Proposed 23-ID-10

Committee: Infectious Disease

Proposed Title: Update to Public Health Reporting and National Notification for Non-congenital and Congenital Zika Virus Disease

☒ Check this box if this position statement is an update to an existing standardized surveillance case definition and include the most recent position statement number here: 16-ID-01.

Synopsis:

- This position statement updates the standardized surveillance case definitions for non-congenital and congenital Zika virus disease (previous position statement 16-ID-01) to address changes in Zika virus epidemiology and an improved understanding of the clinical and laboratory findings associated with Zika virus disease.
- Updates include:
    - Revisions to the clinical criteria for the non-congenital subtype to remove complications of pregnancy other than fetal loss to prevent double counting of cases.
    - Revisions to the clinical criteria for the congenital Zika virus disease subtype to provide more specific descriptions of clinical findings associated with congenital Zika virus disease.
    - Revisions to the laboratory criteria for case ascertainment and classification for non-congenital and congenital Zika virus disease subtypes to address diagnostic limitations, including cross-reactivity and persistent detection of IgM.
    - Revisions to the epidemiologic linkage criteria for case classification to provide more specificity on the timing of exposure.
    - Removal of Zika virus non-congenital and congenital infection without disease subtypes from the case definition and list of Nationally Notifiable Conditions (NNC).

I. Statement of the Problem

Development of surveillance case definitions for Zika virus infection and disease and addition to the Nationally Notifiable Conditions (NNC) list occurred in 2016 during a rapidly evolving Zika virus disease outbreak in the Western Hemisphere. Since that time, levels of Zika virus transmission in the Americas have declined considerably (1-3). Zika and dengue viruses are closely related flaviviruses that share a similar global geographic distribution and cause diseases with overlapping clinical features (4). Experience has demonstrated that serologic assays often are unable to differentiate antibodies formed against Zika and dengue viruses and other flaviviruses or determine the timing of infection. Enhanced surveillance efforts and prospective follow-up of cohorts of children with congenital Zika virus infection have provided an improved understanding of the clinical implications of congenital infection and the expected frequency of adverse outcomes (5-9). This position statement revises the standardized case definition for Zika virus disease to address the changing epidemiology and current knowledge of the laboratory and clinical findings associated with Zika virus disease. It also removes non-congenital and congenital Zika virus infection without disease from the case definition, thus removing these subtypes from the NNC list.

II. Background and Justification

Zika virus is a flavivirus that was first identified in the Zika Forest, Uganda in a non-human primate in 1947 and from *Aedes africanus* mosquitoes in 1948 (10). Before 2007, there had been only 14 human Zika virus disease cases documented. In 2007, an outbreak of Zika virus disease occurred on Yap Island, Federated States of Micronesia (11). From 2013 to 2014 there was a large outbreak in French Polynesia where *Aedes aegypti* was identified as the most important vector.

Zika virus was first identified in the Western hemisphere in 2015, with large outbreaks in Brazil (12). The virus then spread throughout Central and South America, resulting in several hundred thousand cases. Widespread transmission occurred in Puerto Rico and the United States (U.S.) Virgin Islands, and limited transmission occurred in some counties of Florida and Texas. More than 5,000 travel-associated cases were reported in other U.S. states. Since 2017, the number of reported Zika virus disease cases has declined worldwide, though there have been occasional increases reported from some countries (3).

While Zika virus is primarily transmitted through the bite of an infected *Aedes* species mosquito, intrauterine, perinatal, sexual, laboratory, and transfusion-associated transmission have been reported (13,14). Zika virus has been detected in human milk, but it is unknown whether an infant can become infected through breast milk (15).

