

**SURVEILLANCE GUIDE FOR
REPORTING ARBOVIRAL DISEASES:
HUMAN CASE DATA ONLY**



DIVISION OF VECTOR-BORNE DISEASES

DECEMBER 2021

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GENERAL NOTES ON HUMAN CASE REPORTING

1. CDC requests that all nationally notifiable arboviral conditions (refer to Appendix G) be reported; however, we are also interested in knowing about other arboviral diseases occurring in your jurisdiction. Appendix G provides some additional codes for arboviral diseases that are not nationally notifiable, as well as a condition code (10072) for others not listed.
2. CDC currently distributes domestic arboviral, Zika and chikungunya reports every two weeks during the arboviral transmission season. This same schedule is used for updating West Nile virus, Zika virus and chikungunya case counts on the CDC website and updating the CDC Disease Maps (formerly USGS maps). All cases that are reported and published to ArboNET by close of business Monday of the report week are included in the various updates.
3. Antibody cross-reactivity and similarities in clinical presentation make distinguishing between related flaviviruses difficult, especially in areas where multiple flaviviruses are endemic. Further complicating disease reporting are the overlaps in case definitions for flaviviruses, which can result in the occasional case meeting the case definition criteria for more than one flavivirus disease. We use the specific example of Zika virus disease and dengue below, but the concepts apply to other endemic flavivirus diseases with cross-reactivity (e.g., West Nile virus disease and Saint Louis encephalitis).

For cases meeting the case definition criteria for both Zika virus disease and dengue it may be difficult to distinguish between the two diseases for reporting purposes. For these cases, we request that you do not report the case twice as both a Zika virus disease case and a dengue case.

Our preference is that you make a determination using the best available epidemiological and clinical evidence. In some cases, diagnostic testing on a convalescent specimen may provide additional insight. You can consult with CDC to determine if additional testing would be helpful and warranted.

If the available epidemiological and clinical information are not adequate to permit a best guess for reporting purposes, then report the case as Flavivirus disease, not otherwise specified (Flavivirus NOS) using condition code 50237. It is important to note that this is a disease condition code, not intended for asymptomatic infections.

These Flavivirus NOS cases (with condition code 50237) will not be counted as a Zika or dengue case and will not be reported in NNDSS weekly or annual tables, or included in surveillance data posted on the CDC webpages or maps. For this reason, we request that you use the Flavivirus NOS condition code as infrequently as possible.

4. The MMWR week is the week of the epidemiologic year assigned by the state health department for each reported case. MMWR week may be based on any of several dates (e.g., onset, diagnosis, laboratory result, when reported to public health, or data transmission date), and that assignment may vary by state or condition.

Because of the inconsistent use of the MMWR week variable, the Arboviral Diseases Branch uses 'Onset Date' to calculate the week and year for all reports generated with ArboNET data.

If 'Onset Date' is not provided, 'Specimen Collection Date' or 'Date of Donation' are used.

If none of the above dates are provided, the reported MMWR week and year are used.

NNDSS uses the MMWR week variable reported by the jurisdiction for their published summary tables, and the Arboviral Program uses 'Onset Date' as described above, for this reason, the weekly counts may not match.

CASE REPORT DATA ELEMENTS

State ID: State-assigned primary case identification number (unique ID). States use this field to link back to their own state investigations.

County: The patient's county of residence. For non-U.S. resident cases enter the reporting jurisdiction's county.

Case Disease Imported Code: This variable is intended to collect the most likely location of infection, not the patient's recent travel history.

- Indigenous: indicates that the infection was likely acquired in the patient's state of residence.
- Out of State: indicates that the infection was likely acquired outside of the patient's state of residence but within the United States.

Imported State: If the state of origin is known, choose the appropriate option from the list.

- International: indicates that the infection was likely acquired in another country.

Imported Country: Enter the country of origin here if known. If not known, enter "Unknown". For a person who visited multiple countries and the likely country of origin is unknown based on current known epidemiology, enter "Unknown". This field is used to inform travel guidance, reporting incorrectly could result in a country being considered a risk area for the particular disease when it is not.

Binational Reporting Criteria: This field is to be used if 'Imported From' has a value of 'Acquired out of Country' and the case was imported from Mexico or Canada.

Arbovirus: Virus being reported. Choose the appropriate value from the list.

DENV Serotype: Only used for cases reported with 'Arbovirus' as 'Dengue'. Choose the appropriate option from the list (DENV-1; DENV-2; DENV-3; DENV-4; Unknown; No Answer).

Condition Code: All conditions reported to the National Notifiable Diseases Surveillance System (NNDSS), which includes ArboNET, have associated condition codes. Condition codes are used to help simplify storage and retrieval of information about cases of nationally notifiable diseases. All CDC reports, including arboviral reports, are generated using reported condition codes, so it is important that these are accurately recorded. For a list of condition codes, please refer to Appendix G.

- Some arboviruses have multiple condition codes, based on either clinical presentation (e.g., neurologic vs non-neurologic) or other factors (e.g., congenital vs non-congenital, infection vs disease).
 - Example 1: If you are reporting a West Nile virus disease case with neurological presentation, the condition code should be 10056 and the primary clinical syndrome should be one of the following:
 - Acute flaccid paralysis
 - Encephalitis – including meningoencephalitis
 - Guillain-Barre' syndrome
 - Meningitis
 - Other neuroinvasive presentation
 - Example 2: If you are reporting a dengue disease case, the condition code and primary clinical syndrome should align as follows:
 - Condition code: 10680 - Clinical syndrome: Dengue
 - Condition code: 11704 - Clinical syndrome: Dengue-like illness
 - Condition code: 11705 - Clinical syndrome: Dengue, severe

Onset Date: This should reflect the date the patient developed symptoms of the current acute arboviral illness. If the case is an asymptomatic infection, leave this field blank. The Arboviral Diseases Branch uses 'Onset Date' to calculate the week and year for all reports generated with ArboNET data. If 'Onset Date' is not provided, 'Specimen Collection Date' or 'Date of Donation' are used.

Clinical Syndrome: Select the clinical syndrome which best describes the patient's current clinical illness according to the below guidelines. This variable is considered the "Primary Clinical Syndrome".

