies) and mosquitoes.
- Travelers to affected areas should take steps to prevent bug bites.
- Illness can occur in people of any age and is often mistaken for dengue.

Map: Areas in South America with reported cases of Oropouche (see larger map)

Current Situation

What Travelers Can Do to Protect Themselves and Others

- Travelers to affected areas should take steps to prevent bug bites during travel to protect themselves from infection. They should also prevent bug bites for 3 weeks after travel to avoid possibly spreading the virus to others in the U.S.
  - If travelers are pregnant, they should discuss travel plans, reasons for travel, steps to prevent bug bites, and potential risks with their healthcare provider.

Released Health Alert Network (HAN) Health Advisory

Notifying clinicians and public health authorities of increase in Oropouche virus disease in the Americas

- Advises on evaluating and testing travelers returning from impacted areas with signs and symptoms consistent with Oropouche virus infection
- Raises awareness of possible risk of vertical transmission and associated adverse effects on pregnancy
- Highlights prevention measures to mitigate additional spread of virus and potential importation into unaffected areas

Posting additional web content on CDC's Oropouche page

Guidance for Public Health officials and Considerations for Clinicians

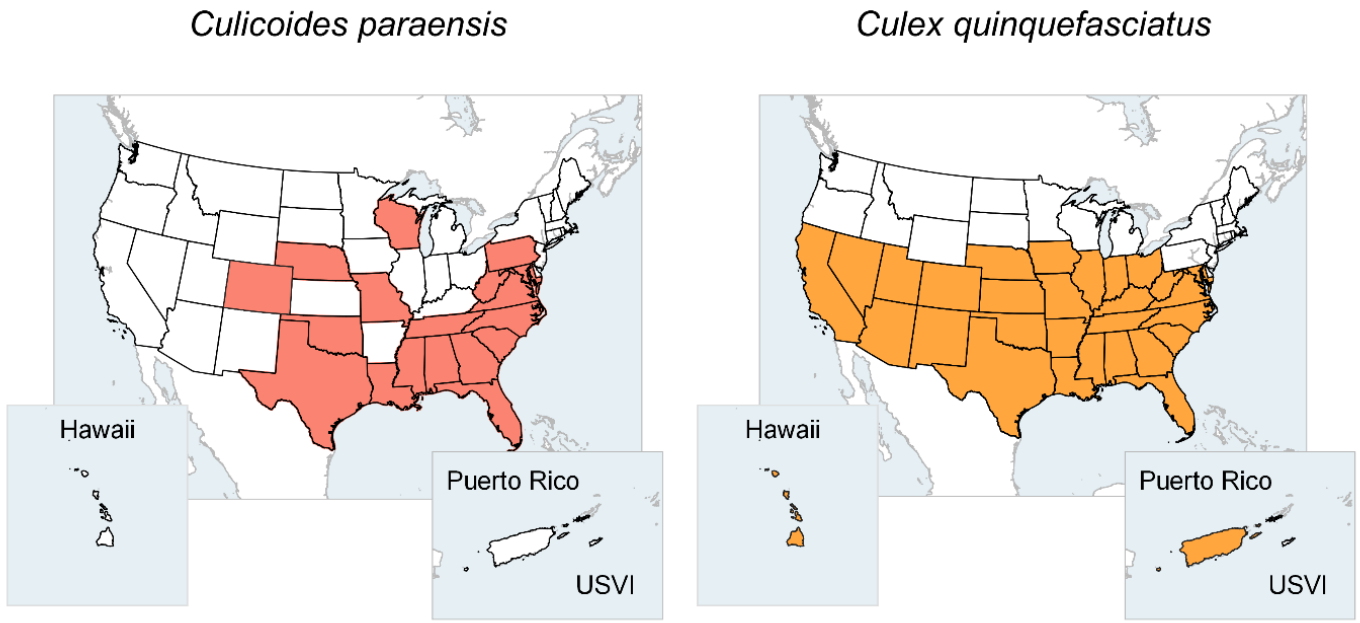
https://www.cdc.gov/oropouche/php/reporting
https://www.cdc.gov/oropouche/hcp/clinical-care-pregnancy

Response to Oropouche virus disease cases in U.S. states and territories in the Americas

- **Intended to assist STLTs investigate and respond to importation and potential transmission**
  - Serves as a reference, not prescriptive or comprehensive
  - Subject to change as we learn more
- **Includes recommendations for**
  - Preventing infections in travelers (including pregnant persons)
  - Responding to travel-associated cases (suspect, probable and confirmed)
  - Assessing for local transmission
  - Responding to local transmission
    - Single case
    - Multiple cases

Response plan appendices*

- Maps showing the estimated range of potential OROV vectors
- Recommendations for entomologic surveillance
- Vector control strategies
- Instructions on modifying CDC Light Traps for biting midges



Distribution of *Culicoides paraensis* and *Culex quinquefasciatus*in based on field observations and modelling. Presence does not imply uniform distribution throughout entire areas. Maps will be updated as more is learned.

