

09-ID-19

Committee: Infectious Disease

Title: Add Dengue Virus Infections to the Nationally Notifiable Conditions List

I. Statement of the Problem

Increasing international travel along with rapidly increasing disease burden world-wide, endemicity in US territories, sporadic instances of autochthonous transmission during outbreaks in the continental United States, and the potential for transfusion-mediated transmission, suggest that the number of dengue cases in the United States is likely to increase in the future. The purpose of this position statement is to add dengue to the National Notifiable Diseases Surveillance System list of nationally notifiable infectious diseases.

II. Background and Justification

Background

Infection with any of the 4 dengue virus serotypes (DENV-1 through DENV-4) can cause disease which may result in a range of clinical illness from asymptomatic infection to severe systemic disease. Dengue viruses are transmitted from person to person through the bite of infected *Aedes* mosquitoes (principally *A. aegypti*, but also *A. albopictus*). Unlike most other arthropod-borne viruses, humans are the main amplifying viral host. The intrinsic incubation period in humans is 3 to 14 days with an acute febrile phase of infection lasting 3 to 7 days. The extrinsic incubation period in mosquitoes is 8 to 12 days depending on environmental factors.

Dengue is endemic throughout the tropics and subtropics, and more than 900,000 cases were reported in the Americas in 2007 alone (1). Dengue is the most common mosquito-borne viral disease of humans (2) and the most common arboviral infection in travelers (3). Dengue is more prevalent than malaria among travelers returning to the United States from the Caribbean, South America, South-central Asia and Southeast Asia (4). An estimated 17 million passengers traveled between the US mainland and dengue-endemic areas of Asia, the Caribbean, Central and South America, and Oceania in 2007 (5). Furthermore, the range of areas of dengue transmission has expanded significantly in recent years (6). Hyperendemicity has been established in many urban centers of the tropics where rapid development has favored vector proliferation. Increasing international travel, ineffective vector control measures, and the lack of a vaccine have likely contributed to the geographic expansion of dengue.

Although dengue is endemic in tropical and subtropical areas and the risk of infection among US residents is frequently associated with travel to these areas, the evolving ecology and epidemiology of dengue infections suggest that it does pose an increasing risk to public health in the continental United States. A recent commentary in JAMA asserted that “widespread appearance of dengue in the continental United States is a real possibility” (7). Historically, dengue transmission occurred within the continental United States as early as the 18th century. More recently, local transmission was documented as early as 1934 in Florida (8). During 1980, after a 2-year period of intense transmission of dengue in Mexico, the first locally transmitted dengue cases in the US since 1945 were believed to have occurred among residents of Texas (9). More recently, locally transmitted infections in south Texas were thought to have occurred in 9 patients during 1986 (10), in 7 patients during 1995 (11), in 2 patients in 1999 (12), and in single

cases of dengue hemorrhagic fever in 2004 (13) and 2005 (14). Recent studies on the Texas/Mexico border have demonstrated a “small, but significant risk for dengue outbreaks in the continental US” (15) and many more infections are believed to occur than are reported (16). Additionally, from July 1943 to July 1944, a total of 1498 locally transmitted cases occurred in Hawaii after dengue was introduced from Fiji (17). In 2001-2002, the Hawaii Department of Health identified 122 infections including the first autochthonous case of dengue fever since 1944 (18). Analysis of data from the Centers for Disease Control and Prevention’s (CDC) passive surveillance system in Puerto Rico has clearly shown that the number of cases of travel-associated dengue identified in 2005 (96 cases) nearly equals the number identified during the preceding 5 years combined (98 cases) (19).