- Acute flaccid paralysis (AFP): AFP is a clinical syndrome characterized by rapid-onset extremity, facial, and/or respiratory weakness with 'flaccid' or decreased muscle tone in the affected areas. AFP may result from diverse conditions affecting the lower motor neurons such as anterior ('polio') myelitis, neuromuscular junction disorders, or acute neuropathies (such as Guillain-Barré syndrome [GBS]). If the case is identified as having GBS, the clinical syndrome should be reported as GBS instead of AFP.
- Asymptomatic: Infected person without any symptoms.
- Congenital infection: Infants who were infected in utero should be reported using this clinical syndrome. Complications in the infant should be recorded under 'Newborn Complications'.
- Dengue: Dengue virus infection in a case that meets the criteria for dengue but does not meet the criteria for severe dengue.
- Dengue-like illness: Dengue virus infection and fever as reported by the patient or healthcare provider in a case that does not meet the criteria for dengue.
- Encephalitis – including meningoencephalitis: Encephalitis is infection or inflammation of the brain tissue. Clinically, it may present with fever, persistent altered mental status, new-onset seizures, and/or focal neurologic deficits (e.g., cranial nerve palsies, aphasia, focal numbness, focal weakness, etc.) Diagnostically, it may be associated with a cerebrospinal fluid (CSF) pleocytosis and/or abnormal brain lesions on magnetic resonance imaging (MRI). Sometimes it may co-exist with infection or inflammation of the meninges (i.e., meningitis) resulting in a meningoencephalitis. Of note, many patients can become confused or have altered mental status due to their fever or other underlying medical conditions or medicines (e.g., liver or kidney disease, use of tacrolimus). Because of this, some consideration should be taken when classifying a patient with altered mental status as having encephalitis to ensure there is some sign of infection or inflammation of the brain.
- Febrile illness: Febrile illness without neurologic involvement. This may include isolated headache without other neurologic symptoms.
- Guillain-Barré syndrome (GBS): GBS is clinical syndrome characterized by an acute immune-mediated attack on multiple peripheral nerves and/or nerve roots (i.e., an acute immune-mediated polyradiculoneuropathy). Clinically, it may present with an acute, bilateral, progressive, flaccid weakness of the extremities and/or cranial nerve muscles and is usually accompanied by reduced or absent reflexes. GBS is one of many causes of acute flaccid paralysis (AFP). If the case is identified as having GBS, the clinical syndrome should be reported as GBS instead of AFP.
- Hepatitis/Jaundice: Inflammation of the liver resulting in elevated liver function enzymes and/or elevated bilirubin. The elevated bilirubin can lead to yellowish discoloration (jaundice) of whites of eyes, skin, and mucous membranes.
- Meningitis: Meningitis is infection or inflammation of the tissues that cover the brain (i.e., the meninges). Clinically, this may present with fever, headache, photophobia or light sensitivity, and/or new nuchal rigidity (the inability to flex one's neck forward). Unless there is a concurrent encephalitis (i.e., meningoencephalitis), pure meningitis should not present with prominent altered mental status or focal neurologic deficits. Diagnostically, it may be associated with a cerebrospinal fluid (CSF) pleocytosis, but brain imaging on CT or MRI may be normal. If meningitis co-exists with an encephalitis (i.e., meningoencephalitis), it should be reported as encephalitis instead.
- Multi-system organ failure: Failure or insufficiency of two or more systems or organs in the body, such as heart, lung, liver, and/or kidney.
- Other neuroinvasive presentation: Other neurologic/neuroinvasive presentations not covered under the categories of AFP, GBS, encephalitis/meningoencephalitis, or meningitis. This category might be selected if there is not sufficient information available to classify a neurologic case as a particular clinical syndrome. Other neuroinvasive presentation is a clinical syndrome that should only be selected for

other neurologic/neuroinvasive presentations that are not covered under the other categories. Some examples of clinical presentations that could fit in the category of other neuroinvasive presentation include blurred vision or unilateral facial paralysis, which might indicate optic neuritis or Bell's palsy, respectively. Other acute neurologic signs without a specific diagnosis that do not clearly fit one of the above categories would also qualify. Please contact the treating physician or CDC if there is any trouble determining which neuroinvasive category is most appropriate.

- Other clinical: For other non-neurologic/non-neuroinvasive presentations that are not consistent with other categories.
- Severe dengue: Dengue virus infection in a case that meets the criteria for dengue and has any one or more of the following: severe plasma leakage, severe bleeding from the gastrointestinal tract or vagina as defined by requirement for medical intervention, and/or severe organ involvement (elevated liver transaminases, impaired level of consciousness and/or diagnosis of encephalitis, encephalopathy, or meningitis, or heart or other organ involvement, including myocarditis, cholecystitis, and pancreatitis).
- Unknown: Insufficient information to assign a clinical syndrome to a case. You can change this at a later date if more information is obtained.

Clinical Syndrome 2: Select a secondary clinical syndrome when appropriate, using the same definitions as above.

Case Status: Choose the appropriate option from the list (Confirmed, Probable, Suspect, or Not a Case). For information on defining the case status for the record reference the appropriate national surveillance case definition in Appendix A-D.

Age: Age at time of illness onset or specimen collection (for asymptomatic cases).

Age Type: If you enter an age, you must choose an age type (e.g., Days, Months, Weeks, Years).

Sex: Choose the appropriate option from the list (Male, Female, or Unknown).

Race: Select **all** appropriate values (American Indian or Alaska Native, Asian, Black or African American, Native Hawaiian or Other Pacific Islander, White, Other, or Unknown).

Ethnicity: Select the appropriate value: Hispanic or Latino, Not Hispanic or Latino, or Unknown.

Country of Birth: Enter country of birth here if known.

Country of Usual Residence: This variable captures the country where the individual usually lives. If the country of usual residence is known, choose the appropriate option from the list.

Hospitalized: Choose the appropriate option from the list (Yes, No, or Unknown).

Fatality: Choose the appropriate option from the list (Yes, No, or Unknown).

Date of Death If you have not entered 'Yes' in 'Fatality', this field will not appear for data entry. You must enter a date that is after the onset date entered.

Publish: The 'Publish' variable (named 'Publish Flag' in Arboviral v1.3 MMG) is used to indicate whether or not a case should be included in CDC reports.

- 'Yes' indicates that CDC should include the case in reports generated with ArboNET data, including the arboviral activity updates, CDC Disease Maps, CDC website case counts, and the NNDSS weekly and annual tables.
- 'No' indicates that CDC should not include the case in reports. You might choose not to publish a case because of pending confirmatory testing, additional data collection needed, or other reasons related to the case investigation. *Please remember to update the 'Publish' field to 'Yes' when you are ready for the case to be included in CDC reports.*

EPIDEMIOLOGIC DATA ELEMENTS

Laboratory Acquired 'Yes' indicates that the patient was possibly infected while working in a laboratory setting.

Identified by Blood Donor Screening 'Yes' indicates that the patient's donated blood tested positive for viral RNA. For more information about reporting positive blood donors, please refer to Appendices E and F.

Blood Donor 'Yes' indicates that the patient donated a blood product within 30 days of illness onset. **This is meant to capture if a case donated blood before or after illness onset, because a case may be viremic before and after illness onset resulting in potentially infectious blood products**

Date of Donation: You should only enter a value if either 'Blood Donor' or 'Identified by Blood Donor Screening' are marked as 'Yes'.

Blood Transfusion: 'Yes' indicates that the patient received a blood product ≤30 days of illness onset. Marking this field as 'Yes' does not necessarily mean that the blood product received was determined to be the source of infection following investigation of the case.

Organ Donor: 'Yes' indicates that the patient donated an organ within 30 days of illness onset.

Organ Transplant Recipient: 'Yes' indicates that the patient received an organ or tissue transplant ≤30 days of onset. Marking this field as 'Yes' does not necessarily mean that the product received was determined to be the source of infection following investigation of the case.