*Subject to change as we learn more

Ongoing priority activities

- **Developing interim guidance for evaluation and management of infants born to pregnant people with confirmed or probable Oropouche virus disease**
- **Drafting response guidance for Oropouche virus disease cases in U.S.**
  - Investigating suspect cases and assessing for potential local transmission
  - Responding to travel-associated and local transmission
- **Working with state partners to share initial travel-associated cases of Oropouche virus disease in U.S. residents**
- **Discussing interim case definitions and status as nationally notifiable**
- **Increasing type of CLIA-approved tests available, rolling out testing capacity, and increasing testing capacity**

https://www.cdc.gov/oropouche/php/reporting/index.html

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

Next Scheduled Call

Monday, October 21
3 PM - 4 PM ET

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

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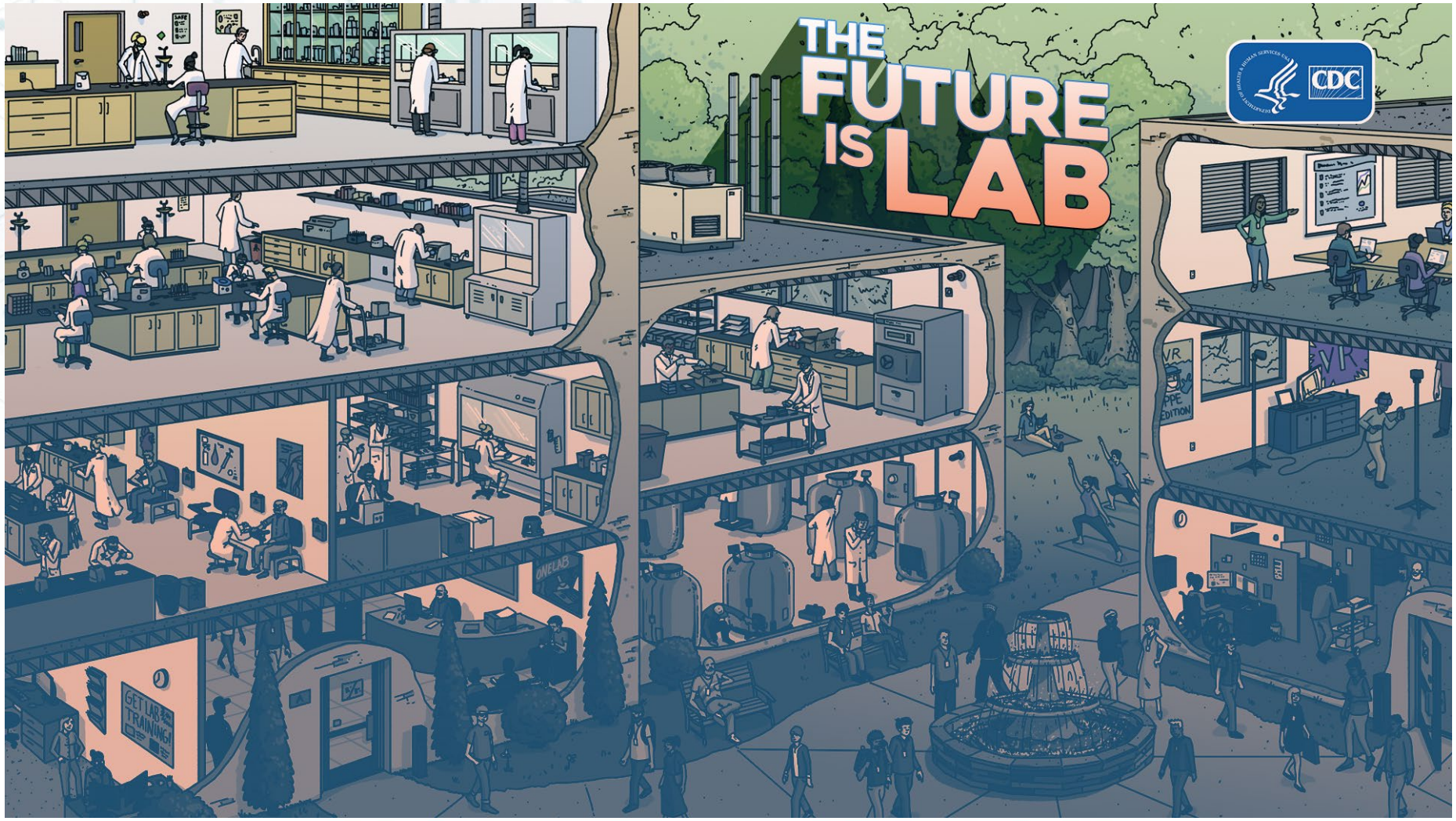
Thank You For Your Time!



For more information, contact CDC
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TTY: 1-888-232-6348 www.cdc.gov