

**West Nile Virus in California:  
Guidelines for Human Testing and Surveillance  
Within the Regional Public Health Laboratory Network**

California Department of Public Health  
Richmond, California

May 2011

**West Nile Virus in California: Guidelines for Human Testing and Surveillance**  
**Within the Regional Public Health Laboratory Network**

**TABLE OF CONTENTS**

Diagnostic Testing Guidelines .....	1
Submitting Specimens to Regional Public Health Laboratory Network for Testing	1
Viral and Rickettsial Disease Laboratory (VRDL) Testing Algorithm .....	2
Laboratory Diagnosis and Test Interpretation .....	2
Case Classification: Regional Public Health Laboratory Network .....	3
Results from Commercial or Reference Laboratories .....	3
West Nile Virus-Associated Fatalities .....	4
Reporting .....	4
Contacts, Links, and Appendices Index .....	7
Appendix A: Instructions for Submitting Specimens .....	8
Appendix B: West Nile Virus Specimen Submittal Form .....	9
Appendix C: VRDL Testing Algorithm – Serum .....	10
Appendix D: WNV Laboratory Testing at VRDL .....	11
Appendix E: Revised National Surveillance Case Definition .....	12
Appendix F: West Nile Virus Infection Case Report .....	14
Appendix G: West Nile Virus Infection Case Report-Supplemental Form ...	15
Appendix H: Report of West Nile-Virus Positive Blood Donor.....	16

## West Nile Virus in California: Guidelines for Human Testing and Surveillance Within the Regional Public Health Laboratory Network

### Diagnostic Testing Guidelines

West Nile virus (WNV) testing within the regional public health laboratory network (i.e., the California Department of Public Health Viral and Rickettsial Disease Laboratory and participating local public health laboratories) is recommended for individuals with the following symptoms, particularly during West Nile virus “season,” which typically occurs from July through October in California:

- A. Encephalitis
- B. Aseptic meningitis (Note: Consider enterovirus for individuals  $\leq 18$  years of age)
- C. Acute flaccid paralysis; atypical Guillain-Barré Syndrome; transverse myelitis; or
- D. Febrile illness\*
  - a. Illness compatible with West Nile fever and lasting  $\geq 7$  days
  - b. Must be seen by a health care provider

---

\* The West Nile fever syndrome can be variable and often includes headache and fever ( $T \geq 38^{\circ}\text{C}$ ). Other symptoms include rash, swollen lymph nodes, eye pain, nausea or vomiting. After initial symptoms, the patient may experience several days of fatigue and lethargy.

Identification of human cases is important early in the West Nile virus season to assess the burden of human illness and target mosquito control and public education activities to reduce exposure risk. However, depending on the volume of tests requested and laboratory capacity, local public health laboratories may need to consider limiting testing to individuals with neuroinvasive disease once West Nile virus is established in a given area.

### Submitting Specimens to Regional Public Health Laboratory Network for Testing

Required specimens:

- Acute serum:  $\geq 2$ cc serum

If a lumbar puncture is performed and residual CSF is available:

- Cerebral spinal fluid (CSF): 1-2cc CSF for further testing at CDC (please note: these results may not be available for several weeks)

If West Nile virus is highly suspected and acute serum is negative or inconclusive, request:

- 2nd serum:  $\geq 2$ cc serum collected 3-5 days after acute serum

Paired acute and convalescent serum specimens are useful for demonstration of sero-conversion to WNV. Paired samples should be collected whenever WNV is suspected. Although a single acute serum may provide evidence of recent WNV infection, a negative acute serum does not necessarily rule out infection. Occasionally, a specimen may be collected too soon to show antibody related to a current illness (e.g. with immunocompromised individuals).

Specimens must be submitted with a completed specimen submittal form (See **Appendix A: Instructions for Submitting Specimens**; and **Appendix B: West Nile Virus Specimen Submittal Form**).

## Viral and Rickettsial Disease Laboratory Testing Algorithm

The Viral and Rickettsial Disease Laboratory [VRDL] will test serum samples for West Nile Virus [WNV].