Breast Fed Infant: 'Yes' indicates that the patient was a breast fed infant at the time of illness onset. If the patient was a breast-feeding woman at the time of illness onset, this field should **NOT** be marked as 'Yes'. Marking this field as 'Yes' does not necessarily mean that breast milk was determined to be the source of infection following investigation of the case.

Transmission Mode Other: Choose an appropriate option from the list when applicable

- Sexual transmission: indicates that the patient was likely infected through sexual contact with an infected person.
- Perinatal transmission: indicates that the patient is an infant that was infected around the time of delivery.
- Transplacental transmission: indicates that the patient is an infant that was infected during pregnancy

PREGNANCY/CONGENITAL INFECTIONS DATA ELEMENTS

Pregnant: 'Yes' indicates that the patient was pregnant at the time of illness onset or at the time of specimen collection in the case of asymptomatic women.

Last Menstrual Period Before Delivery: Date of first day of last menstrual period before delivery for pregnant women

Pregnancy Complications: This variable would only be used on the mother's report (not the infant's report). Choose the appropriate options (can choose multiple values). Values include: microcephaly, intracranial calcification, fetal growth abnormality, and fetus with central nervous system malformation.

Pregnancy Outcomes: This variable would only be used on the mother's report (not the infant's report). Choose the appropriate option. Values include: live birth, premature birth, fetal death, therapeutic abortion, still birth, perinatal death, still pregnant.

Mother-Infant Case ID: This variable would be used on a mother's or infant's report to link the two cases together. The mother's StateID should be entered for the infant's notification and the infant's StateID should be entered for the mother's notification.

Newborn Complications: This variable would only be used on a congenital infection report (not the mother's report). Choose the appropriate options (can choose multiple values). Values include: microcephaly, intracranial calcification, congenital anomaly of central nervous system, ocular defects, limb defects, intrauterine growth retardation, none.

CLINICAL SIGNS AND SYMPTOMS DATA ELEMENTS

None of the clinical signs and symptoms data are required. For all, mark as 'Yes', 'No', or 'Unknown' as appropriate.

Fever: any measured or subjective fever as recorded by the patient or provider.

Chills or Rigors: a subjective fever was recorded by the patient or provider.

Rash

Headache

Fatigue or Malaise

Conjunctivitis

Nausea or Vomiting

Diarrhea

Myalgia

Arthralgia

Arthritis

Paresis or Paralysis

Stiff Neck: a specific type of stiff neck (nuchal rigidity) when a person cannot flex their neck downwards to their chest. This is characteristic of meningitis.

Ataxia: a clinical sign defined as a lack of coordinated voluntary muscle movements. Ataxia may affect the extremities, trunk, eyes, or speech. When affecting gait, ataxia may cause imbalance, unsteadiness, or falls; not all gait abnormalities are caused by ataxia. Terms such as dysmetria, incoordination, or clumsiness describing movements may suggest ataxia.

Altered Mental Status

Parkinsonism or Cogwheel Rigidity: a clinical hypokinetic movement disorder characterized by bradykinesia, postural instability, rigidity, and/or tremor due to multiple different diseases.

Seizures

Retro-orbital Pain

Leukopenia: white blood cell count $<5,000/\text{mm}^3$

Oral ulcers

Other Symptoms: This is a free text field where other symptoms can be listed. There is a 255 character limit.

Additional Signs and Symptoms for Dengue Cases

Abdominal Pain or Tenderness

Liver Enlargement: enlargement >2 centimeters

Severe Organ Involvement: any of the following: 1) Elevated liver transaminases: aspartate aminotransferase (AST) or alanine aminotransferase (ALT) $\geq 1,000$ per liter (U/L); 2) Impaired level of consciousness and/or diagnosis of encephalitis, encephalopathy, or meningitis; or 3) Heart or other organ involvement including myocarditis, cholecystitis, and pancreatitis.

Persisting Vomiting: vomiting ≥ 3 times over 24 hours.

Increasing Hematocrit with Decreased Platelet Count: an increase in hematocrit concurrent with a rapid decrease in platelet count.

Tourniquet Test Positive: positive tourniquet test (capillary fragility test).

Extravascular Fluid Accumulation: pleural or pericardial effusion, ascites.

Severe Plasma Leakage: plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites) with respiratory distress. A high hematocrit value for patient age and sex offers further evidence of plasma leakage.

Mucosal Bleeding: bleeding at any site (e.g., hematemesis, melena)

Severe Bleeding: bleeding from the gastrointestinal tract (e.g., hematemesis, melena) or vagina (menorrhagia) and requiring medical intervention including intravenous fluid resuscitation or blood transfusion.

LABORATORY INFORMATION AND DIAGNOSTIC TESTING RESULTS

This section includes repeating group laboratory variables. Multiple test results can be reported for a single case report. **Laboratory information and diagnostic testing results should pertain only to the arboviral condition that is being reported.** For example, if a West Nile case is being reported, all lab results should be related to West Nile testing, not for other arboviruses (e.g., St. Louis encephalitis) that may have been part of the differential diagnosis.

Test Type: Choose the appropriate option from the list (Serum IgM, Serum PRNT, Serum PCR or NAT, CSF IgM, CSF PRNT, CSF PCR, Immunohistochemical staining, Other specimen PCR, Arboviral antigen).

Test Result: Choose the appropriate option from the list (Positive, Negative, Equivocal, Not Done).

Specimen Type: Choose the appropriate option from the list (acute phase serum, amniotic fluid, blood, body fluid, cerebrospinal fluid, convalescent phase serum, cord blood, fetal cytologic material, fetal tissue, saliva, seminal fluid, serum, placenta, tissue, brain tissue, urine).

Specimen Collection Date: Date of collection of the specimen being reported.

Performing Lab Type: Choose the appropriate option from the list (CDC, State Public Health, Commercial).

Serum Paired Antibody Result: '4-Fold Rise' indicates that there was a four-fold or greater change in virus-specific quantitative antibody titers between acute- and convalescent-phase serum specimens. 'Negative' indicates that there was not a four-fold or greater change in virus-specific quantitative antibody titers between acute- and convalescent-phase serum specimens.

Cerebrospinal Fluid Pleocytosis: 'Yes' (checked box) indicates a CSF white blood cell count ≥ 5 .

APPENDIX A: ARBOVIRAL DISEASES, NEUROINVASIVE AND NON-NEUROINVASIVE CASE DEFINITIONS

The most up to date information can be found at <https://ndc.services.cdc.gov/case-definitions/arboviral-diseases-neuroinvasive-and-non-neuroinvasive-2015/>

2015 Case Definition; CSTE Position Statement 14-ID-04; Subtype(s)

- California Serogroup Virus Diseases
- Chikungunya Virus Disease
- Eastern Equine Encephalitis Virus Disease
- Powassan Virus Disease
- St. Louis Encephalitis Virus Disease
- West Nile Virus Disease
- Western Equine Encephalitis Virus Disease

Background

Arthropod-borne viruses (arboviruses) are transmitted to humans primarily through the bites of infected mosquitoes, ticks, sand flies, or midges. Other modes of transmission for some arboviruses include blood transfusion, organ transplantation, perinatal transmission, breast feeding, and laboratory exposures. More than 130 arboviruses are known to cause human disease. Most arboviruses of public health importance belong to one of three virus genera: *Flavivirus*, *Alphavirus*, and *Orthobunyavirus*.

