RESPONSE TO OROPOUCHE VIRUS DISEASE CASES

in U.S. states and territories in the Americas

CS353598-A

Contents

Summary

This document was developed by the Centers for Disease Control and Prevention (CDC) to assist state, Tribal, local, and territorial (STLT) health departments to investigate and respond to importation and potential transmission of Oropouche virus (OROV). In addition to guidance on identifying and responding to local transmission, information is provided to assist STLT health departments in protecting pregnant women and their infants. This document serves as a reference for public health decision-making and is not meant to be prescriptive or comprehensive, as activities and decisions are jurisdiction- and situation-specific. The response activities outlined in this plan are based on currently available knowledge about OROV, its transmission, and its possible effects on during pregnancy. The CDC is available to support STLT partners and healthcare providers for any inquiries, consultations, or assistance with investigations. The document and activities described within will be updated as needed. Please contact CDC for assistance at eocevent495@cdc.gov.

1. OROV overview

OROV belongs to the Simbu serogroup of the genus *Orthobunyavirus* in the *Peribunyaviridae* family. The virus was first detected in 1955 in Trinidad and Tobago and is endemic in the Amazon basin. Previous disease activity and/or outbreaks have been described in Argentina, Bolivia, Brazil, Colombia, Ecuador, French Guiana, Panama, and Peru; one child was infected in Haiti in 2014. The current outbreak is occurring in endemic areas and new non-endemic areas outside the Amazon basin. As of August 2024, countries reporting locally acquired (autochthonous) cases include Bolivia, Brazil, Colombia, Cuba, and Peru. Travel-associated cases have been identified in the United States and Europe associated with travel to Cuba or Brazil.

Sylvatic (enzootic) transmission of OROV occurs in forested areas between mosquitoes and non-human vertebrate hosts (e.g., sloths and non-human primates). Other vertebrates have been identified as having antibodies against OROV, such as domestic and wild birds and rodents but their role as amplifying hosts is unknown. Humans can become infected while visiting forested areas and are likely responsible for introducing the virus into urban environments as they develop sufficient viremia to serve as hosts. Biting midges (*Culicoides paraensis*) and possibly certain mosquitoes (*Culex quinquefasciatus*) transmit the virus from an infected person to an uninfected person.

Approximately 60% of people infected with OROV become symptomatic. The incubation period is typically less than one week (range: 3–10 days). Initial clinical presentation is similar to diseases caused by dengue, Zika, and chikungunya viruses, with acute onset of fever, chills, headache, myalgia (muscle aches), and arthralgia (joint pain). Other symptoms can include retroorbital (eye) pain, photophobia (light sensitivity), nausea, vomiting, diarrhea, fatigue, maculopapular rash, conjunctival injection (blood shot eyes), and abdominal pain. Early clinical laboratory findings can include lymphopenia and leukopenia, elevated C-reactive protein (CRP), and slightly elevated liver enzymes. Initial symptoms typically resolve after a few days, but a high proportion (about 70%) experience recurrent symptoms days to weeks after resolution of their initial illness. Although illness is typically mild, it is estimated less than 5% of patients develop hemorrhagic (bleeding) manifestations (e.g., epistaxis (nosebleed), gingival bleeding, melena (black stools), menorrhagia (heavy menstrual bleeding), petechiae) or neuroinvasive disease (e.g., meningitis, meningoencephalitis). Neuroinvasive disease symptoms may include intense occipital pain, dizziness, confusion, lethargy, photophobia, nausea, vomiting, nuchal rigidity (neck stiffness), and nystagmus (uncontrolled eye movement). Clinical laboratory findings for patients with neuroinvasive disease include pleocytosis and elevated protein in cerebrospinal fluid (CSF).

People exposed to biting midges or mosquitoes infected with the virus are most at risk for developing disease. Risk factors for more severe OROV disease are not well-defined but likely include those at risk for severe disease from other arboviruses (e.g., people aged 65 years or older, or those with underlying medical conditions, such as immune suppression, hypertension, diabetes, or cardiovascular disease). Earlier this year, Brazil reported two deaths in otherwise healthy non-pregnant women, and five cases in pregnant women with evidence of vertical transmission of the virus to the fetus associated with fetal death or congenital abnormalities, including microcephaly. This was the first report of deaths and OROV vertical transmission and associated adverse birth outcomes. Since the outbreak in Brazil peaked in

January and February of 2024, additional reports of adverse birth outcomes are expected as pregnant women with exposure to OROV during the outbreak approach full term.

No specific antiviral treatments or vaccines are available for OROV disease. Treatment for symptoms can include rest, fluids, and use of analgesics and antipyretics. Acetaminophen is the preferred treatment for fever and pain. 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 close observation and supportive treatment. Pregnant women with laboratory evidence of OROV infection should be monitored during pregnancy and live-born infants should be carefully evaluated.

2. Investigating suspect OROV disease cases

CDC encourages STLT health departments to investigate all patients with suspected OROV disease. The goal of the investigation is to confirm that a case meets clinical criteria of a suspect case, to ensure samples are obtained and sent for testing at the CDC, and to determine potential exposures (e.g., recent travel, resides in an area with other cases, or association with known OROV disease cases). Information collected during the initial investigation of a suspect case should be shared between public health and vector control programs and used to inform coordinated public health action (e.g., vector control efforts and public health communication). STLT health departments can use their standard Arboviral Case Report Forms for the collection of symptom and exposure data. Because clinicians are integral to the surveillance process, health departments should take steps to increase healthcare provider awareness of OROV and ensure testing of suspect cases.

2.1 Suspect case definition

A suspect case is a patient who has been in an area with documented or suspected OROV circulation* within two weeks of initial symptom onset (as patients may experience recurrent symptoms) 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
- Tested negative for other possible diseases, in particular dengue†, AND
- Absence of a more likely clinical explanation.

*If concern exists for local transmission in a non-endemic area, consider if the patient shared an exposure location with a person with confirmed OROV 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 OROV 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.

2.1.1 Other diagnostic considerations

In many countries, outbreaks of dengue are occurring in areas with reported OROV transmission. For patients with suspected OROV disease, it is important to rule out dengue virus infection because proper clinical management of dengue can improve health outcomes. Other diagnostic considerations include

chikungunya, Zika, leptospirosis, malaria, or infections caused by various other bacterial or viral pathogens (e.g., rickettsia, group A streptococcus, rubella virus, measles virus, parvovirus, enteroviruses, adenovirus, Mayaro virus).

2.2 Laboratory testing

Laboratory diagnosis is generally accomplished by testing serum. Cerebrospinal fluid can also be tested in patients with signs and symptoms of neuroinvasive disease. STLT partners are encouraged to review and keep current on CDC's evolving OROV testing and reporting guidance. Currently, testing is limited to those meeting the suspect case definition (Section 2.1), unless a STLT health department requests an exception. Current testing is limited to assays listed in CDC's Infectious Diseases Laboratory Test Directory.

2.3 Interim case definitions

OROV disease is not currently a nationally notifiable condition. CDC is working with the Council or State and Territorial Epidemiologists (CSTE) to provide guidance for OROV case reporting. Interim case definitions have been established for immediate voluntary reporting of OROV cases to ArboNET, the national arboviral disease surveillance system. Of note, the interim case definition for non-congenital Oropouche virus disease incorporates additional assays and testing on specimen types that may become available in the future. Please refer to Reporting cases to ArboNET for up-to-date guidance.