Most people infected with Zika virus have asymptomatic infections or mild clinical disease characterized by acute onset of fever, maculopapular rash, arthralgia, and nonpurulent conjunctivitis. Other common symptoms can include myalgia, headache, edema, vomiting, retroorbital pain, or lymphadenopathy. Hospitalization and death are uncommon. Guillain-Barré syndrome, encephalopathy, meningoencephalitis, myelitis, uveitis, and severe thrombocytopenia rarely occur. Transmission of the virus to the unborn child during pregnancy can lead to congenital Zika virus infection and may cause serious birth defects of the brain and eyes, including severe microcephaly, intracranial calcifications, cerebral or cortical atrophy, chorioretinal abnormalities, and optic nerve abnormalities (5-9, 16). Less specific abnormalities or later onset sequalae seen in children with congenital Zika include body tone abnormalities, hearing loss, vision impairment, seizures, movement abnormalities, swallowing abnormalities and developmental delay.

Transmission during pregnancy can occur regardless of symptoms in the gestational parent, and infants with congenital Zika virus infection may appear asymptomatic at birth but have neuroimaging findings or clinical sequelae (e.g., vision loss) that are only detected after birth (17). Long-term sequelae of congenital Zika virus infection among infants without apparent birth defects remain unclear. However, poor case ascertainment, inconsistent verification across states, diagnostic limitations leading to inaccurate reporting (18-20) and lack of prospective follow-up associated with national surveillance have prompted removal of previously-included reporting of asymptomatic non-congenital and congenital infections. During outbreaks or epidemics, monitoring the burden of asymptomatic infections in both pregnant people and their infants may be necessary to inform public health response and clinical guidance since asymptomatic infection may still present a risk. Enhanced surveillance through sentinel sites or platforms that allow linkage of gestational parent and infant cases, inclusion of asymptomatic cases, and assessment of pregnancy and infant outcomes, such as the Surveillance for Emerging Threats to Pregnant People and Infants Network, should be considered to complement Zika virus disease data collected with this CSTE case definition (21).

III. Statement of the Desired Actions to be Taken

CSTE recommends the following actions:

1. Implement a standardized surveillance case definition for **non-congenital and congenital Zika virus disease**.

    A. Utilize standard sources (e.g., reporting*) for case ascertainment for **non-congenital and congenital Zika virus disease**. Surveillance for **non-congenital and congenital Zika virus disease** should use the recommended sources of data to the extent of coverage presented in Section V.

    B. Utilize standardized criteria for case ascertainment for **non-congenital and congenital Zika virus disease** presented in Section VI and Table VI in Technical Supplement.

    C. Utilize standardized criteria for case classification for **non-congenital and congenital Zika virus disease** presented in Section VII and Table VII in Technical Supplement.

2. Utilize standardized criteria for case ascertainment and classification (based on Sections VI and VII and Technical Supplement of accompanying position statement) for **non-congenital and congenital Zika virus disease, update** non-congenital and congenital Zika disease on the *Nationally Notifiable Condition List* using the following notification** timeframe, and remove non-congenital and congenital Zika virus infection [without disease] from the *Nationally Notifiable Condition List*:
   - ☐ Immediately notifiable, extremely urgent (within 4 hours)
   - ☐ Immediately notifiable, urgent (within 24 hours)
   - ☒ Routinely notifiable (non-congenital and congenital Zika virus disease)
   - ☒ No longer notifiable (non-congenital and congenital Zika virus infection [without disease])

3. CSTE recommends that all States and Territories enact laws (statute or rule/regulation as appropriate) to make non-congenital and congenital Zika virus disease reportable in their jurisdiction. Jurisdictions (e.g., States and Territories) conducting surveillance (according to these methods) should submit case notifications to CDC.

4. Expectations for Message Mapping Guide (MMG) development for a newly notifiable condition: the National Notifiable Diseases Surveillance System (NNDSS) can receive HL7-based messages for case notifications; the specifications for these messages are presented in MMGs. When CSTE recommends a new condition be made nationally notifiable, CDC must obtain Office of Management and Budget Paperwork Reduction Act (OMB PRA) approval prior to accepting case notifications for the new condition. Under anticipated timelines, notification using the Generic V2 MMG would support transmission of the basic demographic and epidemiologic information common to all cases and could begin with the new MMWR year following the CSTE annual conference. Input from CDC programs and CSTE would prioritize development of a disease-specific MMG for the new condition among other conditions waiting for MMG development.