Dengue is endemic in Puerto Rico, the US Virgin Islands, and US territories in the Pacific. In 2007, more than 10,500 cases of dengue were reported among American citizens in the continental United States and its territories. Most of these occurred in Puerto Rico, and extensive travel occurs between Puerto Rico and Puerto Rican communities in the northeastern continental United States and Florida. Similarly, heavy travel and migration along the US/Mexican border increase the possibility that imported cases will continue to occur and that local transmission within the United States could result, particularly in southern and eastern states where mosquito vectors (*Aedes aegypti* and *A. albopictus*) are present. Arizona is experiencing increased presence of *A. aegypti* and health authorities are concerned about increased potential for local dengue transmission because of their proximity to Mexico (20).

The risk of transmission through blood transfusion, as occurred with West Nile virus, is a further public health risk. Because blood donations are not screened for dengue virus, infected persons may unknowingly donate blood, since high levels of viremia can occur before the onset of illness and the majority of dengue infections are asymptomatic. Viremic blood donors infected with dengue virus have been identified (21). In Puerto Rico, 1 in 1300 blood donations were positive for DENV in 2005 (i.e., a non-outbreak year).

Currently WHO criteria classify symptomatic dengue infections into 1) undifferentiated fever or viral syndrome, 2) classic dengue fever (DF), 3) dengue hemorrhagic fever (DHF), and 4) dengue shock syndrome (DSS). If these classifications change in the future ArboNET can be modified to accommodate any changes. Undifferentiated fever associated with dengue infection is characterized by mild symptoms that are insufficient to meet DF criteria.

Asymptomatic infections and undifferentiated fevers are the most common manifestation of dengue virus infection and represent 50%-80% of cases. DF is frequently self-limiting although it can be incapacitating and require hospitalization. Treatment is symptomatic and supportive. Severe disease (i.e., DHF or DSS) is rare but may be fatal. Without proper, timely treatment, case fatality can exceed 20% in those with severe disease. With modern intensive supportive therapy, case fatality can be reduced to <1%. Maintenance of the circulating fluid volume and hemodynamic status is the central feature of severe case management. Other, less common clinical syndromes may include myocarditis, pancreatitis, hepatitis, or neuroinvasive disease.

The variability in clinical illness associated with dengue infection and its non-specific symptomatology emphasize the need for laboratory confirmation of all suspected cases. Overlap among the various clinical syndromes is common and the CDC Dengue Branch is available for consultation about appropriate case classification.

Justification

The purpose of this position statement is to add dengue to the National Notifiable Diseases Surveillance System list of nationally notifiable infectious diseases. Dengue is not currently included in the list of nationally notifiable conditions (www.cdc.gov/ncphi/diss/nndss/casedef/arboviral_current.htm). The case definition has not been amended since 1996 and requires updating to reflect current laboratory diagnostic testing as well as World Health Organization (WHO) case criteria. Variation in state-mandated reporting of dengue infections also hinders the collection of representative national surveillance data.

Currently, 26 states mandate the reporting of dengue infections. In an additional 6 states dengue reporting is considered mandatory within the category of arboviruses. In 2006, dengue cases were identified in 12 of the 32 states (37.5%) that mandate reporting, but these cases were not reported to ArboNet. Because state-mandated reporting requirements for dengue do not necessarily result in the submission of cases to ArboNet, current reporting practices do not generate comprehensive national surveillance data on dengue virus infections. Competent mosquito vectors that could transmit dengue have been identified in 21 of the 32 states (65.6%) where dengue is reportable and in 7 of the 18 states (38.8%) where dengue is not reportable.

Dengue reporting in the United States is conducted through two passive surveillance systems maintained by the CDC. The system operated by the CDC Dengue Branch in San Juan, Puerto Rico relies mainly on reports by clinicians to state health departments, which forward patient specimens to CDC for diagnostic testing. Dengue cases are also reported through the ArboNet arbovirus surveillance system. ArboNet officially began to record dengue case reports in July 2004. The ArboNet system relies largely on reports by private laboratories and clinicians to state health departments. Under these circumstances the delay between private laboratory testing and reporting means that specimens are rarely available for confirmatory testing. Analysis of data from these two surveillance systems suggests that there is little overlap of reporting. From 2005 through 2007 each system has received reports of approximately 150 cases per year. However, incomplete demographic information and description of symptoms often limits the usefulness of this information. Without systematic national surveillance it is likely that the number of travel-related dengue cases is significantly underestimated. As a result, national epidemiologic information sufficient to improve knowledge about the risk of dengue infection among US citizens is not available.