California serogroup viruses include:

- California encephalitis
- Jamestown Canyon
- Keystone
- La Crosse
- Snowshoe hare
- Trivittatus viruses

Clinical Description

Most arboviral infections are asymptomatic. Clinical disease ranges from mild febrile illness to severe encephalitis. For the purpose of surveillance and reporting, based on their clinical presentation, arboviral disease cases are often categorized into two primary groups: neuroinvasive disease and nonneuroinvasive disease.

Neuroinvasive disease

Many arboviruses cause neuroinvasive disease such as aseptic meningitis, encephalitis, or acute flaccid paralysis (AFP). These illnesses are usually characterized by the acute onset of fever with headache, myalgia, stiff neck, altered mental status, seizures, limb weakness, or cerebrospinal fluid (CSF) pleocytosis. AFP may result from anterior ("polio") myelitis, peripheral neuritis, or post-infectious peripheral demyelinating neuropathy (i.e., Guillain-Barre' syndrome). Less common neurological manifestations, such as cranial nerve palsies, also occur.

Non-neuroinvasive disease

Most arboviruses are capable of causing an acute systemic febrile illness (e.g., West Nile fever) that may include headache, myalgias, arthralgia, rash, or gastrointestinal symptoms. Some viruses also can cause more characteristic clinical manifestations, such as severe polyarthralgia or arthritis due to Chikungunya virus or other alphaviruses (e.g., Mayaro, Ross River, O'nyong-nyong).

Clinical Criteria

A clinically compatible case of arboviral disease is defined as follows:

Neuroinvasive disease

- Meningitis, encephalitis, acute flaccid paralysis, or other acute signs of central or peripheral neurologic dysfunction, as documented by a physician, AND

- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis and/ or nuchal rigidity.

Non-neuroinvasive disease

- Fever (chills) as reported by the patient or a health-care provider, AND
- Absence of neuroinvasive disease, AND
- Absence of a more likely clinical explanation. Other clinically compatible symptoms of arbovirus disease include: headache, myalgia, rash, arthralgia, vertigo, vomiting, paresis and/ or nuchal rigidity.

Laboratory Criteria for Diagnosis

Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR

- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF or serum.

Case Classification

Probable

Neuroinvasive disease

A case that meets the above clinical criteria for neuroinvasive disease and the following laboratory criteria:

- Virus-specific IgM antibodies in CSF or serum but with no other testing.

Non-neuroinvasive disease

A case that meets the above clinical criteria for non-neuroinvasive disease and the laboratory criteria for a probable case:

- Virus-specific IgM antibodies in serum but with no other testing.

Confirmed

Neuroinvasive disease

A case that meets the above clinical criteria for neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

- Isolation of virus from, or demonstration of specific viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, OR
- Four-fold or greater change in virus-specific quantitative antibody titers in paired sera, OR
- Virus-specific IgM antibodies in serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, OR
- Virus-specific IgM antibodies in CSF, with or without a reported pleocytosis, and a negative result for other IgM antibodies in CSF for arboviruses endemic to the region where exposure occurred.

Non-neuroinvasive disease

A case that meets the above clinical criteria for non-neuroinvasive disease and one or more of the following laboratory criteria for a confirmed case:

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

Comment(s)

Imported arboviral diseases

Human disease cases due to Dengue or Yellow fever viruses are nationally notifiable to CDC using specific case definitions. However, many other exotic arboviruses (e.g., Japanese encephalitis, Tick-borne encephalitis, Venezuelan equine encephalitis, and Rift Valley fever viruses) are important public health risks for the United States as competent vectors exist that could allow for sustained transmission upon establishment of imported arboviral pathogens. Health-care providers and public health officials should maintain a high index of clinical suspicion for cases of potentially exotic or unusual arboviral etiology, particularly in international travelers. If a suspected case occurs, it should be reported to the appropriate local/state health agencies and CDC.

Interpreting arboviral laboratory results:

- **Serologic cross-reactivity:** In some instances, arboviruses from the same genus produce cross-reactive antibodies. In geographic areas where two or more closely-related arboviruses occur, serologic testing for more than one virus may be needed and results compared to determine the specific causative virus. For example, such testing might be needed to distinguish antibodies resulting from infections within genera, e.g., flaviviruses such as West Nile, St. Louis encephalitis, Powassan, Dengue, or Japanese encephalitis viruses.
- **Rise and fall of IgM antibodies:** For most arboviral infections, IgM antibodies are generally first detectable at 3 to 8 days after onset of illness and persist for 30 to 90 days, but longer persistence has been documented (e.g., up to 500 days for West Nile virus). Serum collected within 8 days of illness onset may not have detectable IgM and testing should be repeated on a convalescent-phase sample to rule out arboviral infection in those with a compatible clinical syndrome.
- **Persistence of IgM antibodies:** Arboviral IgM antibodies may be detected in some patients months or years after their acute infection. Therefore, the presence of these virus-specific IgM antibodies may signify a past infection and be unrelated to the current acute illness. Finding virus-specific IgM antibodies in CSF or a fourfold or greater change in virus-specific antibody titers between acute- and convalescent-phase serum specimens provides additional laboratory evidence that the arbovirus was the likely cause of the patient's recent illness. Clinical and epidemiologic history also should be carefully considered.
- **Persistence of IgG and neutralizing antibodies:** Arboviral IgG and neutralizing antibodies can persist for many years following a symptomatic or asymptomatic infection. Therefore, the presence of these antibodies alone is only evidence of previous infection and clinically compatible cases with the presence of IgG, but not IgM, should be evaluated for other etiologic agents.
- **Arboviral serologic assays:** Assays for the detection of IgM and IgG antibodies commonly include enzyme-linked immunosorbent assay (ELISA), microsphere immunoassay (MIA), or immunofluorescence assay (IFA). These assays provide a presumptive diagnosis and should have confirmatory testing performed. Confirmatory testing involves the detection of arboviral-specific neutralizing antibodies utilizing assays such as plaque reduction neutralization test (PRNT).
- **Other information to consider.** Vaccination history, detailed travel history, date of onset of symptoms, and knowledge of potentially cross-reactive arboviruses known to circulate in the geographic area should be considered when interpreting results.

APPENDIX B: DENGUE VIRUS INFECTIONS CASE DEFINITION

The most up to date information can be found at <https://ndc.services.cdc.gov/case-definitions/dengue-virus-infections-2015/>

2015 Case Definition; CSTE Position Statement 14-ID-10; Subtype(s)

- Dengue
- Dengue-like illness
- Severe dengue

Background

Dengue is a potentially fatal acute febrile illness caused by infection with any of four dengue viruses (DENV-1, -2, -3, and -4). Dengue is a major public health problem worldwide, where an estimated 400 million DENV infections and 100 million clinically apparent dengue cases occurred in 2010. Although ~75% of individuals infected with a DENV will be asymptomatic, ~5% of individuals that develop dengue will progress to severe dengue, an illness characterized by plasma leakage leading to hypovolemic shock, hemorrhage, and potentially death. The case-fatality rate for individuals with severe dengue can be as high as 10% if untreated, or 0.1% with appropriate clinical management.