Confirmed case

A case that meets the suspect case definition and one or more of the following laboratory criteria:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera
- Virus-specific IgM antibodies in CSF or serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen

Probable case

A case that meets the suspect case definition and one of the following laboratory criteria:

- Virus-specific IgM antibodies in CSF or serum
- Virus-specific neutralizing antibodies in a single CSF or serum specimen

3. Pregnancy and birth defects surveillance

Based on limited data from Brazil, vertical transmission of OROV is possible. However, it is not known how frequent vertical transmission occurs during pregnancy and if the timing of OROV disease during pregnancy increases the risk of an adverse outcome. CDC is ready to assist STLT health departments with protecting and educating pregnant women at risk because of travel-associated or local biting midge or mosquito-borne transmission of OROV. STLT health departments are encouraged to track cases of OROV disease during pregnancy, link to data sources with pregnancy outcomes (e.g., spontaneous abortions, stillbirths, and congenital anomalies) and live-born infant outcomes, and assist with provider outreach and education. CDC encourages STLT partners to consider enhanced surveillance efforts to monitor

longitudinally pregnancies and their infants, such as through SET-NET (Surveillance for Emerging Threats to Pregnant People and Infants). Please contact CDC for assistance at setnet@cdc.gov.

4. Recommendations to prevent infections among travelers to areas at risk for OROV

All STLT health departments should advise their residents who might travel to areas at risk for OROV circulation on how to prevent becoming infected (e.g., use of insect repellent). Specific outreach should be considered to travel medicine and other healthcare providers located in areas where a high probability of travel-associated cases can be expected based on international travel patterns of community residents. STLT health departments should work to inform the public and healthcare providers on how to prevent, diagnose, manage, and report suspected OROV cases. Specific recommendations include:

- Public
    - Travelers to areas with a risk of OROV transmission should protect themselves against insect bites during, and for 3 weeks after travel to prevent further spread of the virus and possible importation into the Unites States. When used as directed, EPA-registered insect repellents are proven safe and effective, including for pregnant and breastfeeding women. Use EPA-registered repellents labeled for flies, biting flies, or *Culicoides*.
    - Pregnant travelers should discuss travel plans, reasons for travel, steps to prevent insect bites, and potential risk with their healthcare provider.
    - Pregnant women considering travel to countries with an OROV Level 2 Travel Health Notice should reconsider non-essential travel. If travel is unavoidable, pregnant travelers should strictly follow OROV prevention recommendations to prevent insect bites during travel.
- Healthcare providers
    - Consider and discuss possible OROV testing with your STLT health departments for travelers who meet the suspect case definition.
    - Inform pregnant women of the possible risks to the fetus when considering travel to areas with reported OROV transmission and to counsel these patients to consider the destination, reason for traveling, and their ability to prevent insect bites.
    - Advise people to reconsider non-essential travel to areas with an OROV Level 2 Travel Health Notice during pregnancy. If a pregnant woman decides to travel, counsel them to **strictly** prevent insect bites during travel.
    - Report all suspected OROV disease infections to your STLT health department to facilitate diagnosis and mitigate risk of local transmission. For after-hours contact information for health departments please visit: https://www.cste.org/page/EpiOnCall. Please follow standard procedures for reporting during normal business hours.
- Travelers with symptoms compatible with OROV disease
    - Seek medical care and tell their healthcare provider when and where they traveled.
    - Do not take aspirin or other NSAIDS (e.g., ibuprofen) to reduce the risk of bleeding.

- Prevent insect bites during the first week of illness to avoid further spread, especially in areas where biting midges or mosquitoes or are active.

5. Responding to travel-associated OROV case(s)

5.1 Recommended actions for areas with suspect travel-associated case(s)

For suspect travel-associated cases, the level of public health intervention will depend on several factors:

- when the case returned from an area with OROV transmission relative to their symptoms onset;
- presence of potentially competent vectors in the area where the case resides;
- ability of suspect case to avoid vector bites;
- climatic variables (e.g., season); and
- jurisdictional assessment of the need and capacity to respond.

If the returning traveler became ill while traveling and arrives back to the United States more than 7 days after their initial illness onset, investigation into possible subsequent local transmission would typically not be warranted as data suggest most persons do not have culturable virus in their blood beyond the first week, including during possible recurrence of symptoms. However, if the person is immunocompromised consider whether additional investigation is warranted based on their underlying condition and likelihood of prolonged viremia.

CDC is currently investigating the potential vector competence of domestic biting midge and mosquito species to determine the most likely vectors to transmit the virus in the United States. Based on the current understanding of vectors previously implicated in transmission, many U.S. states could have vectors capable of transmitting the virus in areas of their state (Appendix A). If the infected traveler is returning during a period when vectors are not active in their region (i.e., winter), then there is limited to no risk.

In response to a suspect travel-associated case, STLT health departments in collaboration with vector control programs should consider if public health interventions or messaging is warranted based on the initial case investigation and index of suspicion of the risk of subsequent local transmission. STLT health departments should communicate potential infection zones to public, vector control, and healthcare providers. Messaging and interventions could include:

- Public
  - Advise people in the local area to protect themselves against insect bites and to seek care if they develop symptoms.
    - When used as directed, EPA-registered insect repellents are proven safe and effective, including for pregnant and breastfeeding women.
    - Advise people in the local area to use screens in windows and doors, repair screens that have tears or holes in them, and keep doors to the outside closed to prevent insect bites. Biting midges can be excluded using mesh window screens 20 (or 20 x 20 mesh), that is 20 openings in one linear inch.
- Healthcare providers

  - Consider and discuss possible OROV testing with STLT health departments for individuals who meet the suspect case definition.
  - Report all suspected OROV disease infections to your STLT health department to facilitate diagnosis and mitigate risk of local transmission. For after-hours contact information for health departments please visit: https://www.cste.org/page/EpiOnCall. Please follow standard procedures for reporting during normal business hours.
- Suspect travel-associated cases
  - Advise to avoid biting midge and mosquito bites for the first week of their illness and any travel companions who are asymptomatic should avoid biting midge bites or mosquito bites for 3 weeks after travel (to account for potential incubation period and any viremic phase).

5.2 Recommended actions for areas with probable or confirmed travel-associated case(s)

If a travel-associated case-patient has laboratory evidence of recent OROV infection, the local jurisdiction should assess the likelihood of local transmission based on the factors used to assess a suspect travel-associated case (e.g., timing of illness onset relative to travel and presence of vector and supportive climatic factors). Based on the assessment of potential risk, measures noted above should be considered and potentially implemented if there is concern for local spread. STLT health departments can also consider:

- Inquire about any known contacts, including household occupants, who might have clinically compatible symptoms. If any are noted, attempts should be made to obtain a sample and determine the contact's history of travel and type of contact with the confirmed or probable travel-associated case.
- If public health and vector control program officials determine there is an increased risk of local transmission based on the timing of illness onset relative to travel and presence of vector and supportive climatic factors, the following activities could be considered:
  - Conduct event-based surveillance for fever of unknown origin. Educate providers to be vigilant for unexplained clusters of febrile illness and to report the finding to public health.
  - Implement syndromic surveillance in healthcare facilities in and around the area of concern.
  - Sample houses around the case-patient's household (or other likely exposure location(s)) to determine if there are any other individuals who have had recent symptoms compatible with OROV disease. If anyone is found to have compatible symptoms, obtain specimens for OROV testing and refer for clinical care. The geographic scope and intensity of the surveillance will depend on local circumstances, such as population density, potential vector abundance, number and locations of travel-associated cases, and other risk factors (e.g., lack of air conditioning or screens). CDC is available to provide additional guidance to STLT health departments as requested. Contact eocevent495@cdc.gov for assistance.
  - Distribute information on vector bite prevention (e.g., door hangers, pamphlets on personnel protective measures) in the area of the travel-associated disease case-patient's household.
  - Consider using social media, TV, radio, newspapers, and other media outlets to distribute information on bite prevention.