5. CDC should publish data on non-congenital and congenital Zika virus disease as appropriate (see Section IX). CSTE recommends the following case statuses be included in the CDC Print Criteria:
   - ☒Confirmed
   - ☒Probable
   - ☐Suspect
   - ☐Unknown

6. CSTE recommends that all jurisdictions (e.g., States, Localities, or Territories) with legal authority should conduct public health surveillance and use the case classifications included in this standardized surveillance position statement.

** Reporting: process of a healthcare provider, laboratory, or other entity submitting a report (case information) of a condition under public health surveillance to local, state, or territorial public health.*

*** Notification: process of a local or state public health authority submitting a report (case information) of a condition on the* Nationally Notifiable Conditions List *to CDC.*

IV. Goals of Surveillance

To provide information on the temporal, geographic, and demographic occurrence of Zika virus and indicators of morbidity and mortality, including hospitalization, associated with Zika virus disease to facilitate prevention and control.

V. Recommended Data Sources and Methods for Surveillance

Surveillance for non-congenital and congenital Zika virus disease should use the following recommended sources of data and/or methodologies and the extent of coverage listed in Table V.

Table V. Recommended Sources of Data, Surveillance Methods, and Extent of Coverage for Ascertainment of Cases of non-congenital and congenital Zika virus disease.

Source of Data/Methodology for Case Ascertainment	Coverage	
	Population-Wide	Sentinel Sites
Clinician reporting	X	
Laboratory reporting	X	
Reporting by other entities, specify: Hospitals	X	
Death certificates	X	
Hospital discharge or outpatient records	X	
Data from electronic medical records	X	
Telephone or online survey		
School-based survey		
Other, specify: N/A		

VI. Criteria for Case Ascertainment

Case ascertainment is the process through which public health identifies potential cases of a disease or condition using data reported or provided to public health by healthcare, laboratories, and other reporting entities This public health reporting is triggered by the case ascertainment criteria (a single criterion or a combination of criteria) included in this position statement, and each initial report sent to public health should include common data elements and disease-specific data elements. Case ascertainment criteria are not intended to be used for clinical diagnosis purposes.

A. Narrative: A description of suggested criteria for case ascertainment of a specific condition and recommended reporting procedures.

Recommended reporting procedures for Zika virus disease:

- All cases of non-congenital and congenital Zika virus disease should be reported.
- Reporting should be ongoing and routine.
- Frequency of reporting should follow the state health department's reporting schedule.

Report the following to public health authorities:

- Any person meeting at least one criterion in both the clinical and epidemiologic linkage criteria for reporting sections below (A1 and A3).
- Any person meeting at least one laboratory criterion for reporting below (A2).
- Any person meeting the vital records criterion for reporting below (A4).
- Any person meeting the healthcare record criterion for reporting below (A5).

A1. Clinical Criteria for Reporting

- Acute onset of one or more of the following symptoms: fever (measured or reported), generalized rash, arthralgia, or non-purulent conjunctivitis; **OR**
- Guillain-Barré syndrome; **OR**
- Loss of a fetus at greater or equal to 20 weeks gestation; **OR**
- Congenital anomalies of the brain or eye or neurologic sequelae in an infant.

A2. Laboratory Criteria for Reporting

- Detection of Zika virus, viral antigen, or viral RNA in body fluid or tissue; **OR**
- Detection of Zika virus IgM antibodies in blood or cerebrospinal fluid (CSF).

A3. Epidemiologic Linkage Criteria for Reporting
- Resided in or traveled to an area with a possible risk[1] of Zika virus transmission; **OR**
- Laboratory exposure to Zika virus; **OR**
- Receipt of blood, blood products, organ transplant, or tissue transplant; **OR**
- Sexual contact with a person who has either been diagnosed with Zika virus infection or returned from traveling to an area with a possible risk[1] of Zika virus transmission; **OR**
- Met any of the epidemiologic linkage criteria above during pregnancy.

A4. Vital Records Criteria for Reporting
- A person whose death certificate lists Zika virus infection or disease as an underlying cause of death or a significant condition contributing to death.