DENVs are transmitted primarily through the bite of *Aedes aegypti* and *Ae. albopictus* mosquitoes. Because these mosquitoes are endemic throughout the tropics and sub-tropics, an estimated 40% of the world's population is at risk for DENV infection. These mosquitoes are also present in the United States. *Ae. aegypti* is present throughout southern Florida, southern Louisiana, parts of New Mexico and Arizona, southern and central Texas (most prominently around urban centers such as Houston, Dallas, and Austin) [4], and have recently been detected in central California and southern Utah. *Ae. albopictus* is widely present throughout most of the southern United States and as far north as Illinois and New York.

Clinical Criteria

Dengue is defined by fever as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms:

- Nausea/vomiting
- Rash
- Aches and pains (e.g., headache, retro-orbital pain, joint pain, myalgia, arthralgia)
- Tourniquet test positive
- Leukopenia (a total white blood cell count of $<5,000/\text{mm}^3$), **or**
- Any warning sign for severe dengue:
 - Abdominal pain or tenderness
 - Persistent vomiting
 - Extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites)
 - Mucosal bleeding at any site
 - Liver enlargement >2 centimeters
 - Increasing hematocrit concurrent with rapid decrease in platelet count

Laboratory Criteria for Diagnosis

- **Confirmatory:**
 - Detection of DENV nucleic acid in serum, plasma, blood, cerebrospinal fluid (CSF), other body fluid or tissue by validated reverse transcriptase-polymerase chain reaction (PCR), or
 - Detection of DENV antigens in tissue by a validated immunofluorescence or immunohistochemistry assay, or
 - Detection in serum or plasma of DENV NS1 antigen by a validated immunoassay; or
 - Cell culture isolation of DENV from a serum, plasma, or CSF specimen; or

- Detection of IgM anti-DENV by validated immunoassay in a serum specimen or CSF in a person living in a dengue endemic or non-endemic area of the United States without evidence of other flavivirus transmission (e.g., WNV, SLEV, or recent vaccination against a flavivirus (e.g., YFV, JEV)); or
 - Detection of IgM anti-DENV in a serum specimen or CSF by validated immunoassay in a traveler returning from a dengue endemic area without ongoing transmission of another flavivirus (e.g., WNV, JEV, YFV), clinical evidence of co-infection with one of these flaviviruses, or recent vaccination against a flavivirus (e.g., YFV, JEV); or
 - IgM anti-DENV seroconversion by validated immunoassay in acute (i.e., collected <5 days of illness onset) and convalescent (i.e., collected >5 days after illness onset) serum specimens; or
 - IgG anti-DENV seroconversion or ≥ 4 -fold rise in titer by a validated immunoassay in serum specimens collected >2 weeks apart, and confirmed by a neutralization test (e.g., plaque reduction neutralization test) with a >4-fold higher end point titer as compared to other flaviviruses tested.
- **Probable:**
 - Detection of IgM anti-DENV by validated immunoassay in a serum specimen or CSF in a person living in a dengue endemic or non-endemic area of the United States with evidence of other flavivirus transmission (e.g., WNV, SLEV), or recent vaccination against a flavivirus (e.g., YFV, JEV).
 - Detection of IgM anti-DENV in a serum specimen or CSF by validated immunoassay in a traveler returning from a dengue endemic area with ongoing transmission of another flavivirus (e.g., WNV, JEV, YFV), clinical evidence of co-infection with one of these flaviviruses, or recent vaccination against a flavivirus (e.g., YFV, JEV).
 - **Suspected:**
 - The absence of IgM anti-DENV by validated immunoassay in a serum or CSF specimen collected <5 days after illness onset and in which molecular diagnostic testing was not performed in a patient with an epidemiologic linkage.

Epidemiologic Linkage

- Travel to a dengue endemic country or presence at location with ongoing outbreak within previous two weeks of onset of an acute febrile illness or dengue, or
- Association in time and place (e.g., household member, family member, classmate, or neighbor) with a confirmed or probable dengue case.

Criteria to Distinguish a New Case from an Existing Case

DENV infection results in long-lasting immunity to symptomatic infection (dengue) with that DENV-type. However, cross-protective (heterotypic) immunity against dengue is short-lived with estimated durations of 1-3 years. In dengue endemic areas where infection pressure is high, individuals have been shown to infrequently have sequential episodes of dengue with two different infecting serotypes.

Based on these data, a person with two clinical episodes of dengue occurring at least two weeks apart and shown to be due to different infecting DENV-types confirmed by molecular diagnostic testing would be classified as two different cases.

However, for two clinical episodes of dengue in the same person diagnosed only by IgM anti-DENV on the second episode; to be considered separate cases, they would have to occur >90 days apart due to the persistence of detectable IgM anti-DENV for ~90 days.

Exposure

- During the two weeks prior to onset of fever, travel to a dengue endemic country or presence in a location experiencing an ongoing dengue outbreak, OR
- Association in time and place with a confirmed or probable dengue case.

Endemicity

The largest burden of dengue in the United States is in the territories of Puerto Rico and the U.S. Virgin Islands where it is endemic. As such, the majority of reported dengue cases in the U.S. come from these two territories, where existing surveillance systems are in place to capture both the incidence and to some degree the spectrum of disease. Other areas of the US where dengue is or has been endemic include American Samoa, the Northern Marianas, and Guam. In addition, hundreds of travel-associated dengue cases occur each year, primarily in the 50 United States and the District of Columbia.

Subtype(s) Case Definition

Dengue

Clinical Description: Dengue is defined by fever as reported by the patient or healthcare provider and the presence of one or more of the following signs and symptoms:

- Nausea/vomiting
- Rash
- Aches and pains (e.g., headache, retro-orbital pain, joint pain, myalgia, arthralgia)
- Tourniquet test positive
- Leukopenia (a total white blood cell count of $<5,000/\text{mm}^3$), or
- Any warning sign for severe dengue:
 - Abdominal pain or tenderness
 - Persistent vomiting (≥ 3 times in a 24-hour period)
 - Extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites)
 - Mucosal bleeding at any site
 - Liver enlargement >2 centimeters
 - Increasing hematocrit concurrent with rapid decrease in platelet count

Dengue-like illness

Clinical Description: Dengue-like illness is defined by fever as reported by the patient or healthcare provider.

Comments

* In June 2014, the Council of State and Territorial Epidemiologists (CSTE) recommended Dengue-like illness become nationally notifiable. Dengue-like illness will be added to the list of National Notifiable Infectious Conditions when the CDC receives Office of Management and Budget (OMB) Paperwork Reduction Act (PRA) approval to receive data for this condition.