CSTE position statement 07-ID-06 adopted in 2006 and entitled “Events that May Constitute a Public Health Emergency of International Concern” specifically included dengue as an example of a disease that can spread rapidly internationally and cause substantial morbidity and mortality. The need for domestic surveillance to detect such diseases when they occur, consistent with international public health reporting obligations under the newly adopted International Health Regulations (IHR, 2005), necessitates improved dengue surveillance reporting.

Dengue meets the following criteria for a nationally and **standard** notifiable condition, as specified in CSTE position statement 08-EC-02:

- A majority of state and territorial jurisdictions—or jurisdictions comprising a majority of the US population—have laws or regulations requiring **standard** reporting of dengue to public health authorities
- CDC requests **standard** notification of dengue to federal authorities.
- CDC has condition-specific policies and practices concerning the agency’s response to, and use of, notifications.

III. Statement of the Desired Action(s) to be Taken

1. Designate dengue a nationally notifiable condition by adding it to the National Notifiable Disease Surveillance System list of nationally notifiable conditions.
2. Update the existing 1996 dengue case definition and standardize laboratory diagnostic criteria.

IV. Goals of Surveillance

1. Use data from a more comprehensive dengue surveillance system to monitor trends, identify areas of risk and risk factors to US travelers, target prevention efforts, and inform vaccination recommendations when vaccines become available.
2. Enhance surveillance and increase laboratory testing of suspected human cases of dengue to improve knowledge of dengue epidemiology and more accurately assess the public health burden of illness among US citizens.
3. Enhance healthcare provider awareness of dengue so that cases can be rapidly identified, thereby reducing the possibility of local transmission or establishment of endemicity in the US.
4. Potentially improve clinical management of severe dengue infections.

V. Methods for Surveillance

Case ascertainment will be conducted through passive, population-based surveillance. Dengue case reports will derive from laboratory and clinician reporting to state and local health departments, which will conduct individual follow-up consistent with available resources. CDC laboratories in San Juan, Puerto Rico and Fort Collins will continue to offer free diagnostic testing for specimens submitted by state, county, or city health departments.

Table V. Recommended sources of data and extent of coverage for ascertaining cases of dengue

Source of data for case ascertainment	Coverage	
	Population-wide	Sentinel sites
clinician reporting	X	
laboratory reporting	X	
reporting by other entities (e.g., hospitals, veterinarians, pharmacies)	X	
death certificates	X	
hospital discharge or outpatient records	X	
extracts from electronic medical records	X	
telephone survey		
school-based survey		
other _____		

VI. Criteria for Reporting

A. Narrative

Reporting of dengue is to be on-going and routine and is not limited to occurrences of multiple cases or outbreaks. Date of onset of illness (e.g., first day patient is febrile) is critical for guiding appropriate laboratory testing and is therefore required before samples can be processed if they are forwarded to CDC laboratories for testing. Confirmatory testing by CDC laboratories is not required for cases to be classified as confirmed. Any laboratory test results meeting the criteria outlined in the case definition section (below) are acceptable for case classification.