A5. Healthcare Record Criteria for Reporting
- A person whose healthcare record contains a diagnosis of Zika virus infection or disease.

B. Disease-Specific Data Elements to be Included in the Initial Report
Disease-specific data elements should be included in addition to the common data elements that are to be reported for all initial individual case reports (see CSTE Position Statement 09-SI-01 "Common Core Data Elements for Case Reporting and Laboratory Result Reporting" https://cdn.ymaws.com/www.cste.org/resource/resmgr/PS/09-SI-01.pdf). Public health authorities do not expect that an initial report will contain all the information necessary for case investigation and case classification.
- Pregnancy status
- Exposure history (e.g., prenatal, blood transfusion, laboratory, travel, and sex)
- Congenital anomalies
- Fetal demise
- Hospitalized
- Fatality

VII. Case Definition for Case Classification

This case definition for case classification is intended solely for public health surveillance purposes and does not recommend criteria for clinical diagnosis purposes. Once a public health agency has ascertained data on potential cases of a disease or condition from reporting entities, the public health agency assigns case statuses based on the case classifications included within this position statement.

A. Narrative: A description of criteria to determine how public health should classify a case of non-congenital and congenital Zika virus disease.

A1. Clinical Criteria
Non-congenital Zika virus disease:
To meet the clinical criteria for non-congenital Zika virus disease, the person should have one or more of the following not explained by another etiology.
- Acute onset of one or more of the following symptoms: fever (measured or reported), generalized rash, arthralgia, or non-purulent conjunctivitis,
- Guillain-Barré syndrome,
- Loss of a fetus at greater or equal to 20 weeks gestation.

[1] A geographic area with a possible risk of Zika virus transmission is defined as an area with past or current Zika virus transmission or the primary mosquito vector (*Aedes aegypti*).

Congenital Zika virus disease[2]:
To meet the clinical criteria for congenital Zika virus disease, the liveborn infant must not have an identified genetic or other cause for the findings, including a positive test for another likely etiology^, and should have one or more of the following brain or eye anomalies or neurological sequelae specific for congenital Zika virus disease and typically identifiable in the neonatal period:

- microcephaly (occipital frontal circumference >2 standard deviations below the mean for age and sex) at birth or postnatal onset,
- cortical hypoplasia or abnormal gyral patterns (polymicrogyria, lissencephaly, heterotopia),
- increased volume of cerebrospinal fluid (CSF) (hydrocephalus ex vacuo, unspecified hydrocephalus, ventriculomegaly) due to loss of brain parenchyma,
- intracranial calcifications (most commonly between the cortex and subcortex),
- congenital contractures of major joints (arthrogryposis) associated with structural brain anomalies,
- congenital paralysis of the diaphragm associated with structural brain anomalies,
- corpus callosum agenesis/hypoplasia,
- cerebellar hypoplasia,
- scarring of the macula with coarse deposits of pigment in the retina (focal retinal pigmentary mottling),
- other structural eye anomalies (microphthalmia, cataracts, chorioretinal atrophy, optic nerve hypoplasia).

^ ***Other clinical considerations for congenital Zika virus disease****: Among congenital infections, cytomegalovirus infection has clinical findings most consistent with Zika virus infection and should be ruled out by diagnostic testing. While other infectious etiologies (e.g., rubella virus, varicella zoster virus, herpes simplex virus, lymphocytic choriomeningitis virus,* Toxoplasma gondii*, or* Treponema pallidum*) have clinical findings less consistent with congenital Zika virus disease, testing for these infections should be considered as part of the complete evaluation for congenital disease.*

A2. Laboratory Criteria*

Non-congenital Zika virus disease:

Confirmatory laboratory evidence:

- Detection of Zika virus, viral antigen, or viral RNA in a body fluid or tissue; **OR**
- Detection of anti-Zika virus IgM antibodies in blood or CSF, with positive Zika virus-specific neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred[3].