Severe dengue

Clinical Description: Severe dengue is defined as dengue with any one or more of the following scenarios:

- Severe plasma leakage evidenced by hypovolemic shock and/or extravascular fluid accumulation (e.g., pleural or pericardial effusion, ascites) with respiratory distress. A high hematocrit value for patient age and sex offers further evidence of plasma leakage.
- Severe bleeding from the gastrointestinal tract (e.g., hematemesis, melena) or vagina (menorrhagia) as defined by requirement for medical intervention including intravenous fluid resuscitation or blood transfusion.
- Severe organ involvement, including any of the following:
 - Elevated liver transaminases: aspartate aminotransferase (AST) or alanine aminotransferase (ALT) $\geq 1,000$ per liter (U/L)
 - Impaired level of consciousness and/or diagnosis of encephalitis, encephalopathy, or meningitis
 - Heart or other organ involvement including myocarditis, cholecystitis, and pancreatitis

Case Classification

Suspected: A clinically compatible case of dengue-like illness, dengue, or severe dengue with an epidemiologic linkage, as defined above.

Probable: A clinically compatible case of dengue-like illness, dengue, or severe dengue with laboratory results indicative of probable infection, as defined above.

Confirmed: A clinically compatible case of dengue-like illness, dengue, or severe dengue with confirmatory laboratory results, as defined above.

Comment(s)

The 2009 CSTE Dengue Position Statement included the reporting of DENV-positive asymptomatic blood donors identified through pilot screening projects in dengue endemic areas. However, these screening projects have ended, no cases were reported, and the "Asymptomatic Blood or Tissue Donor" reporting category will be deleted, limiting reporting to persons with symptomatic DENV infection (i.e., dengue).

APPENDIX C: YELLOW FEVER CASE DEFINITION

The most up to date information can be found at <https://ndc.services.cdc.gov/case-definitions/yellow-fever-2019/>

2019 Case Definition; CSTE Position Statement 18-ID-04

Clinical Criteria

A clinically compatible case of yellow fever is defined as:

- Acute illness with at least one of the following: fever, jaundice, or elevated total bilirubin ≥ 3 mg/dl AND Absence of a more likely clinical explanation.

Laboratory Criteria

Confirmatory laboratory evidence:

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

Presumptive laboratory evidence:

- Yellow fever virus-specific IgM antibodies in CSF or serum, and negative IgM results for other arboviruses endemic to the region where exposure occurred.

Epidemiologic Linkage

Epidemiologically linked to a confirmed yellow fever case, or visited or resided in an area with a risk of yellow fever in the 2 weeks before onset of illness.

Case Classifications

Confirmed:

A case that meets the above clinical criteria and meets one or more of the following:

- Isolation of yellow fever virus from, or demonstration of yellow fever viral antigen or nucleic acid in, tissue, blood, CSF, or other body fluid, AND no history of yellow fever vaccination within 30 days before onset of illness unless there is molecular evidence of infection with wild-type yellow fever virus.
- Four-fold or greater rise or fall in yellow fever virus-specific neutralizing antibody titers in paired sera, AND no history of yellow fever vaccination within 30 days before onset of illness.
- Yellow fever virus-specific IgM antibodies in CSF or serum with confirmatory virus-specific neutralizing antibodies in the same or a later specimen, AND no history of yellow fever vaccination.

Probable:

A case that meets the above clinical and epidemiologic linkage criteria, and meets the following:

- Yellow fever virus-specific IgM antibodies in CSF or serum, AND negative IgM results for other arboviruses endemic to the region where exposure occurred, AND no history of yellow fever vaccination.

APPENDIX D: ZIKA VIRUS INFECTIONS CASE DEFINITION

The most up to date information can be found at <https://ndc.services.cdc.gov/case-definitions/zika-virus-disease-and-zika-virus-infection-2016-06-01/>

2016 Case Definition; CSTE Position Statement 16-ID-01; Subtype(s)

- Zika virus disease, congenital
- Zika virus disease, non-congenital
- Zika virus infection, congenital
- Zika virus infection, non-congenital

Background

Zika virus (ZIKV), a flavivirus transmitted by *Aedes* species mosquitoes, was first identified in the Zika Forest by the Virus Research Institute in Uganda in a non-human primate in 1947 and from *Aedes africanus* mosquitoes in 1948. Before 2007, there had been only 14 human ZIKV disease cases documented. In 2007, an outbreak of ZIKV disease occurred on Yap Island, Federated States of Micronesia and the ensuing investigation included the first population-based epidemiological study of ZIKV infection and disease. It was estimated that 75% (attack rate) of the island's inhabitants were infected with ZIKV resulting in 18% symptomatic and 82% asymptomatic infections. The most common symptoms documented in this outbreak were maculopapular rash, fever, arthralgia, and conjunctivitis. From 2013 to 2014 there was a large outbreak in French Polynesia where *Aedes aegypti* was considered the most important vector. There continues to be ongoing transmission in the Pacific Islands.

Due to the rapidly evolving epidemic of Zika virus infection, the Council of State and Territorial Epidemiologists (CSTE) Executive Board developed an interim position statement to establish standardized case definitions for Zika virus disease and ZIKV congenital infection dated February 26, 2016, and to add these conditions to the Nationally Notifiable Diseases List. As laboratory testing for ZIKV has been more widely performed, limitations of the interpretation of serologic test results, including plaque reduction neutralization testing have been recognized, necessitating revisions to the laboratory criteria of the case definitions. Additionally, numerous asymptomatic persons, particularly pregnant women are tested for ZIKV infection and will meet laboratory criteria for infection. Because asymptomatic infection might be epidemiologically significant, revisions to the interim surveillance case definitions are proposed to include ZIKV infections without disease. Public health jurisdictions are encouraged to evaluate, report, and monitor identified ZIKV infections, particularly in pregnant women, that don't meet the clinical criteria of the confirmed and probable congenital and non-congenital disease case classifications.

Laboratory Criteria for Diagnosis

Recent ZIKV infection

- Culture of ZIKV from blood, body fluid, or tissue; **OR**
- Detection of ZIKV antigen or viral ribonucleic acid (RNA) in serum, cerebrospinal fluid (CSF), placenta, umbilical cord, fetal tissue, or other specimen (e.g., amniotic fluid, urine, semen, saliva), **OR**
- Positive ZIKV immunoglobulin M (IgM) antibody test in serum or CSF **with** positive ZIKV neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred

Recent flavivirus infection, possible ZIKV

- Positive ZIKV IgM antibody test of serum or CSF with positive neutralizing antibody titers against ZIKV and dengue virus or other flaviviruses endemic to the region where exposure occurred
- Positive ZIKV IgM antibody test **AND** negative dengue virus IgM antibody test with no neutralizing antibody testing performed

Epidemiologic Linkage

- Resides in or recent travel to an area with known ZIKV transmission; **OR**

- Sexual contact with a confirmed or probable case within the infection transmission risk window of ZIKV infection or person with recent travel to an area with known ZIKV transmission; **OR**
- Receipt of blood or blood products within 30 days of symptom onset; **OR**
- Organ or tissue transplant recipient within 30 days of symptom onset; **OR**
- Association in time and place with a confirmed or probable case; **OR**
- Likely vector exposure in an area with suitable seasonal and ecological conditions for potential local vectorborne transmission

Subtype(s) Case Definition

Zika virus disease, congenital

Clinical Criteria

Liveborn infant with congenital microcephaly, or intracranial calcifications, or structural brain or eye abnormalities, or other congenital central nervous system-related abnormalities not explained by another etiology.