- Consider conducting vector surveillance activities (Appendix B) such as setting traps, identifying potential vectors to species, and when appropriate, conducting real time reverse transcription polymerase chain reaction (RT-PCR) testing.
- Consider conducting vector control activities (Appendix C) such as identifying potential infection zones, applying insecticides, and conducting door-to-door inspections for vectors when appropriate.

6. Assessing for potential local OROV transmission

For all suspect cases, investigators should inquire about recent travel and attempt to identify other cases by inquiring about other symptomatic persons in the same place of residence (i.e. household, shelter, etc.) and recommend testing of symptomatic individuals that meet the suspect case definition. During case investigations, persons with suspected OROV infection and their household members should be provided directions to prevent further transmission, identify and eliminate possible vector habitats around the household (i.e., water holding containers), and instructions on when to seek additional care or testing if symptomatic. Investigators should determine whether the suspect case has visited an area with active OROV transmission.

If a confirmed or probable case is thought to be locally acquired, the transmission route should be thoroughly investigated. Investigators should determine if biting midges (*Culicoides* spp) or mosquito (*Culex quinquefasciatus*) vectors that transmit OROV have been documented in the area (see Appendix B Entomological Surveillance) and inquire about other less common modes of non-vector-borne transmission such as transmission through recent receipt of blood, organ, or tissues or through occupational exposure (e.g., needlestick or mucosal exposure to OROV in a hospital or laboratory). Sexual transmission should also be considered but has not been documented as a route of OROV transmission. To assess for possible sexual transmission, investigators should inquire about:

- recent sexual contacts (vaginal, anal, or oral),
- use of condoms or other barrier methods, and
- partner travel history and symptom status.

A **confirmed case of local vector-borne transmission** is defined as a person without any travel to an area with OROV circulation or other known exposure to potentially infected blood, organs, or tissues, and who meets the interim confirmed case definition (see Section 2). Once a locally acquired case is confirmed, follow recommendations outlined in the next section. A jurisdiction may decide to implement the recommendations when a probable case is identified and no further testing is possible, and the clinical presentation and available test results, other exposures, and local epidemiology indicate there is the possibility of local transmission.

7. Responding to local OROV transmission

Local transmission by vectors should be assumed, if it is seasonally appropriate, whenever a case is confirmed and other routes of exposure (e.g., travel, transfusion, sex, laboratory exposure) have been evaluated and ruled out. Under these circumstances, STLT health departments should implement surveillance for OROV disease around the home of the confirmed, locally acquired case and any other

likely sites (e.g., work or recreation) of transmission identified through the case investigation. The principal objectives of this surveillance should be to define the frequency and geographic extent of local transmission.

7.1 Confirmed local transmission

In response to a single case of local vector-borne transmission, STLT health departments should:

- Coordinate with CDC and other agencies and authorities regarding local OROV transmission event and response.
- Identify the physical location of the case patient's most likely place(s) of exposure (e.g., home, work, other US location if recent travel).
- Implement targeted epidemiologic surveillance activities in suspected area(s) of local transmission to identify additional cases, including:
    - Assess other household members for symptoms of OROV disease and collect serum to test for recent OROV infection.
    - Consider a house-to-house survey of neighborhood households, workplaces or other likely exposure locations(s) to identify any recently symptomatic people and, if symptomatic, obtain specimens to test for recent OROV infection. As stated in Section 5.2, the geographic scope and intensity of enhanced surveillance will depend on local circumstances. CDC is available to provide additional guidance to STLT health departments as requested. Contact eocevent495@cdc.gov for assistance.
    - Consider implementing syndromic surveillance in healthcare facilities in and around the area of concern.
- Assess the need for vector control and surveillance measures, which could include (see Appendices B and C for more details):
    - Using case report data to determine infection dates and potential infection zones.
    - Intensify vector control and surveillance in the identified geographic area(s), which may include focal or area-wide application of insecticides, door-to-door inspections, and source reduction (i.e., removal or modification of biting midge or mosquito larval habitats).
    - Given the importance of identifying the vectors responsible for transmission, consider vector testing in the immediate areas around cases (i.e., residence and place of work).
- Develop standing communication channels with vector control leads/officials to share vital information and coordinate surveillance and vector control efforts.
- Communicate with blood and tissue collection establishments.
- Provide testing guidance to the public and healthcare providers, including those who care for pregnant women.
- Prepare and issue a media statement in coordination with CDC and involved local health departments.
- Hold press conferences/events about confirmed local transmission, ongoing investigations, and updates.
- Augment clinician outreach and communication activities to healthcare providers in the county or jurisdiction through existing local channels for urgent infectious disease alerts (e.g., messages

through local medical societies and local chapters, Health Alert Network messages [HANs], conference calls).
- Consider implementing enhanced surveillance for persons presenting to clinical care with clinically compatible illness.
- Communicate with clinicians caring for pregnant women and infants about the risks of OROV and disseminate CDC guidance for these populations.
- Ensure that state and local maternal and child health and birth defects programs are integrated into OROV planning and response activities.
- Provide information to pregnant women and persons of reproductive age about the presence of OROV in the local area and what precautions they should take to prevent being infected with or avoid OROV exposure during pregnancy.
- Voluntarily report the case to ArboNET using interim case definitions.
- Monitor local news stories and social media posts to determine if information is accurate, identify messaging gaps, and adjust communication materials as needed.
- Implement community outreach efforts by adapting predeveloped messages to encourage care seeking (and testing for confirmation, when appropriate) of people with clinically compatible illnesses.
- Ensure engagement of public health, clinical, and community organizations to socialize and implement response plans.

7.2 Confirmed local transmission involving more than one case

The definition of multi-person local transmission is based on a limited understanding of potential vectors in the United States and is subject to change as more is learned. At this time, multi-person local transmission should be suspected when two or more probable or confirmed cases, without travel history to areas with known virus circulation, occur in different households or workplaces located within one mile of each other and have <45 days between onset of their illness (which is approximately the length of three incubation periods in humans and insect vectors). If a common exposure within a mile cannot be identified or the illness onset for the cases is ≥45 days apart, those cases can be considered individual confirmed local cases (see Section 7.1: Confirmed local transmission). If a STLT health department has concerns about suspected multi-person local transmission that does not meet this definition, please contact eocevent495@cdc.gov for consultation.

For confirmed multi-person local transmission, the level of public health intervention will depend on multiple factors:

- number of cases identified in the community,
- abundance of competent vectors, and
- characteristics and size of risk area (i.e., population density, urban vs. rural, proximity to neighboring communities, and geographic features).