Presumptive laboratory evidence:

- Detection of anti-Zika virus IgM antibodies in blood or CSF with a negative anti-dengue virus IgM antibody test in the same specimen with no neutralizing antibody testing performed; **OR**
- Four-fold or greater rise in anti-Zika virus-specific neutralizing antibody titers in paired blood specimens; **OR**
- In the setting of a Zika virus outbreak[4] with minimal circulation of other endemic flaviviruses, detection of anti-Zika virus IgM antibodies in blood or CSF.

Congenital Zika virus disease:

Confirmatory laboratory evidence:

- Detection of Zika virus, viral antigen, or viral RNA in infant CSF, blood, urine, or postmortem tissue**; **OR**
- Detection of anti-Zika virus IgM antibodies in infant CSF or blood**, with positive anti-Zika virus-specific neutralizing antibody titers.

[2] Clinical findings can be observed during prenatal or postnatal evaluations. Consult with CDC as needed for assistance with congenital Zika virus disease clinical determinations.
[3] If Zika and dengue virus IgM antibodies are detected and neutralizing antibodies are unable to differentiate flaviviruses, consider reporting as *Flavivirus disease, not otherwise specified* (See ArboNET Surveillance Guide).
[4] Consult with CDC as needed for assistance with outbreak status determinations.

Presumptive laboratory evidence:

- Detection of Zika virus, viral antigen, or viral RNA in amniotic fluid, placenta, umbilical cord, or cord blood**; **OR**
- Detection of anti-Zika virus IgM antibodies in infant CSF or blood** with no neutralizing antibody testing performed.

** Note: The categorical labels used here to stratify laboratory evidence are intended to support the standardization of case classifications for public health surveillance. The categorical labels should not be used to interpret the utility or validity of any laboratory test methodology.*
*** To prevent misclassifying postnatal Zika virus infections as congenital cases, in Zika virus endemic areas specimens should be collected within 4 weeks after birth.*

A3. Epidemiologic Linkage Criteria

- Resided in or traveled to an area with a risk[5] of Zika virus transmission in the 14 days before the onset of symptoms, in the 28 days before the onset of Guillain-Barré syndrome, or during pregnancy; **OR**
- Laboratory exposure to Zika virus before onset of symptoms or during pregnancy; **OR**
- Receipt of blood, blood products, organ transplant, or tissue transplant within 30 days of symptom onset or during pregnancy from a person who has either been diagnosed with Zika virus infection or returned from traveling to an area with risk of Zika virus transmission; **OR**
- Sexual contact, within 14 days of symptom onset or during pregnancy, with a person who in the last 90 days has either been diagnosed with Zika virus infection or has returned from traveling to an area with a risk of Zika virus transmission.

A4. Case Classifications

Non-congenital Zika virus disease

Confirmed:

- Meets the epidemiologic linkage criteria, and clinical and confirmatory laboratory criteria for non-congenital Zika virus disease.

Probable:

- Meets the epidemiologic linkage criteria, and clinical and presumptive laboratory criteria for non-congenital Zika virus disease.

Congenital Zika virus disease

Confirmed:

- Meets the clinical criteria for congenital Zika virus disease, **AND**
- Meets confirmatory laboratory criteria for congenital Zika virus disease, **AND**
- Whose gestational parent meets:
    - epidemiologic linkage criteria, **OR**
    - confirmatory laboratory criteria for non-congenital Zika virus disease during this pregnancy.

Probable:

- Meets the clinical criteria for congenital Zika virus disease, **AND**
- Meets presumptive laboratory criteria for congenital Zika virus disease, **AND**
- Whose gestational parent meets:
    - epidemiologic linkage criteria, **OR**
    - confirmatory laboratory criteria for non-congenital Zika virus disease during this pregnancy.

B. Criteria to Distinguish a New Case of Zika virus disease from Reports or Notifications which Should Not be Enumerated as a New Case for Surveillance

A person not previously enumerated as a case that meets the confirmed or probable case classification.

Note: Infection with Zika virus is expected to provide lifelong immunity. However, in persons who are severely immunocompromised, viral persistence following infection may occur, which can lead to persistent disease. Immunocompromised individuals may also be vulnerable to reinfection with Zika virus.

[5] Consult with CDC as needed for assistance with geographic risk determinations.