- Immunofluorescence assay (IFA) may be done as an adjunct test on serum (IFA is not done on CSF)
- In addition to serum, VRDL encourages submission of CSF if a lumbar puncture is performed and residual CSF is available. VRDL requests that WNV testing on CSF only be requested for individuals who have a screening test positive (serum IgM+). CSF will be sent to CDC for testing; CSF results may not be available for several weeks, but results for serum tested at VRDL can be available within 14 calendar days from receipt of sample.
- When previously untested serum and CSF are received, enzyme immunoassay (EIA) is performed on serum (CSF is stored in case additional confirmatory testing at the CDC is needed)
  - If the IgM is negative in the serum sample but you strongly suspect WNV, another serum sample should be collected 2-3 days after the first serum. WNV IgM is usually present in immunocompetent individuals by day 5 of illness onset.
  - In immunocompromised individuals the WNV antibody response may be delayed. For these patients, additional testing is warranted, please consult with VRDL for guidance.
  - Please consult with VRDL for guidance any time WNV is strongly suspected, regardless of previous test results.
- Plaque reduction neutralization testing (PRNT) is done to resolve indeterminate results, or by request (*Note: At VRDL, PRNT is not currently validated for diagnostic purposes; these results are to be used for surveillance purposes only*)
- Enterovirus PCR may also be done on CSF specimens on a seasonal basis, depending on the availability of resources at VRDL
  - Call 510-307-8606 to find out whether the most current algorithm includes enterovirus PCR
- See **Appendix C: VRDL WNV Testing Algorithm – Serum** and **Appendix D: WNV Laboratory Testing at VRDL**

## Laboratory Diagnosis and Test Interpretation

- IFA is a more subjective assay than EIA and should be interpreted with caution
- IgG(+) result only (i.e., negative for IgM) typically indicates previous infection of a flavivirus
  - Check case history for travel to flavivirus-endemic areas, length of time between onset of symptoms and collection of specimen, vaccination history, etc.
  - If current infection is still suspected, obtain convalescent serum to test for seroconversion
- VRDL is always available for consultation on test results with local public health laboratories

Interpretation of West Nile virus antibody test results\*

Tests	Results	Interpretation
IgM IgG	negative negative	Antibody not detected
IgM IgG	negative positive	Infection at undetermined time
IgM IgG	positive negative	Possible evidence of recent or current infection; further testing necessary**
IgM IgG	positive positive	Evidence of recent or current infection***
IgM IgG	indeterminate negative	Inconclusive ‡request convalescent serum

\* Due to heterotypic antibody responses and/or cross-reactions, serologic results should be interpreted on the basis of clinical and epidemiological information

\*\* Note the possibility of a false positive IgM result (EIA)

\*\*\* Note that some individuals may have persisting antibodies from the previous WNV season

‡ Paired acute and convalescent serum samples may be useful for demonstration of seroconversion