In response to a suspected multi-person local transmission event for OROV, STLT health departments should

- In coordination with CDC, define geographic areas with OROV transmission risk and the need for vector control activities.
- Prepare and issue a media statement in coordination with CDC and involved local health departments.
- Intensify efforts to determine the risk of ongoing local transmission and adjust the geographic area(s) for public health interventions as necessary. If indicated by available epidemiologic, entomologic, and environmental information, the identified geographic area(s) may be expanded or reduced with consideration of other factors.
- Continue and possibly expand epidemiologic surveillance activities as described in Section 7.1: Confirmed local transmission to identify other possible cases of local transmission.
- Continue vector control and surveillance measures as guided by the entomologic evaluation of the area (Appendix B and C).
- Recommend testing of pregnant women and other people meeting the suspect case definition who live in or travel to the impacted area.
- Implement expanded jurisdictional intervention plans for reducing risk and target messages for all vulnerable populations, specifically:
    - Pregnant women
    - Persons at risk for unintended pregnancy
    - Persons who choose to delay or avoid pregnancy during the outbreak
    - Persons planning pregnancy
    - Individuals with an increased risk of vector exposure (e.g., unhoused and outdoor workers)
- Identify statewide resources for caring for infants and children with OROV-associated birth defects, developmental concerns, and other related outcomes.
- Encourage providers to keep abreast of recommendations and advisory updates from the American College of Obstetricians and Gynecologists/ Society for Maternal and Fetal Medicine/ American Academy of Pediatrics (ACOG/SMFM/AAP).
- Communicate with blood and tissue collection establishments regarding risk areas.
- Conduct risk communication activities, with CDC assistance, that ensure information and prevention recommendations reach intended audiences within their jurisdictions, including people who live in, work in, or plan to travel to the area where transmission is thought to be occurring, as well as to other relevant stakeholders (e.g., laboratories, healthcare partners/providers, blood and tissue collection establishments, neighboring states, tribal leaders). Communication activities should:
    - Describe the area where OROV transmission is thought to be occurring based on the best available epidemiologic, entomologic, and environmental information.
    - Identify an estimated date when local transmission began.
    - Describe all surveillance and response efforts taking place in the affected area.
    - Provide objective assessments of the situation and scale of the public health threat.
    - Provide advice about ways to reduce mosquito and biting midge populations around the home.
    - Provide guidance to laboratories, as needed.

    - Engage early with businesses, including blood and tissue collection establishments, and labor stakeholders to prepare for the potential short- and long-term effects (e.g., economic, infrastructure, supply).
    - Provide recommendations for employers with worksites in a designated area.
    - Provide recommendations for travelers going to and from affected areas (e.g., whether to avoid travel).
- Voluntarily report cases to ArboNET using interim case definitions.
- Continue to monitor the status of local transmission on, at a minimum, a weekly basis.
    - The geographic area(s) OROV intervention should be adjusted based on current information.
    - Environmental conditions not conducive to biting midge or mosquito activity, or other evidence (e.g., more than 45 days without a case) that indicates the risk of OROV transmission has been reduced, should also be considered when scaling down interventions.
- Implement a protocol and communication strategy when interventions are changed.

8. Other considerations

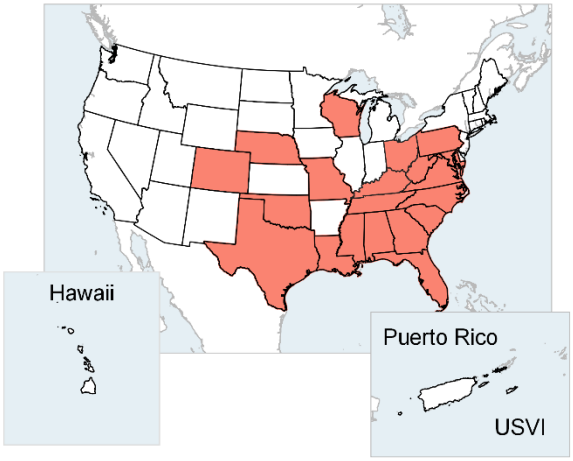
STLT health departments may consider utilizing wastewater surveillance as an adjunct to other surveillance approaches previously described. Wastewater surveillance may have the potential to aid in determining whether there is a risk of disease transmission in their communities. The limitations of the approach include:

- Inability to inform whether local transmission is occurring because virus detection cannot distinguish between the presence of travel-associated case(s) or locally acquired cases in the community.
- The duration of viral shedding in infected individuals is unknown. This would limit the usefulness of the approach in determining ongoing risk.
- Since the limit of detection for OROV is not established, negative findings may not indicate the absence of infections in the community.

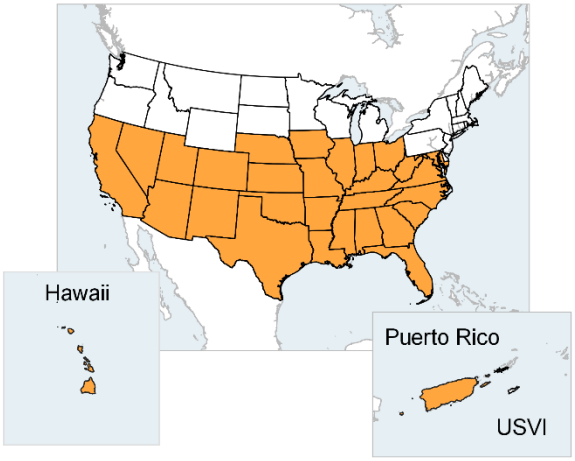
Appendix A Estimated range of potential vectors

Distribution of *Culicoides paraensis* and *Culex quinquefasciatus* in the United States and select territories based on field observations and modelling. Presence of vectors in a jurisdiction does not imply uniform distribution throughout the entire geographic areas. These maps will be updated as more is learned about the specific vectors that contribute to transmission in U.S. states and territories in the Americas. There is a zone where *Culex quinquefasciatus* hybridizes with other *Culex* species; this is not accounted for in the map because there have been no vector competence studies on these species.

Culicoides paraensis



Culex quinquefasciatus



Map references:

Cu. paraensis

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Pappas LG, Moyer S, Pappas CD. Tree hole Culicoides (Diptera: *Ceratopogonidae*) of the Central Plains in the United States. J Am Mosq Control Assoc. 1991;7(4):624-7. PubMed PMID: 1787409.

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Wirth WW, Dyce AL, Peterson BV. An atlas of wing photographs, with a summary of the numerical characters of the Nearctic species of Culicoides (Diptera: *Ceratopogonidae*). Contributions of the American Entomological Institute, 1985. 22(4):1-46.

Cx. quinquefasciatus

Darsie RFJ, Ward RA. Identification and geographical distribution of the mosquitoes of North America, North of Mexico. Gainesville, Florida: University Press of Florida; 2005.

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Appendix B Recommendations for Entomological Surveillance

Below are interim recommendations until vector competence work is completed to inform more specific guidance for the US and Puerto Rico. Published literature that reports work using strains of OROV circulating prior to 2024, and field detections of infected vectors, indicates the primary vectors are *Culicoides paraensis* and *Culex quinquefasciatus* in areas where outbreaks have occurred in South America.

Surveillance for potential vectors of OROV should include 1) trapping of biting midges and mosquitoes, 2) identification of vectors to species, and when warranted, 3) pooling of vectors for PCR testing.

Trapping

Biting Midges- *Culicoides spp.*

There are commercially available traps sold by John W Hock that are designed to attract and contain biting midges. https://www.johnwhock.com/products/mosquito-sandfly-traps/downdraft-blacklight-uv-trap/

CDC Miniature Light Traps that are commonly used in mosquito control programs can be used to sample biting midge populations. The holding chambers utilize screening or netting designed to contain mosquitoes, but biting midges can escape through the mesh. Modifications can be made by replacing netting and/or screening with a finer mesh material. **Appendix D** provides instructions on how to make these modifications.

Host-seeking female biting midges are attracted to carbon dioxide. Use of carbon dioxide in the vicinity of the trap will increase the likelihood of collecting biting midges.

Mosquitoes- *Culex quinquefasciatus*

The American Mosquito Control Association (AMCA) has published best practices for surveillance of mosquitoes, including *Culex* mosquitoes in CONUS. https://www.mosquito.org/bmp/

Virtual training for best management practices in integrated mosquito management can be accessed here: AMCA's Best Practices for Integrated Mosquito Management Virtual Training Program (ce21.com)

CDC guidance developed for surveillance of West Nile vectors, specific for adult *Culex quinquefasciatus,* is provided below.