VIII. Period of Surveillance

Surveillance should be ongoing.

IX. Data Sharing/Release and Print Criteria

CSTE recommends the following case statuses* be included in the 'case' count released outside of the public health agency:

☒Confirmed
☒Probable
☐Suspect
☐Unknown
**Which case statuses are included in case counts constitute the "print criteria."*

Jurisdictions (e.g., States and Territories) conducting surveillance under this case definition can voluntarily submit de-identified case information to CDC, if requested and in a mutually agreed upon format.

Production of national data summaries and national data re-release for non-NNCs:

- Prior to release of national data summaries CDC should follow the CDC/ATSDR Policy on Releasing & Sharing Data, issued on April 16, 2003 and referenced in 11-SI-01 and custodians of such data should consult the CDC-CSTE Intergovernmental Data Release Guidelines Working Group report (www.cste2.org/webpdfs/drgwgreport.pdf) which contains data release guidelines and procedures for CDC programs re-releasing state, local, or territorial-provided data.
- CDC programs have a responsibility, in collaboration with states, localities, and territories, to ensure that CDC program-specific data re-release procedures meet the needs of those responsible for protecting data in the states and territories.

X. Revision History

Position Statement ID	Section of Document	Revision Description
23-ID-10	Section V. Recommended Data Sources and Methods for Surveillance, Table V	REMOVED "Reporting by other entities" as a source of data for case ascertainment
23-ID-10	Section VI. A. A description of suggested criteria for case ascertainment of specific condition and recommended reporting procedures	UPDATED clinical, laboratory, epidemiologic criteria for case ascertainment.
23-ID-10	Section VI. B. Disease-Specific Elements to be included in the Initial Report	CHANGED "Pregnant" to "Pregnancy Status" EDITED Outcome of pregnancy options
23-ID-10	Section VII. A1. Clinical criteria	Significantly REVISED clinical criteria for non-congenital and congenital Zika virus disease. These changes were based on the current knowledge of the clinical findings associated with non-congenital and congenital Zika virus disease. For congenital Zika virus disease ADDED the requirement that there are no other positive tests for another etiology or identified genetic or other causes for the clinical findings. ADDED Other clinical considerations.
23-ID-10	Section VII. A2. Laboratory criteria	Significantly REVISED laboratory criteria for non-congenital and congenital Zika virus disease. Revised criteria were

		developed with an understanding of the diagnostic challenges associated with Zika virus disease, including cross-reactivity with other flaviviruses and prolonged antibody detection.
23-ID-10	Section VII. A3. Epidemiologic Linkage Criteria	ADDED timeframes for exposure.
23-ID-10	Section VII. A5. Case Classifications	Significantly REVISED case classifications based on revised clinical, laboratory and epidemiologic criteria. REMOVED Zika virus non-congenital and congenital infection without disease subtypes from the case definition.
16-ID-01 (Interim)	16-ID-01	Established a surveillance case definition for non-congenital and congenital Zika virus disease and Zika virus infection; added non-congenital and congenital Zika virus disease and Zika virus infection to the *Nationally Notifiable Conditions List* as routinely notifiable for confirmed and probable cases.
N/A	16-ID-01 (Interim)	Established an interim surveillance case definition for Zika virus disease and added Zika virus disease to the Nationally Notifiable Conditions List as routinely notifiable for confirmed and probable cases.

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Council of State and Territorial Epidemiologists
Technical Supplement

Table VI. Table of criteria to determine whether a case should be reported to public health authorities.