Table VI-B: Criteria for reporting a potential case of dengue

Criterion	Reporting		
	Confirmed	Probable	Suspected
<i>Clinical Presentation Dengue Fever (DF)</i>			
Fever lasting from 2 to 7 days	N	N	N
Retro-orbital or ocular pain	O	O	O
Headache	O	O	O
Rash	O	O	O
Myalgia	O	O	O
Arthralgia	O	O	O
Leukopenia	O	O	O
Hemorrhagic manifestations (e.g., petechiae; purpura/ecchymosis; epistaxis; gum bleeding; blood in vomitus, urine, or stool; or vaginal bleeding) or positive tourniquet test*	O	O	O
<i>Clinical Presentation Dengue Hemorrhagic Fever (DHF)</i>	Confirmed	Probable	Suspected
Fever lasting from 2 to 7 days	N		
Evidence of hemorrhagic manifestation or a positive tourniquet test*	N		
Thrombocytopenia ($\leq 100,000$ cells per mm^3)	N		
Evidence of plasma leakage shown by hemoconcentration (an increase in hematocrit $\geq 20\%$ above average for age or a decrease in hematocrit $\geq 20\%$ of baseline following fluid replacement therapy), or pleural effusion, or ascites or hypoalbuminemia or hypoproteinemia.	N		
<i>Clinical Presentation Dengue Shock Syndrome (DSS)</i>	Confirmed	Probable	Suspected
Fever lasting from 2-7 days	N		
Evidence of hemorrhagic manifestation or a	N		

positive tourniquet test*			
Thrombocytopenia ($\leq 100,000$ cells per mm^3)	N		
Evidence of plasma leakage shown by hemoconcentration (an increase in hematocrit $\geq 20\%$ above average for age or a decrease in hematocrit $\geq 20\%$ of baseline following fluid replacement therapy), or pleural effusion, or ascites or hypoproteinemia.	N		
Rapid and weak pulse and narrow pulse pressure (< 20 mm Hg); OR age-specific hypotension and cold, clammy skin and restlessness.	N		
<i>Laboratory findings</i>	Confirmed	Probable	Suspected
Isolation of virus from or demonstration of specific arboviral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid by polymerase chain reaction (PCR) test, immunofluorescence, or immunohistochemistry, OR	S		
Seroconversion from negative for dengue-specific serum IgM antibody in an acute phase (≤ 5 days after symptom onset) specimen to positive for dengue-specific serum IgM antibodies in a convalescent-phase specimen collected ≥ 5 days after symptom onset, OR	S		
Demonstration of a ≥ 4 -fold rise in reciprocal IgG antibody titer or hemagglutination inhibition titer to dengue antigens in paired acute and convalescent serum samples, OR	S		
Demonstration of a ≥ 4 -fold rise in PRNT (plaque reduction neutralization test) end point titer (as expressed by the reciprocal of the last serum dilution showing a 90% reduction in plaque counts compared to the virus infected control) between dengue viruses and other flaviviruses tested in a convalescent serum sample, OR	S		
Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF	S		
Dengue-specific IgM antibodies present in serum with a P/N ratio ≥ 2 .		N	
<i>Epidemiological risk factors</i>	Confirmed	Probable	Suspected
Travel to an dengue endemic country or presence at location with ongoing outbreak within previous two weeks of dengue-like illness, OR			N
Association in time and place with a confirmed or probable dengue case.			N

S = This criterion alone is sufficient to report a case

N = All “N” criteria in the same column—in conjunction with at least one of any “O” criteria in each category (e.g., clinical presentation) in the same column—are required to report a case.
O = At least **two** of any “O” criteria in each category (e.g., clinical presentation) in the same column—in conjunction with all other “N” criteria in the same column—is required to report a case.

*The tourniquet test is performed by inflating a blood pressure cuff on the upper arm to a point midway between the systolic and diastolic pressures for 5 minutes. A test is considered positive when 10 or more petechiae per 2.5 cm² (1 in²) are observed after the cuff pressure has been released for 2 minutes. The test may be negative or mildly positive during the phase of profound shock. It usually becomes positive, sometimes strongly positive, if the test is conducted after recovery from shock.

B. Disease-specific data reporting elements

The following information is needed to identify instances of autochthonous transmission (i.e., locally acquired cases) versus dengue cases resulting from importation from another country (i.e., travel-associated dengue infections).