Specimen Collection and Traps

Light traps collect a wide range of mosquito species (McCardle et al. 2004), providing information about both primary and secondary vectors and a better understanding of the species composition in an area. *Culex quinquefasciatus* can be collected in light traps. CDC miniature light traps (Sudia and Chamberlain 1962) are lightweight and use batteries to provide power to a light source and fan motor. CO2 (usually dry ice) is frequently used as an additional attractant. Light traps collections may consist largely of unfed, nulliparous individuals, which greatly reduces the likelihood of detecting arboviruses.

Gravid traps can be useful for sampling *Culex quinquefasciatus,* particularly in urban areas (Andreadis and Armstrong 2007, Reisen et al. 1999). Because gravid females have previously taken a blood meal, this increases the likelihood of capturing infected mosquitoes and detecting virus. Gravid traps can be baited with attractants such as fresh or dry grass clipping infusions, rabbit chow infusions, cow manure, fish oil, or other materials that mimic the stagnant water in habitats where these species lay eggs. These vary in attractiveness depending on the type of infusion and its preparation (Burkett et al. 2004, Lampman et al. 1996).

Collecting resting mosquitoes provides a good representation of vector population structure since unfed, gravid, and blood-fed females (as well as males) may be collected. Resting mosquitoes can be collected using suction traps such as the CDC resting trap (Panella et al. 2011), and by using handheld or backpack mechanical aspirators (Nasci 1981) to remove mosquitoes from natural resting harborages or artificial resting structures (e.g., wooden resting boxes, red boxes, fiber pots, and other similar containers). Because of the wide variety of resting sites and the low density of resting mosquitoes in most locations, sampling resting populations is labor intensive and sufficient sample sizes are often difficult to obtain.

Identification of mosquitoes and biting midges to species

There are numerous regional and state guides (taxonomic keys) available for identifying mosquitoes in specific regions and states. The *Identification and geographical distribution of the mosquitoes of North America, north of Mexico,* covers all mosquito species documented in North America as of 2005. For the most precise information about potential vectors, identification to species level is necessary.

Some identification keys for *Culicoides* include:

A systematic review of the genus *Culicoides* (Diptera: Ceratopogonidae) of Virginia with a geographic catalog of the species occurring in the eastern United States north of Florida (Battle and Turner, 1971).

The sand flies (Culicoides) of Florida (Diptera: Ceratopogonidae). (Blanton and Wirth, 1979).A photographic key to the adult female biting midges (Diptera: Ceratopogonidae: *Culicoides*) of Florida (Blosser et al, 2024).

The West Indian Sandflies of the Genus *Culicoides* (Diptera: Ceratopogonidae) (Wirth and Blanton 1974).

Vector Testing

Vector testing is encouraged to identify the vectors responsible for transmission. When responding to a locally acquired case, if vector testing for OROV is not available at a local or state agency, contact CDC to discuss options by emailing: entomology-adb@cdc.gov. Biting midges or mosquitoes can be processed using these procedures:

Preservation of specimens for nucleic acid detection

Specimens may be kept frozen, at 4 °C, and/or on chill tables during the sorting process. Mosquitoes and biting midges should be separated by species, collection date, and site. Once sorted, specimens should be stored at one of the following conditions until tested:

- Dry, frozen at -80 °C
- Dry, or in 70-95% non-denatured ethanol, frozen at -20 °C
- In 70-95% non-denatured ethanol, at 4 °C (least preferred)

Real time RT-PCR testing for OROV

Homogenize specimens in a buffer suitable for RNA extraction, such as cell culture media, viral transport media, or PBS. Pool 1-50 individual specimens and add 1 mL homogenization buffer. Centrifuge the homogenate to separate and clarify the supernatant. Extract RNA from an aliquot of clarified supernatant using a commercially available RNA or total nucleic acid extraction kit. Use the primers, probe, and thermocycling conditions to conduct OROV real-time RT-PCR as described in Naveca et al. 2017.

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Appendix C Vector control strategies

Below are interim recommendations until vector competence work is completed to inform more specific guidance for the US and Puerto Rico. Published literature that reports work using strains of OROV circulating prior to 2024, and field detections of infected vectors, indicates the primary vectors are *Culicoides paraensis* and *Culex quinquefasciatus* in areas where outbreaks have occurred in South America.

Specific strategies for control of biting midges are currently being evaluated. There is existing guidance that targets *Culex quinquefasciatus* mosquitoes because of their role in West Nile virus transmission. The AMCA Manual of Best Management Practices that includes control of *Culex* mosquitoes can be accessed here: https://www.mosquito.org/assets/pdf/hr_november_2021_amca_bmp_ma/

Virtual training for best management practices in integrated mosquito management can be accessed here: AMCA's Best Practices for Integrated Mosquito Management Virtual Training Program (ce21.com)

Integrated vector management (IVM) should be used to prevent and control OROV disease. IVM is a comprehensive program that applies the principles of integrated pest management. More information on IVM can be found in the Guidelines for West Nile Virus Surveillance and Control.

Vector Control for responding to case(s) of OROV disease

Educate all vector control personnel involved in responding to a case of OROV disease about the disease and prevention measures. Staff going to the field should take steps to lower their risk of infection, such as wearing permethrin treated long sleeve shirts and pants and using EPA-registered insect repellent.

The basis of the strategies listed here are adapted from Florida's Lee County Mosquito Control District response plan and CDC's Guidelines for West Nile Virus Surveillance and Control.

- Work with epidemiologist(s) to determine approximate infection dates and potential sites of exposure to infected vectors (e.g., residence, workplace, places of recreation).
- Set traps to collect both biting midges and mosquitoes up to a one-mile radius of infection zones (see Appendix B for more information on trapping and Appendix D for information on modifying CDC light trap chambers to collect both mosquitoes and biting midges).
- Identify to species and prepare mosquito and biting midge pools separately if OROV testing is planned (see Appendix B).
- Work with local public health to communicate ways that community members can assist in controlling mosquito larval habitats (e.g., disposing of discarded tires or other trash containers, emptying or treating unmaintained swimming pools).
- Consider messaging (e.g., newspaper release, interviews, conducting townhall meeting) in collaboration with public health officials to raise awareness about the risk of OROV in the community and address questions and concerns regarding community level vector control measures.
- Assist in the distribution of materials about OROV prevention (e.g., doorhangers, flyers) around the suspected infection site.

- Implement vector control measures. Most of the control measures targeting biting midges in the US has been in the context of animal (livestock) health. Evaluation of methods to control biting midges to prevent human disease should be undertaken. Control measures can include:
    - Aerial or ground adulticide using ultra-low-volume (ULV) technology up to a one square mile polygon, ; alternating between pyrethroids and organophosphates for subsequent applications;
    - Ground larvicide (LV truck) up to a one-mile radius around suspected site of infection; and
    - Barrier treatments on foliage, tree holes, fences, and other potential biting midge resting areas at least one acre around the suspected site of infection.
    - All products used for larval or adult control (ULV or barrier treatments) of vectors should be EPA-registered and labeled for the control of the target pest, e.g. *Culicoides* or *Culex* mosquitoes.
- Conduct vector surveillance and control measures until local transmission is no longer occurring. The decisions to decrease or stop activities should be made in conjunction with STLT health department and might include >45 days since the illness onset of the last reported human disease case. lo

In addition to the activities outlined above, consideration should be given to other aspects of IVM, including safety of vector control pesticides and practices, quality of vector control, maintaining good records of vector control efforts, and monitoring of insecticide resistance in mosquitoes. The CDC Bottle Bioassay is recommended to test for insecticide resistance in mosquitoes but has not been evaluated for use on biting midges. Resistance testing should be conducted before a product is first used. Resistance testing should follow published protocols to provide standardized results. A quick resistance assessment should be conducted prior to emergency adulticiding. Insecticide resistance test kits can be requested from the CDC by sending an email to USbottleassaykit@cdc.gov and requesting an order form. The instruction manual for use of the CDC Bottle Bioassay is located here: CDC Bottle Bioassay | Mosquitoes | CDC.