Criterion	Non-Congenital Zika virus disease		Congenital Zika virus disease			
Clinical Criteria for Reporting						
Acute onset of one or more of the following symptoms: • Fever (measured or reported) • Arthralgia • Generalized rash • Non-purulent conjunctivitis		O				
Guillain-Barré syndrome		O				
Loss of a fetus at ≥20 weeks gestation		O				
Congenital brain or eye anomalies or neurologic sequelae				N		
Infant			N	N	N	N
Laboratory Criteria for Reporting						
Detection of Zika virus, viral antigen, or viral RNA in body fluid or tissue	S		O			
Detection of Zika virus IgM antibodies in blood or cerebrospinal fluid	S		O			
Epidemiological Linkage Criteria for Reporting						
Resided in or traveled to an area with a possible risk[1] of Zika virus transmission		O				
Laboratory exposure to Zika virus		O				
Receipt of blood, blood products, organ transplant, or tissue transplant		O				
Sexual contact with a person who has either been diagnosed with Zika virus infection or has returned from traveling to an area with a possible risk[1] of Zika virus transmission		O				
Gestational parent resided in or traveled to an area with a possible risk[1] of Zika virus transmission during pregnancy				O		
Gestational parent had a laboratory exposure to Zika virus during pregnancy				O		
Gestational parent received blood, blood products, organ transplant, or tissue transplant during pregnancy				O		
Gestational parent had sexual contact during pregnancy with a person who has either been diagnosed with Zika virus infection or has returned from traveling to an area with a possible risk[1] of Zika virus transmission				O		
Vital Records Criteria for Reporting						
A person whose death certificate lists Zika virus infection or disease as an underlying cause of death or a significant condition contributing to death	S				N	
Healthcare Record Criteria for Reporting						
A person whose healthcare record contains a diagnosis of a Zika virus infection or disease	S					N
						2023 Template

Notes:
S = This criterion alone is SUFFICIENT to report a case.
N = All "N" criteria in the same column are NECESSARY to report a case.
O = At least one of these "O" (ONE OR MORE) criteria in each category (categories=clinical, laboratory, epidemiologic linkage, vital records, etc.) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.
[1] A geographic area with a possible risk of Zika virus transmission is defined as an area with past or current Zika virus transmission or the primary mosquito vector (*Aedes aegypti*).

Table VII.A. Classification Table: Criteria for defining a case of non-congenital and congenital Zika virus disease.

Criterion	Non-congenital Zika virus disease		Congenital Zika virus disease					
	Confirmed	Probable	Confirmed			Probable		
Clinical Evidence								
Acute onset of one or more of the following symptoms: • Fever (measured or reported) • Arthralgia • Generalized rash • Non-purulent conjunctivitis	O	O						
Guillain-Barré syndrome	O	O						
Loss of a fetus at ≥20 weeks gestation	O	O						
Clinical evidence not explained by another etiology	N	N						
Liveborn infant			N	N	N	N	N	N
No identified genetic or other cause for the findings, including a positive test for another likely etiology^			N	N	N	N	N	N
Microcephaly (occipital frontal circumference >2 standard deviations below the mean for age and sex) at birth or postnatal onset			O	O	O	O	O	O
Cortical hypoplasia or abnormal gyral patterns (polymicrogyria, lissencephaly, heterotopia)			O	O	O	O	O	O
Increased volume of cerebrospinal fluid (CSF) (hydrocephalus ex vacuo, unspecified hydrocephalus, ventriculomegaly) due to loss of brain parenchyma			O	O	O	O	O	O
Intracranial calcifications (most commonly between the cortex and subcortex)			O	O	O	O	O	O
Congenital contractures of major joints (arthrogryposis) associated with structural brain anomalies			O	O	O	O	O	O
Congenital paralysis of the diaphragm associated with structural brain anomalies			O	O	O	O	O	O
Corpus callosum agenesis/hypoplasia			O	O	O	O	O	O
Cerebellar hypoplasia			O	O	O	O	O	O
Scarring of the macula with coarse deposits of pigment in the retina (focal retinal pigmentary mottling)			O	O	O	O	O	O
Other structural eye anomalies (microphthalmia, cataracts, chorioretinal atrophy, optic nerve hypoplasia)			O	O	O	O	O	O
Laboratory Evidence								
Detection of Zika virus, viral antigen, or viral RNA in a body fluid or tissue	O			N[#]			N[#]	
Detection of anti-Zika virus IgM antibodies in blood or CSF, with positive Zika virus-specific neutralizing antibody titers and negative neutralizing antibody titers against dengue or other flaviviruses endemic to the region where exposure occurred	O				N[#]			N[#]
Detection of anti-Zika virus IgM antibodies in blood or CSF with a negative anti-dengue virus IgM antibody test in the same specimen with no neutralizing antibody testing performed		O						
Four-fold or greater rise in anti-Zika virus-specific neutralizing antibody titers in paired blood specimens		O						
In the setting of a Zika virus outbreak** with minimal circulation of other endemic flaviviruses, detection of anti-Zika virus IgM antibodies in blood or CSF		O						
Detection of Zika virus, viral antigen, or viral RNA in infant CSF, blood, urine, or postmortem tissue***			O	O	O			