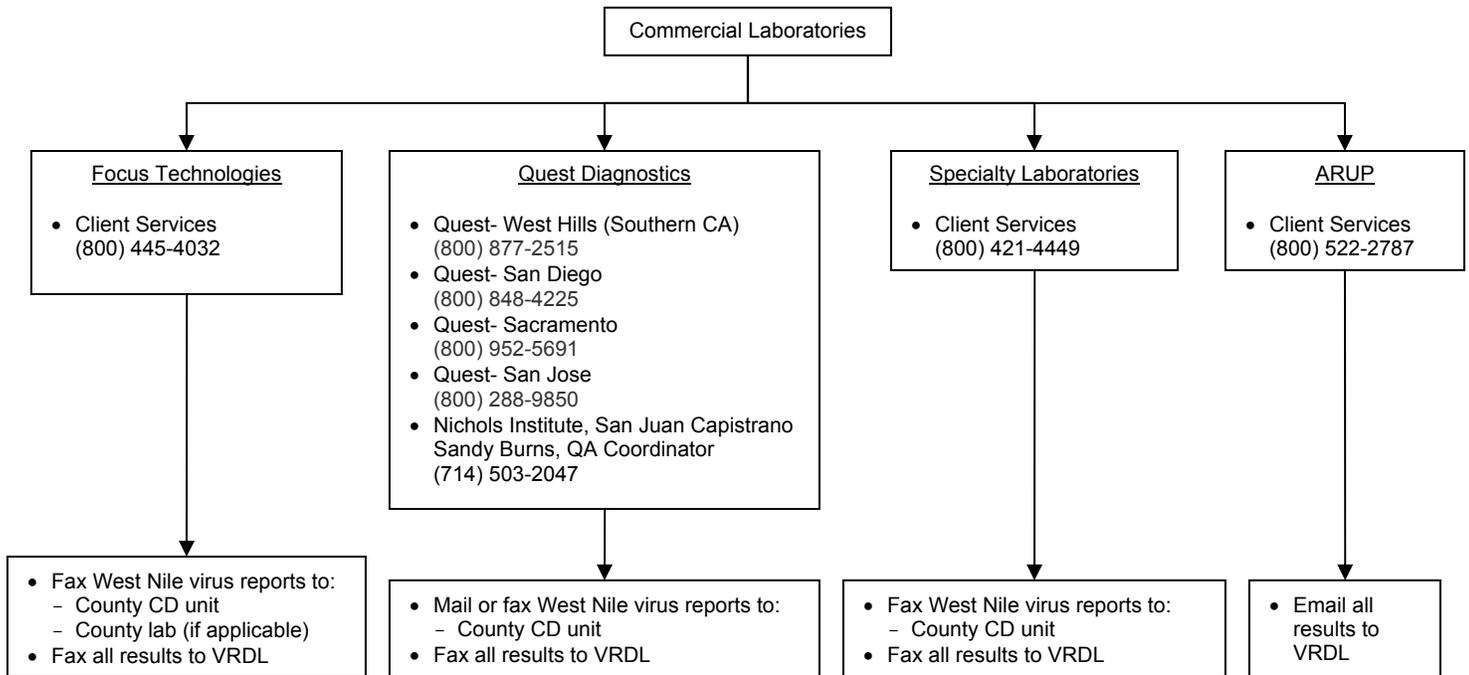
### Case Classification: Regional Public Health Laboratory Network

A case is considered to be WNV positive if the patient has a clinically compatible illness (see **Appendix E** for case definition) and has the following laboratory results:

- IgM(+) by two different assays (e.g. EIA and IFA); or
- IgM(+) and IgG(+) by EIA; or
- IgM(+) and IgG(+) by IFA; or
- Rising IgG antibodies

### Results from Commercial or Reference Laboratories

- California Code of Regulations, Title 17, Section 2505 requires laboratories to report positive West Nile virus test results to the local health department
- Local health departments should follow up on IgM(+) results from commercial labs
  - If a patient has clinically compatible illness and is IgM-positive *and* IgG-positive, the commercial lab results are sufficient to conclude that patient is infected with WNV – however, for the first few cases of the WNV season, it is recommended that positive results from commercial labs be verified by repeat/confirmatory testing at the local public health lab and/or VRDL
  - If patient is IgM-positive and IgG-negative, be aware that IgM can be falsely positive; follow-up testing is suggested
- IgG-positive result only (i.e., IgM-negative) typically indicates previous infection
- When in doubt, try to obtain either the original specimen or a convalescent sample to forward to the local public health lab or to VRDL for repeat/confirmatory testing
- Public health reporting by commercial laboratories is being facilitated by VRDL (see below)