More information about IVM-associated activities, legal action to achieve access or control, and continuing education can be found in the Guidelines for West Nile Virus Surveillance and Control.

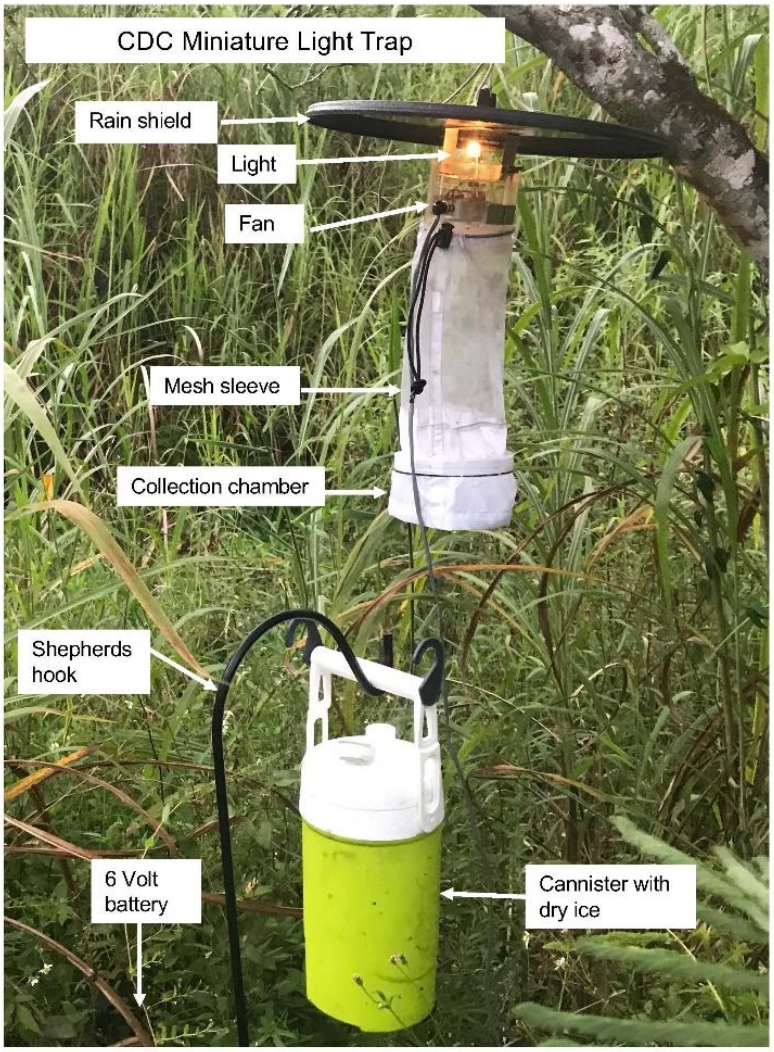
Appendix D Modifying CDC Light Trap Chambers for Mosquito and No-see-um Collection (Protocol courtesy of Dr. Nathan Burkett-Cadena, University of Florida)

Modifying CDC Light Trap Chambers for Mosquito and No-see-um Collection

Nathan Burkett-Cadena, PhD
Associate Professor
University of Florida
Florida Medical Entomology Laboratory

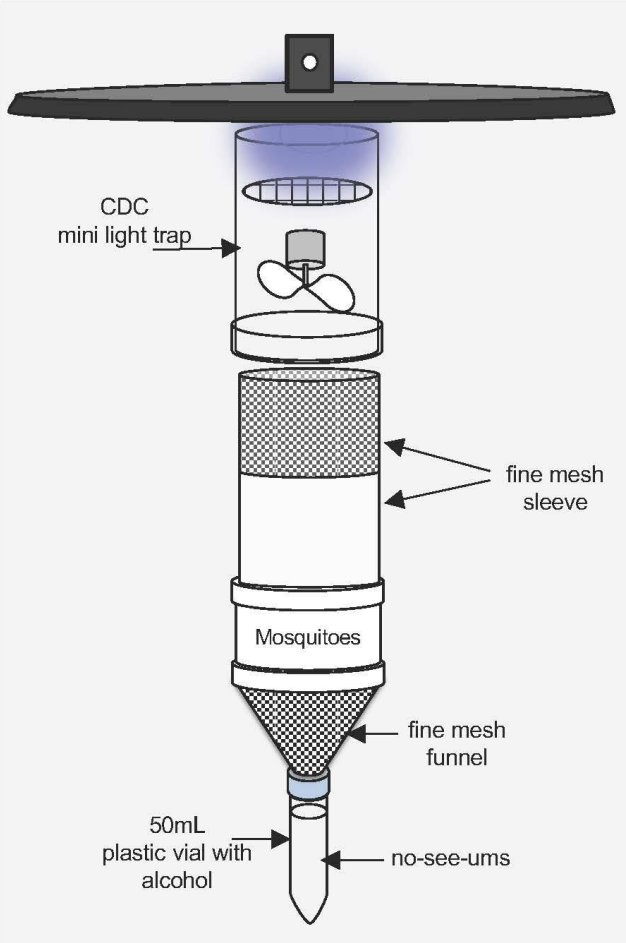
Mosquito and no-see-um sampling using
"The CDC Miniature Light Trap"

- The CDC Miniature Light Trap (CDC-LT) is an effective insect trap.
- The CDC-LT captures a diverse insects, including mosquitoes and biting midges.
- The CDC-LT uses light to attract these over short distances.
- A battery-powered fan sucks insects into a collection net / chamber.
- When baited with carbon dioxide, larger numbers of host-seeking female mosquitoes and no-see-ums can be captured.



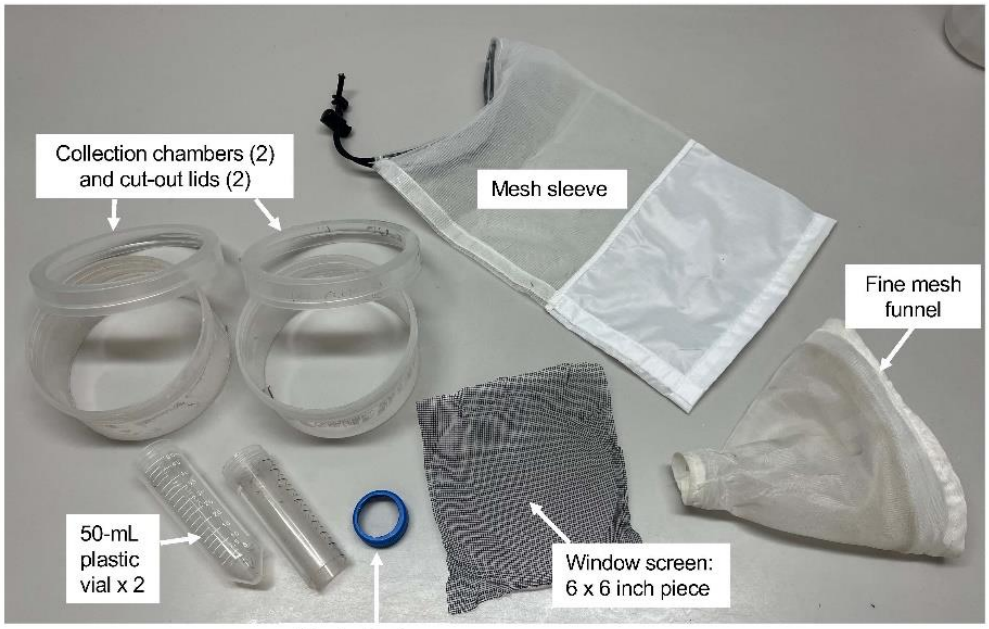
Modified Capture Chamber for CDC Miniature Light Trap for Collecting Biting Midges (no-see-ums)

- The CDC-LT collects mosquitoes in appropriate condition, but small no-see-ums can escape from the collection chamber through the metal mesh at the bottom of the chamber, or dry out in the collection chamber.
- No-see-ums are typically preserved and identified in alcohol solution. Standard isopropyl alcohol (90%) is good for preservation of morphological features of adult no-see-ums.
- Modifying the collection chamber to accept a plastic vial below the mosquito capture chamber permits collection and preservation of no-see-ums in alcohol while maintaining mosquitoes dry.