(As part of the complete evaluation of congenital microcephaly or other central nervous system [CNS] birth defects, testing for other congenital infections such as syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection, and herpes simplex virus infections should be considered. An assessment of potential genetic and other teratogenic causes of the congenital anomalies should also be performed.)

Case Classification

Probable

A neonate meets clinical criteria for congenital disease; **AND**

The neonate's mother has an epidemiologic linkage or meets laboratory criteria for recent ZIKV or flavivirus infection; **AND**

The neonate has laboratory evidence of ZIKV or flavivirus infection by:

- Positive ZIKV IgM antibody test of serum or CSF collected within 2 days of birth; **AND**
 - positive neutralizing antibody titers against ZIKV and dengue or other flaviviruses endemic to the region where exposure occurred; **OR**
 - negative dengue virus IgM antibody test and no neutralizing antibody testing performed.

Confirmed

A neonate meets the clinical criteria for congenital disease **AND** meets one of the following laboratory criteria:

- ZIKV detection by culture, viral antigen, or viral RNA in fetal tissue, umbilical cord blood, or amniotic fluid; or neonatal serum, CSF, or urine collected within 2 days of birth; **OR**
- Positive ZIKV IgM antibody test of umbilical cord blood, neonatal serum or CSF collected within 2 days of birth **with** positive ZIKV neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

Zika virus disease, non-congenital

Clinical Criteria

A person with one or more of the following not explained by another etiology:

- Clinically compatible illness that includes
 - acute onset of fever (measured or reported), **OR**
 - maculopapular rash, **OR**
 - arthralgia, **OR**
 - conjunctivitis
- Complication of pregnancy
 - fetal loss; **OR**

- fetus or neonate with congenital microcephaly, congenital intracranial calcifications, other structural brain or eye abnormalities, or other congenital central nervous system-related abnormalities including defects such as clubfoot or multiple joint contractures
- Guillain-Barré syndrome or other neurologic manifestations

Case Classification

Probable

Meets clinical criteria for non-congenital disease; **AND**

Has an epidemiologic linkage; **AND**

Has laboratory evidence of recent ZIKV or flavivirus infection by:

- Positive ZIKV IgM antibody test of serum or CSF with:
 - positive neutralizing antibody titers against ZIKV and dengue or other flaviviruses endemic to the region where exposure occurred; **OR**
 - negative dengue virus IgM antibody test and no neutralizing antibody testing performed.

Confirmed

Meets clinical criteria for non-congenital disease; **AND**

Has laboratory evidence of recent ZIKV infection by:

- Detection of ZIKV by culture, viral antigen or viral RNA in serum, CSF, tissue, or other specimen (e.g. amniotic fluid, urine, semen, saliva); **OR**
- Positive ZIKV IgM antibody test of serum or CSF **with** positive ZIKV neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

Zika virus infection, congenital

Case Classification

Probable

A neonate who does not meet clinical criteria for a congenital disease case; **BUT**

The neonate's mother has an epidemiologic linkage or meets laboratory criteria for recent ZIKV or flavivirus infection; **AND**

The neonate has laboratory evidence of ZIKV or flavivirus infection by:

- Positive ZIKV IgM antibody test of serum or CSF collected within 2 days of birth; **AND**
 - negative dengue IgM antibody test and no neutralizing antibody testing performed; **OR**
 - positive neutralizing antibody titers against ZIKV and dengue or other flaviviruses endemic to the region where exposure occurred.

Confirmed

A neonate who does not meet clinical criteria for a congenital disease case; **BUT**

The neonate has laboratory evidence of recent ZIKV or flavivirus infection by:

- ZIKV detection by culture, viral antigen or viral RNA in fetal tissue, umbilical cord blood, or amniotic fluid; or neonatal serum, CSF, or urine collected within 2 days of birth; **OR**
- Positive ZIKV IgM antibody test of umbilical cord blood, neonatal serum or CSF collected within 2 days of birth **with** positive ZIKV neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

Zika virus infection, non-congenital

Case Classification

Probable

A person who does not meet clinical criteria for non-congenital disease; **BUT**

Has an epidemiologic linkage; **AND**

Has laboratory evidence of recent ZIKV infection by:

- Positive ZIKV IgM antibody test of serum or CSF with:
 - positive neutralizing antibody titers against ZIKV and dengue or other flaviviruses endemic to the region where exposure occurred; **OR**
 - negative dengue IgM antibody test and no neutralizing antibody testing performed.

Confirmed

A person who does not meet clinical criteria for non-congenital disease; **AND**

Has laboratory evidence of recent ZIKV infection by:

- Detection of ZIKV by culture, viral antigen or viral RNA in serum, CSF, tissue, or other specimen (e.g. amniotic fluid, urine, semen, saliva); **OR**
- Positive ZIKV IgM antibody test of serum or CSF **with** positive ZIKV neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred.

Comments

CSTE approved position statement 16-ID-01 in June 2016, which modified the previous February 2016 interim case definition and naming convention from "Zika virus, congenital infection" to "Zika virus disease, congenital" and from "Zika virus disease, non-congenital infection" to "Zika virus disease, non-congenital".

APPENDIX E: REPORTING WEST NILE VIRUS INFECTION IN BLOOD DONORS

CDC encourages state and local health departments to report West Nile virus (WNV) infections in blood donors. These infections may be identified in two ways:

- 1) A WNV disease case-patient may notify public health authorities that he or she donated blood in the 30 days prior to the onset of illness.
- 2) A blood donor may be identified as a presumptive viremic donor (PVD) by nucleic acid-amplification test (NAT) screening of his or her donation by a blood collection agency. A PVD is a person with a blood donation that meets at least one of the following criteria:
 - a) One reactive NAT with a signal-to-cutoff (S/CO) ratio ≥ 17 . Note that this is specific to using the WNV transcription-mediated Amplification Assay (Hologic/Gen-Probe and Novartis).
 - b) Two reactive NATs.

Reporting of donors who do not meet these criteria should wait until follow-up testing is completed.

Consider the following examples. When reporting donors like these to ArboNET, please use the guidelines provided in the table:

- **Blood Donor A:** A WNV disease case-patient who reports that he or she donated blood within 30 days of illness onset (*blood donor status was self-reported; symptomatic*)
- **Blood Donor B:** A PVD identified by blood donation screening who never develops WNV illness (*reported by blood collection agency; asymptomatic*)
- **Blood Donor C:** A PVD identified by blood donation screening who develops WNV disease (*reported by blood collection agency; symptomatic*)

	Onset Date	Condition Code	Case Status	Blood Donor	ID'd by Blood Donation Screening	Donation Date	Clinical Syndrome
Donor A	Date of illness onset	10049 or 10056	Confirmed or Probable	Yes	No	Date of donation	Meningitis, encephalitis, or febrile illness
Donor B	Date of donation	10049	Not a Case	Yes	Yes	Date of donation	Asymptomatic
Donor C	Date of illness onset	10049 or 10056	Confirmed	Yes	Yes	Date of donation	Meningitis, encephalitis, or febrile illness

Condition Code, Clinical Syndrome, and Case Status:

All WNV PVDs should be entered as 'Asymptomatic' and 'Not a Case' with 10049 entered in the 'Condition Code' field unless they meet the clinical case definition for neuroinvasive or non-neuroinvasive disease. If the patient is symptomatic, the 'Clinical Syndrome' field should reflect the nature of illness, the 'Case Status' field should be either 'Confirmed' or 'Probable' based on the criteria specified in the [case definition](#), and the 'Condition Code' field should contain 10049 if the patient has non-neuroinvasive disease and 10056 if the patient has neuroinvasive disease. If illness develops after the PVD is first reported, please update the patient's status.