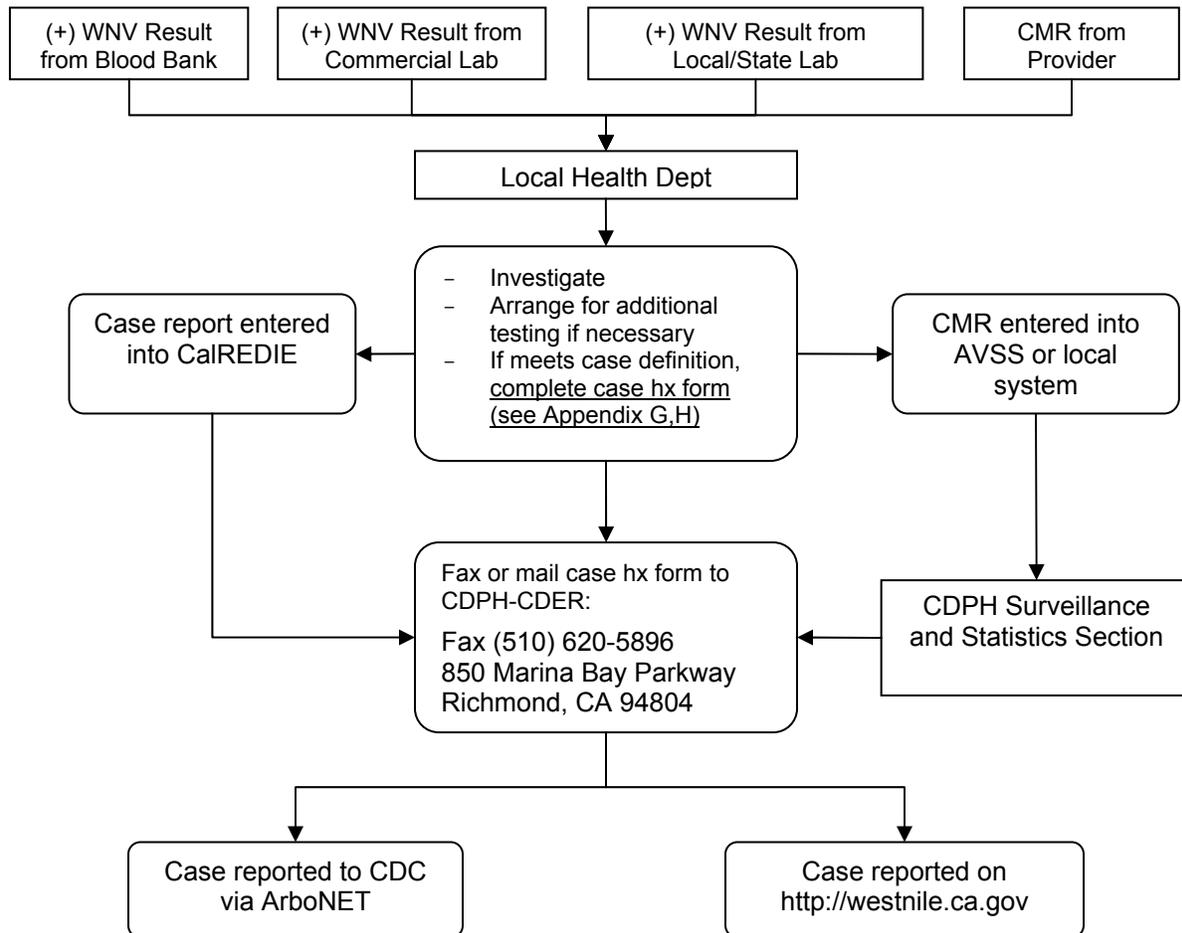
### West Nile Virus-Associated Fatalities

Determining whether or not West Nile virus infection has played a causal role in a fatality can be difficult. West Nile virus may not always be listed as a contributory or underlying cause of death on death certificates. Patients often have many underlying conditions and preexisting medical problems that also may be related to the immediate causes of death. In general, if a patient was diagnosed with West Nile virus and never recovered from the sequelae (e.g. was discharged to convalescent hospital until date of death), a health department may consider designating the patient as a WNV-associated fatality.

### Reporting

Since West Nile virus infection is a laboratory diagnosis, and since West Nile surveillance is a multi-component system maintained nationwide through ArboNet (CDC's source for WNV data), reporting human cases of West Nile virus to the California Department of Public Health is done through slightly different routes than regular disease reporting. The algorithm below outlines the various paths through which West Nile virus infections may be reported.