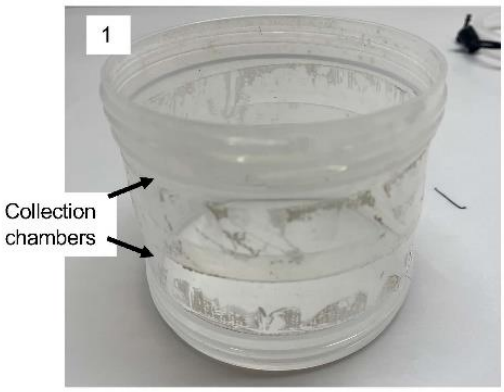
Modified Capture Chamber for CDC Miniature Light Trap for Collecting Biting Midges (no-see-ums)

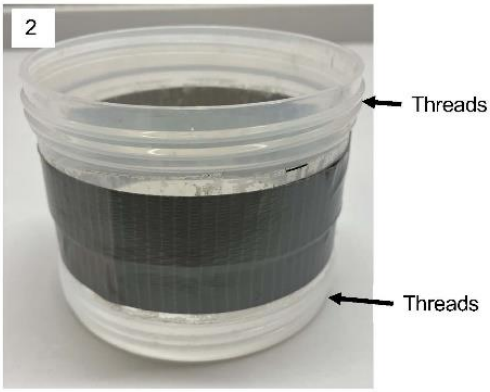
- Modifying the CDC-LT collection chamber to collect mosquitoes and no-see-ums can be done in many different ways.
- This protocol describes one successful way that we routinely use for collecting and separating mosquitoes from no-see-ums.



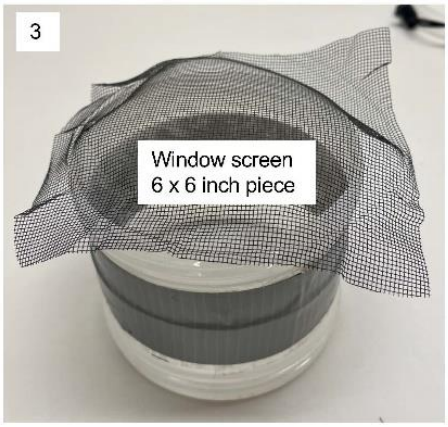
Modified Capture Chamber for CDC Miniature Light Trap for Collecting Biting Midges (no-see-ums)

1. Cut bottoms from 2 collection chambers, then...
2. Join together with duct tape so that threads are on tops and bottoms of champer.

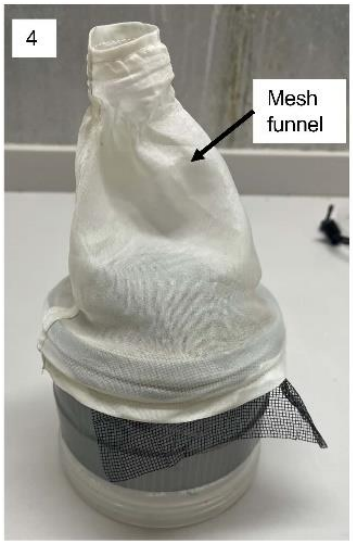




3. Place window screen on one end of chamber, then...
4. Slide mesh funnel over window screen.



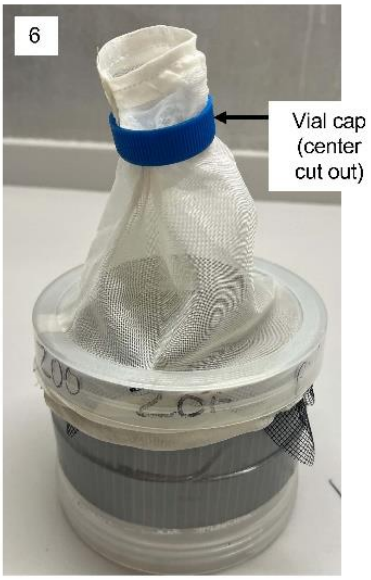
This will become the bottom side of the collection chamber



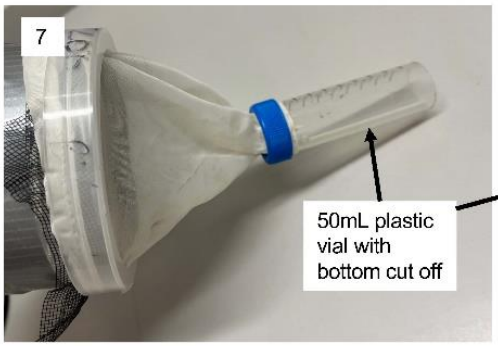
The mesh funnel can be made of pantyhose or other flexible, fine mesh material.
Ours were hand-sewn from polyester fabric.

Modified Capture Chamber for CDC Miniature Light Trap for Collecting Biting Midges (no-see-ums)

5. Screw the cutout chamber lid into place over the mesh funnel, then...
6. Slide the cutout plastic vial lid over the narrow end of the mesh funnel.



7. Screw plastic vial into cut-out cap (blue). The bottom of this vial should be cut off.
8. Attach 2nd vial with alfcohol (when in field).



Having the bottom of this vial cut off allows easy placement and removal of another vial with alcohol in the field.

Modified Capture Chamber for CDC Miniature Light Trap for Collecting Biting Midges (no-see-ums)

View from
top (inside)