- Name, Age, sex, race, ethnicity
- Current residence and country of origin
- Date of symptom onset
- Recent travel history
- History of Yellow Fever Virus vaccination
- History of prior infection with dengue virus or West Nile virus
- History of transfusion, organ transplantation or blood donation
- Clinical signs and symptoms including presence of plasma leakage and hemorrhagic manifestations (DF, DHF, DSS). See description below.
- Initial results of diagnostic testing
- Fatality, hospitalizations, or need for intensive care

VII. Case Definition

A. Clinical description

Dengue fever (DF) is most commonly an acute febrile illness defined by the presence of fever and two or more of the following, retro-orbital or ocular pain, headache, rash, myalgia, arthralgia, leukopenia, or hemorrhagic manifestations (e.g., positive tourniquet test, petechiae; purpura/ecchymosis; epistaxis; gum bleeding; blood in vomitus, urine, or stool; or vaginal bleeding) but not meeting the case definition of dengue hemorrhagic fever. Anorexia, nausea, abdominal pain, and persistent vomiting may also occur but are not case-defining criteria for DF.

Dengue hemorrhagic fever (DHF) is characterized by all of the following

- Fever lasting from 2-7 days
- Evidence of hemorrhagic manifestation or a positive tourniquet test
- Thrombocytopenia ($\leq 100,000$ cells per mm³)
- Evidence of plasma leakage shown by hemoconcentration (an increase in hematocrit $\geq 20\%$ above average for age or a decrease in hematocrit $\geq 20\%$ of baseline following fluid replacement therapy), or pleural effusion, or ascites or hypoproteinemia.

Dengue shock syndrome (DSS) has all of criteria for DHF plus circulatory failure as evidenced by

- Rapid and weak pulse and narrow pulse pressure (<20mm Hg) **or**
- Age-specific hypotension and cold, clammy skin and restlessness.

B. Laboratory criteria for diagnosis

1. Confirmatory

- a. Isolation of virus from or demonstration of specific arboviral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid by polymerase chain reaction (PCR) test, immunofluorescence, or immunohistochemistry, *or*
- b. Seroconversion from negative for dengue-specific serum IgM antibody in an acute phase (≤ 5 days after symptom onset) specimen to positive for dengue-specific serum IgM antibodies in a convalescent-phase specimen collected ≥ 5 days after symptom onset, *or*
- c. Demonstration of a ≥ 4 -fold rise in reciprocal IgG antibody titer or hemagglutination inhibition titer to dengue antigens in paired acute and convalescent serum samples, *or*
- d. Demonstration of a ≥ 4 -fold rise in PRNT (plaque reduction neutralization test) end point titer (as expressed by the reciprocal of the last serum dilution showing a 90% reduction in plaque counts compared to the virus infected control) between dengue viruses and other flaviviruses tested in a convalescent serum sample, *or*
- e. Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF.

2. Presumptive/Probable

- a. Dengue-specific IgM antibodies present in serum with a P/N ratio ≥ 2 .

3. Criteria for Epidemiologic Linkage

- a. Travel to an dengue endemic country or presence at location with ongoing outbreak within previous two weeks of dengue-like illness, *OR*
- b. Association in time and place with a confirmed or probable dengue case.

Table VII-A: Guide to Interpretation and Classification of Common Dengue Laboratory Tests^s