### West Nile Virus Reporting Algorithm



### Important Issues about Reporting

- West Nile virus infection is reportable by both laboratories and providers
- Fax or mail case report forms (See **Appendix F: West Nile Virus (WNV) Infection Case Report**; **Appendix G: West Nile Virus (WNV) Infection Supplemental Form**; and **Appendix H: Report of West Nile Virus-Positive Blood Donor**) to the California Department of Public Health Communicable Disease Emergency Response Branch (CDER) – please indicate, either on form or by phone/email, that individual has tested positive for WNV:  
Fax (510) 620-5896; CDER-West Nile, 850 Marina Bay Parkway, Richmond, CA 94804
- **Only cases reported to CDPH-CDER are entered into ArboNET and posted on the California WNV website** – If a local agency uses AVSS or another local system for their disease surveillance, they will enter West Nile infections separately into those systems, as well as send a case history form to CDPH-CDER
  - The following AVSS classifications can be used to enter cases:
    - ENCP-WNV: For West Nile encephalitis cases
    - MENG-WNV: For West Nile meningitis cases

- WNV-FVR: For West Nile fever cases
- WNV-AFP: For West Nile acute flaccid paralysis cases
- WNV-ASYM: For WNV infections detected via blood bank with no accompanying illness
- WNV-UNK: For cases with unknown or undeterminable clinical status
- CDPH-CDER will check CalREDIE for new case reports
- CDPH-CDER will check AVSS for reported WNV infections that may not have been previously reported
- Health departments should notify their local vector control agency of any confirmed human West Nile virus activity as soon as possible, so that enhanced mosquito surveillance and control measures can be implemented
- A line list of locally acquired WNV cases will be maintained and updated biweekly on the California WNV website (<http://westnile.ca.gov>)
- Report clinical syndrome as West Nile fever, neuroinvasive disease (specify encephalitis, meningitis, acute flaccid paralysis, or other), unknown, or asymptomatic (not a case)
- Contact CDER (510) 620-3987 if local lab or health department knows of a case that is not on website or ArboNET

#### **Important Issues about VRDL Results**

- All VRDL results are faxed and mailed to submitting local public health lab, and faxed to local health department of patient's residence
- Non-diagnostic results, or results that are to be used for surveillance purposes only (e.g. PRNT), will be faxed and mailed separately
- Local health departments need to report West Nile virus results to providers
- VRDL results are routinely reported to local health departments/labs
  - Positive results relayed immediately by phone or email, then followed up with fax/mail
  - Negative results faxed/mailed to labs 1-2 times/week
- Fax requests for results (include patient name and identifier e.g. date of birth) to: (510) 307-8599, Attn: West Nile Virus Project

**Contacts**

Communicable Disease Emergency Response Branch

Cynthia Jean Yen, MPH ..... (510) 620-3987  
Carol Glaser, DVM, MD (for clinical consultation)..... (510) 307-8613  
Pager (510) 720-0078  
West Nile Virus Surveillance Project Fax ..... (510) 620-5896

Viral and Rickettsial Disease Laboratory

Maria Salas, MPH..... (510) 307-8606  
Katharine King..... (510) 307-8562  
Heather Sheriff..... (510) 307-8608

Vector Borne Disease Section

West Nile Virus Hotline ..... (877) 968-2473

**Links**

California West Nile Virus Website ..... <http://westnile.ca.gov>  
CDC West Nile Virus Website ..... <http://www.cdc.gov/ncidod/dvbid/westnile/>

**Appendices**

- A. Instructions for Submitting Specimens
- B. West Nile Virus Specimen Submittal Form
- C. Viral and Rickettsial Disease Laboratory West Nile Virus Testing Algorithm – Serum
- D. West Nile Virus Laboratory Testing – Viral and Rickettsial Disease Laboratory
- E. Revised (2004) National Surveillance Case Definition of Domestic Arboviral Disease
- F. West Nile Virus Infection Case Report
- G. West Nile Virus Infection Case Report- Supplemental Investigation Form
- H. West Nile Virus-Positive Blood Donor Report Form