Mosquito and no-see-um sampling using the CDC Miniature Light Trap

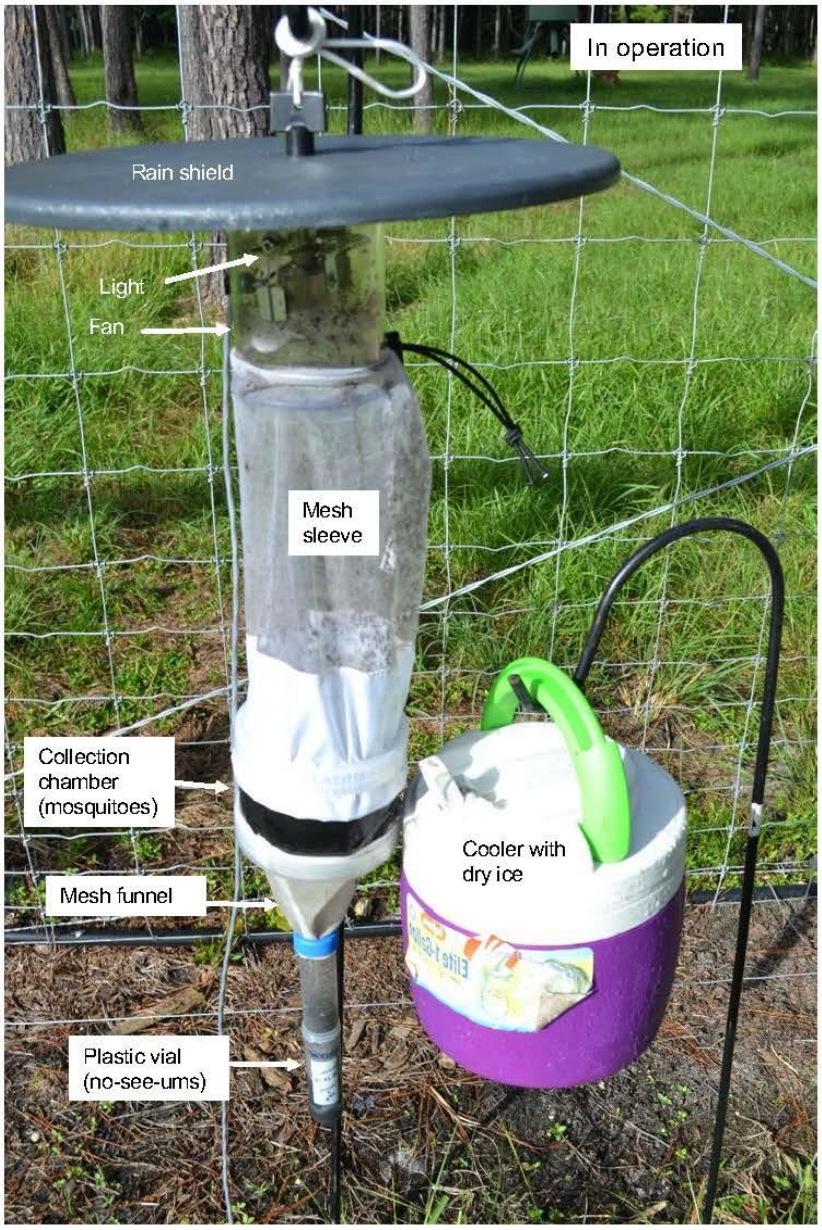
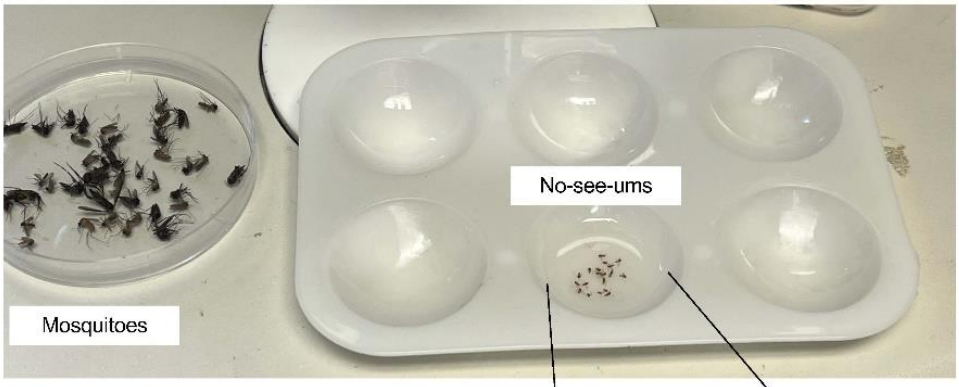


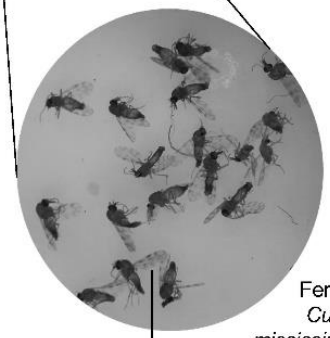
Photo by K. Sloyer

Handling and preserving mosquitoes and no-see-ums

- Mosquitoes and no-see-ums are handled and preserved differently in the laboratory
- Mosquitoes are often handled "dry", while no-see-ums are handled "wet", usually in alcohol (isopropyl alcohol or ethanol).



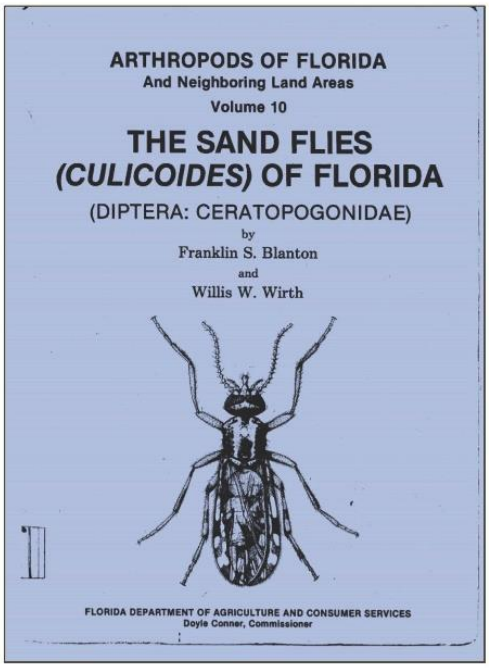
- No-see-ums are principally identified by patterns of dark and pale spots on their wings. These patterns are best observed in wet or slide mounted specimens.



Females of *Culicoides mississippiensis*

Culicoides mississippiensis wing

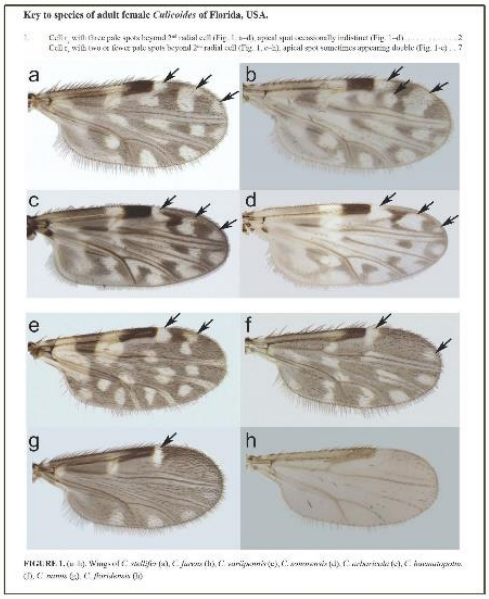
Resources for no-see-um identification in Florida



Blanton FS, Wirth WW. 1979. The sand flies (Culicoides) of Florida (Diptera: Ceratopogonidae). Arthropods of Florida and Neighboring Land Areas; Volume 10. Florida Department of Agriculture and Consumer Services. Gainesville, FL. 204 pg. http://palmm.digital.flvc.org/islandora/object/uf%3A46466#page/cover/mode/1up

Comprehensive resource on no-see-ums in Florida, with chapters on

- Historical and economic importance
- Disease transmission
- Control measures
- Biology
- Colonization
- Morphology
- Classification
- Key to species (not illustrated)
- Diagnostic tables
- Species descriptions (with maps)
- Plates (wing atlas)



Blosser EM, McGregor BL, Burkett-Cadena ND. 2024. A photographic key to the adult female biting midges (Diptera: Ceratopogonidae: Culicoides) of Florida, USA. Zootaxa. 5;5433(2):151-82. https://mapress.com/zt/article/view/zootaxa.5433.2.1

A photographic key to adult females with synopsis of important information

- Morphology
- Classification
- Key to species - photographic
- Summary of medical and veterinary importance

John W. Hock Company sells a product called the "1.20 - Killing Jar and Assembly" that may be useful for capturing no-see-ums with light traps.
https://www.johnwhock.com/products/accessories-options/

UF / FMEL does not endorse this or other products

End of document

Protocol: Burkett-Cadena Lab (University of Florida, USA)