Laboratory test	Days post-onset of sample collection	Interpretation of positive result	Explanation
Real Time-PCR	≤ 5 days	Confirmatory (*Note)	Patient viremic while febrile; days 0-7
IgM (paired specimens, acute and convalescent)	≤ 5 days for acute specimen, > 5 days for convalescent. Ideally 2 specimens should be collected 2 weeks apart	Confirmatory	Negative IgM in an acute specimen followed by a positive IgM in a convalescent specimen
IgG (paired specimens, acute and convalescent)	≤ 5 days for acute specimen, > 5 days for convalescent. Ideally 2 specimens should be collected 2 weeks apart	Confirmatory	Must be 4 fold increase in titer between acute and convalescent specimen
IgM (single serum specimen)	> 5 days	Presumptive	IgM can remain positive for ≥ 3 months in cases of acute dengue infection
<p>*Note: Only PCR for dengue or IgM ELISA-based antibody test can be used for diagnosis of dengue in single serum specimens.</p>			
<p>NB: Previous flavivirus infections and the high prevalence of dengue IgG antibody in some populations (e.g., those resident in, or long-term visitors of dengue endemic countries) complicate interpretation of dengue serological test results. Therefore, a SINGLE serum sample tested using a dengue-specific IgG or combined IgM/IgG (“all antibody”) test is generally not helpful for diagnosis of confirmed or probable cases of dengue. For this reason suspect cases are defined clinically and epidemiologically, without IgG or combined IgG/IgM serological testing. If only a single serum sample is available for testing, a test for dengue-specific IgM antibody test is preferred.</p>			

C. Classification Tables:

Table VII-B. Criteria for classifying a case of dengue.

Criterion	Reporting		
	Confirmed	Probable	Suspected
<i>Clinical Presentation of Dengue Fever (DF)</i>	Confirmed	Probable	Suspected
Fever lasting 2 to 7 days	N	N	N
Retro-orbital or ocular pain	O	O	O
Headache	O	O	O
Rash	O	O	O
Myalgia	O	O	O
Arthralgia	O	O	O
Leukopenia	O	O	O
Hemorrhagic manifestations (e.g., petechiae; purpura/ecchymosis; epistaxis; gum bleeding; blood in vomitus, urine, or stool; or vaginal bleeding) or a positive tourniquet test	O	O	O
<i>Clinical Presentation of Dengue Hemorrhagic Fever (DHF)</i>	Confirmed	Probable	Suspected
Fever lasting 2 to 7 days	N		
Evidence of hemorrhagic manifestation or a positive tourniquet test*	N		
Thrombocytopenia ($\leq 100,000$ cells per mm^3)	N		
Evidence of plasma leakage shown by hemoconcentration (an increase in hematocrit $\geq 20\%$ above average for age or a decrease in hematocrit $\geq 20\%$ of baseline following fluid replacement therapy), or pleural effusion, or ascites or hypoproteinemia.	N		
<i>Clinical Presentation of Dengue Shock Syndrome (DSS)</i>	Confirmed	Probable	Suspected
Fever lasting from 2-7 days	N		
Evidence of hemorrhagic manifestation or a positive tourniquet test	N		
Thrombocytopenia ($\leq 100,000$ cells per mm^3)	N		
Evidence of plasma leakage shown by hemoconcentration (an increase in hematocrit $\geq 20\%$ above average for age or a decrease in hematocrit $\geq 20\%$ of baseline following fluid replacement therapy), or pleural effusion, or ascites or hypoalbuminemia, or hypoproteinemia.	N		
Rapid and weak pulse and narrow pulse pressure ($< 20\text{mm Hg}$); OR Age-specific hypotension and cold, clammy skin and restlessness.	N		
<i>Laboratory findings</i>	Confirmed	Probable	Suspected

Isolation of virus from or demonstration of specific arboviral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid by polymerase chain reaction (PCR) test, immunofluorescence, or immunohistochemistry. <i>Or</i>	S		
Seroconversion from negative for dengue-specific serum IgM antibody in an acute phase (≤ 5 days after symptom onset) specimen to positive for dengue-specific serum IgM antibodies in a convalescent-phase specimen collected ≥ 5 days after symptom onset, <i>or</i>	S		
Demonstration of a ≥ 4 -fold rise in reciprocal IgG antibody titer or hemagglutination inhibition titer to dengue antigens in paired acute and convalescent serum samples, <i>or</i>	S		
Demonstration of a ≥ 4 -fold rise in PRNT (plaque reduction neutralization test) end point titer (as expressed by the reciprocal of the last serum dilution showing a 90% reduction in plaque counts compared to the virus infected control) between dengue viruses and other flaviviruses tested in a convalescent serum sample <i>or</i>	S		
Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF	S		
Dengue-specific IgM antibodies present in serum with a P/N ratio ≥ 2 .		N	
<i>Epidemiological risk factors</i>	Confirmed	Probable	Suspected
Travel to an dengue endemic country or presence at location with ongoing outbreak within previous two weeks of dengue-like illness <i>or</i>			N
Association in time and place with a confirmed or probable dengue case.			N