Publish:

WNV infections in blood donors are important surveillance events. CDC encourages reporting jurisdictions to make these reports available in the public domain. If you want to make a report available in the public domain, simply leave the 'Publish' field at the default setting ('True'). If you do not want a report to be in the public domain, set the 'Publish' field to 'False.'

APPENDIX F: REPORTING ZIKA VIRUS INFECTION IN BLOOD DONORS

CDC encourages state and local health departments to report Zika virus (ZIKV) infections in blood donors. These infections may be identified to public health authorities in two ways:

1. A ZIKV disease patient or their healthcare provider may notify public health authorities directly or the blood collection agency that they donated blood in the 14 days before illness onset (or identification of infection).
2. A blood collection agency may notify public health authorities of a ZIKV-reactive donation identified through blood donation screening.

In July 2018, [FDA issued revised guidance](#) recommending that blood centers in all states and U.S. territories screen donated blood and blood components with a blood screening ZIKV nucleic acid test (NAT) licensed for use by FDA. Screening could be performed by pooling samples from multiple donations (i.e., minipool (MP) nucleic acid testing or MP NAT) with triggering to individual donation (ID NAT) when there is increased risk for local, mosquito-borne transmission of Zika virus. In May 2021, [FDA withdrew this guidance](#) after determining that ZIKV was no longer a “relevant transfusion-transmitted infection.” Accordingly, blood establishments could discontinue blood donation screening for ZIKV with a requirement to report this change to FDA, noting the date testing was discontinued.

Health departments should conduct epidemiologic investigations of PVDs. Donors should be reported to ArboNET if, in addition to the initial reactive ID NAT or MP NAT result, they meet one or more of the following laboratory criteria:

- Detection of ZIKV RNA in any specimen, including a reactive result by the same or alternate NAT assay on the same or a follow-up sample; OR
- Positive ZIKV IgM antibody test in serum or CSF with positive ZIKV neutralizing antibody titers in the same or a follow-up sample; OR
- Detection of ZIKV or viral antigen in any specimen

Note: Blood collection agencies should provide health departments with all screening and confirmatory test results to aid in the investigation.

Consider the following examples. When reporting donors to ArboNET, use the guidelines provided in the table:

1. **Blood Donor A:** Asymptomatic, initial ZIKV NAT reactive, ZIKV IgM positive, ZIKV neutralizing antibodies detected
2. **Blood Donor B:** Symptomatic, initial ZIKV NAT reactive, ZIKV IgM positive, ZIKV and dengue neutralizing antibodies detected
3. **Blood Donor C:** Identified retrospectively to be a donor (symptomatic, ZIKV RT-PCR positive)

	Onset date	Condition Code	Case status	Blood donor	ID'd by blood donation screening	Donation date	Clinical Syndrome
Donor A	Date of donation	50221	Confirmed	Yes	Yes	Date of donation	Asymptomatic
Donor B	Date of illness onset	50223	Confirmed	Yes	Yes	Date of donation	Febrile Illness (or other appropriate response)
Donor C	Date of illness onset	50223	Confirmed	Yes	No	Date of donation	Febrile Illness (or other appropriate response)

Condition Code, Clinical Syndrome, and Case Status:

All ZIKV PVDs should be entered as ‘Asymptomatic’ with 50221 entered in the ‘Condition Code’ field unless they meet the clinical case definition for ZIKV virus disease. If the patient is symptomatic, 50233 should be entered as the ‘Condition Code’ and the appropriate ‘Clinical Syndrome’ field should be selected. If illness develops after the PVD is first reported, please update the patient’s ‘Condition Code’ and ‘Clinical Syndrome’ fields.

APPENDIX G: ARBOVIRAL CONDITION CODES

Condition Code	Condition Name	Nationally Notifiable
10058	Cache Valley virus disease, neuroinvasive	No
10066	Cache Valley virus disease, non-neuroinvasive	No
11718	California encephalitis virus disease	Yes
10054	California serogroup virus diseases, neuroinvasive	Yes
10061	California serogroup virus diseases, non-neuroinvasive	Yes
10073	Chikungunya virus diseases	Yes
10093	Colorado tick fever virus disease	No
10680	Dengue	Yes
11705	Dengue, severe	Yes
11704	Dengue-like illness	Yes
10053	Eastern equine encephalitis virus disease, neuroinvasive	Yes
10062	Eastern equine encephalitis virus disease, non-neuroinvasive	Yes
50237	Flavivirus disease, not otherwise specified	No
10078	Jamestown Canyon virus disease, neuroinvasive	Yes
10079	Jamestown Canyon virus disease, non-neuroinvasive	Yes
10059	Japanese encephalitis virus disease, neuroinvasive	No
10068	Japanese encephalitis virus disease, non-neuroinvasive	No
11712	Keystone virus disease	Yes
10081	La Crosse virus disease, neuroinvasive	Yes
10082	La Crosse virus disease, non-neuroinvasive	Yes
10072	Other arboviral disease, not otherwise specified (Alkhurma virus, Barmah Forest virus, Bourbon virus, Heartland virus, Highlands J virus, Kyasanur Forest virus, Mayaro virus, Murray Valley encephalitis virus, O'nyong-nyong virus, Oropouche virus, Rift Valley Fever virus, Rocio virus, Ross River virus, Sindbis virus, Tahyna virus, Toscana virus, Usutu virus, Other Arbovirus)	No
10057	Powassan virus disease, neuroinvasive	Yes
10063	Powassan virus disease, non-neuroinvasive	Yes
11734	Snowshoe hare virus disease	Yes
10051	St. Louis encephalitis virus disease, neuroinvasive	Yes
10064	St. Louis encephalitis virus disease, non-neuroinvasive	Yes
10074	Tick-borne encephalitis viruses	No
11724	Trivittatus virus disease	Yes
10055	Venezuelan equine encephalitis virus neuroinvasive disease	No
10067	Venezuelan equine encephalitis virus non-neuroinvasive disease	No
10056	West Nile virus disease, neuroinvasive	Yes
10049	West Nile virus disease, non-neuroinvasive	Yes
10052	Western equine encephalitis virus disease, neuroinvasive	Yes
10065	Western equine encephalitis virus disease, non-neuroinvasive	Yes
10660	Yellow fever	Yes
50224	Zika virus disease, congenital	Yes
50223	Zika virus disease, non-congenital	Yes
50222	Zika virus infection, congenital	Yes
50221	Zika virus infection, non-congenital	Yes