Detection of anti-Zika virus IgM antibodies in infant CSF or blood***, with positive anti-Zika virus-specific neutralizing antibody titers			O	O	O			
Detection of Zika virus, viral antigen, or viral RNA in amniotic fluid, placenta, umbilical cord, or cord blood***						O	O	O
Detection of anti-Zika virus IgM antibodies in infant CSF or blood*** with no neutralizing antibody testing performed						O	O	O
Epidemiologic Linkage Evidence								
Resided in or traveled to an area with a risk** of Zika virus transmission in the 14 days before the onset of symptoms or in the 28 days before the onset of Guillain-Barré syndrome	O	O						
Laboratory exposure to Zika virus before onset of symptoms	O	O						
Receipt of blood, blood products, organ transplant, or tissue transplant within 30 days of symptom onset from a person who has either been diagnosed with Zika virus infection or returned from traveling to an area with risk** of Zika virus transmission	O	O						
Sexual contact, within 14 days of symptom onset, with a person who in the last 90 days has either been diagnosed with Zika virus infection or has returned from traveling to an area with a risk** of Zika virus transmission	O	O						
Has a gestational parent who resided in or traveled to an area with a risk** of Zika virus transmission during pregnancy			O			O		
Has a gestational parent with a laboratory exposure to Zika virus during pregnancy			O			O		
Has a gestational parent who received blood, blood products, organ transplant, or tissue transplant during pregnancy from a person who has either been diagnosed with Zika virus infection or returned from traveling to an area with risk** of Zika virus transmission			O			O		
Has a gestational parent who had sexual contact during pregnancy with a person who in the last 90 days has either been diagnosed with Zika virus infection or has returned from traveling to an area with a risk** of Zika virus transmission			O			O		

Notes:
N = All "N" criteria in the same column are NECESSARY to classify a case.
O = At least one of these "O" (ONE OR MORE) criteria in each category (categories=clinical evidence, laboratory evidence, and epidemiologic evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case.
^ *Other clinical considerations for congenital Zika virus disease: Among congenital infections, cytomegalovirus infection has clinical findings most consistent with Zika virus infection and should be ruled out by diagnostic testing. While other infectious etiologies (e.g., rubella virus, varicella zoster virus, herpes simplex virus, lymphocytic choriomeningitis virus,* Toxoplasma gondii, *or* Treponema pallidum*) have clinical findings less consistent with congenital Zika virus disease, testing for these infections should be considered as part of the complete evaluation for congenital disease.*
** If Zika and dengue virus IgM antibodies are detected and neutralizing antibodies are unable to differentiate flaviviruses, consider reporting as Flavivirus disease, not otherwise specified (See ArboNET Surveillance Guide).*
*** Consult with CDC as needed for assistance with outbreak status or geographic risk determinations.*
**** To prevent misclassifying postnatal Zika virus infections as congenital cases, in Zika virus endemic areas specimens should be collected within 4 weeks after birth.*
 # Diagnostic results apply to the gestational parent. Results must be obtained during the current pregnancy.

Table VII.B. Classification Table: Criteria to distinguish a new case of non-congenital and congenital Zika virus disease from reports or notifications which should not be enumerated as a new case for surveillance.

Criterion	Non-Congenital Zika virus disease		Congenital Zika virus disease	
	Confirmed	Probable	Confirmed	Probable
Criteria to distinguish a new case				
A person not previously enumerated as a case that meets the confirmed or probable case classification	S	S	S	S

S = This criterion alone is SUFFICIENT to enumerate as a new case.