S = This criterion alone is sufficient to report a case

N = All "N" criteria in the same column—in conjunction with at least one of any "O" criteria in each category (e.g., clinical presentation) in the same column—are required to report a case.

O = At least **two** of any "O" criteria in each category (e.g., clinical presentation) in the same column—in conjunction with all other "N" criteria in the same column—is required to report a case.

D. Summary of Dengue Case Definition and Classification

Confirmed

A clinically compatible case of DF, DHF, or DSS with confirmatory laboratory results

Probable

A clinically compatible case of DF, DHF, or DSS with laboratory results indicative of presumptive infection

Suspect

A clinically compatible case of DF, DHF or DSS that is epidemiologically linked to a confirmed case

Asymptomatic Blood or Tissue Donor

Specific viral antigen or genomic sequences demonstrated in donated blood or organs during screening and confirmatory testing in the absence of clinically compatible illness in the donor.

Final Comment

Dengue viruses are members of the *Flaviviridae* and have sufficient antigenic similarity to yellow fever virus, Japanese encephalitis virus, and West Nile virus that previous infection or vaccination may raise cross-reactive serum antibodies. After a primary infection with a heterologous flavivirus, subsequent antibody testing by ELISA may produce false positive results for a different flavivirus. PRNT can often resolve cross-reactive serum antibodies in this situation and identify the infecting virus. However, high-titered cross-reactive antibody levels produced from multiple previous flavivirus infections cannot be resolved by PRNT. This demonstrates the complexity inherent in serological diagnosis and differentiation in populations living in regions where more than one flavivirus co-circulates. However, a small proportion of the US population has evidence of previous flavivirus infection (or vaccination) so that cross-reactive flavivirus antibodies should not be a significant limitation to dengue diagnosis among most US travelers. Among US residents, most testing for dengue is done through private clinical laboratories using IgM or IgG detection techniques. To assist state and local health departments in the interpretation of commonly performed serology testing, see VII-B-2 for test interpretation.

Reference testing is available from CDC's Dengue Branch, Division of Vector-Borne Infectious Diseases, National Center for Infectious Diseases, 1324 Calle Cañada, San Juan, PR 00920-3860, telephone 787-706-2399, fax 787-706-2496

VIII. Period of Surveillance:

Surveillance should be ongoing.

IX. Data sharing/release and Print criteria:

- CDC requests standard notification of suspect, probable, and confirmed cases.
- Data flow will proceed from state and local health departments to CDC and WHO. Only fully de-identified case data will be released to the general public. Suspect case data will not be included in final case counts. Case report data will not be used or released until verification procedures are complete and all states have finalized their case counts.
- Data will be used to determine the burden of illness due to dengue, identify areas of risk and risk factors to US travelers, target prevention efforts, and inform vaccination recommendations when vaccines become available. Electronic reports of dengue will be summarized in the MMWR.
- State-specific compiled data will be posted on the EpiX Forum on a monthly basis. Content of this report to the states and territories will be dependent on the current epidemiologic situation and identified needs of stakeholders. Additional methods of data

dissemination including CDC website posting, email notices, and maps highlighting where infection contracted will be investigated.

- State-specific compiled data will be published in MMWR reports. All cases will be verified with the states before publication.

X. References:

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XI. Coordination:

Agencies for Response:

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