## Appendix A

### Instructions for Submitting Specimens

- Refrigerated specimens should be sent on **cold pack** using an overnight courier
  - If CSF needs to be stored ≤72 hours before submittal, store at 2 to 8°C and ship on cold pack.
  - If CSF needs to be stored >72 hours before submittal, freeze at -70°C or colder and ship on dry ice.
- Each specimen should be clearly labeled with **patient name**, **specimen type**, and **date of specimen collection**
- **Specimens must be submitted with a specimen submittal form.** The following information is asked for on the specimen submittal form because it is important for accurate interpretation of results:
  - Onset date
  - Unusual immunological status of patient, if any
  - County of residence
  - History of travel to flavivirus-endemic areas
  - History of prior vaccination against flavivirus disease
  - Brief clinical summary including clinical diagnosis
- **Please include any West Nile virus test results obtained by the local public health laboratory or a commercial reference laboratory**
  - **Other laboratory results affect the VRDL testing algorithm; Specimens that have screened positive or indeterminate for WNV IgM antibodies at another laboratory will be immediately tested with the heterophile subtract procedure**
- **Do not send specimens on Fridays for weekend delivery** (VRDL Specimen Receiving Hours M-F 8-5)
- Address specimens for VRDL to:  
Specimen Receiving/ West Nile  
850 Marina Bay Parkway  
Richmond, CA 94804

## Appendix B: Specimen Submittal Form (version for use by local public health labs)

West Nile virus testing is recommended on individuals with the following:

- A. Encephalitis
- B. Aseptic meningitis (Note: Consider enterovirus for individuals ≤ 18 years of age)
- C. Acute flaccid paralysis; atypical Guillain-Barré Syndrome; transverse myelitis; or
- D. Febrile illness compatible with West Nile fever\* and lasting ≥ 7 days (must be seen by health care provider):

\* The West Nile fever syndrome can be variable and often includes headache and fever ( $T \geq 38C$ ). Other symptoms include rash, swollen lymph nodes, eye pain, nausea or vomiting. After initial symptoms, the patient may experience several days of fatigue and lethargy.

1. **Required specimens:**

- Acute Serum:** ≥ 2cc serum
- Cerebrospinal Fluid (CSF):** 1-2cc CSF may be submitted with acute serum for further testing at CDC if lumbar puncture is performed and residual CSF is available (Please note: these results may not be available for several weeks)

2. If West Nile virus is highly suspected and acute serum is negative or inconclusive:

- 2<sup>nd</sup> Serum:** ≥ 2 cc serum collected 3-5 days after acute serum

- Each specimen should be labeled with **date of collection**, **specimen type**, and **patient name**
- Refrigerated specimens should be sent on **cold pack** using an overnight courier
- Frozen specimens should be sent on **dry ice** using an overnight courier
- CSF that cannot be shipped within 72 hours of collection should be stored frozen at -70°C or colder.
- Serum that cannot be shipped within 48 hours of collection may be stored at 4°C or frozen at -20°C or colder.
- Please do not send specimens on Fridays (Specimen Receiving Hours: M-F 8-5)
- Send specimens to CDPH VRDL: **Specimen Receiving – West Nile Virus**

**850 Marina Bay Parkway  
Richmond, CA 94804**

- Local Public Health Laboratory West Nile **IFA/EIA IgM results** (or attach copy of results):

Specimen	Date Collected	IgM Assay Method	Results			
			Negative	Reactive	Indeterminate	Not Tested
		<input type="checkbox"/> IFA <input type="checkbox"/> EIA				
		<input type="checkbox"/> IFA <input type="checkbox"/> EIA				

**\*\* IMPORTANT: THE INFORMATION BELOW MUST BE COMPLETED AND SUBMITTED WITH SPECIMENS \*\***

<b>Patient's last name, first name:</b>			<b>Patient Information</b>			
			Address _____			
Age or DOB:	Sex (circle): M   F	Onset Date:	City _____ Zip _____ County _____			
			Phone Number (____) _____			
<b>Clinical findings:</b> <input type="checkbox"/> Encephalitis <input type="checkbox"/> Meningitis <input type="checkbox"/> Acute flaccid paralysis <input type="checkbox"/> Febrile illness <input type="checkbox"/> Other: _____			Other information (immunocompromised, travel hx, hx of flavivirus infection, etc.):			
Other tests requested:			<b>This section for Laboratory use only. Date received by VRDL and State Accession Number</b>			
1 <sup>st</sup>	Specimen type and/or specimen source	Date Collected	1 <sup>st</sup>			
2 <sup>nd</sup>	Specimen type and/or specimen source	Date Collected	2 <sup>nd</sup>			
3 <sup>rd</sup>	Specimen type and/or specimen source	Date Collected	3 <sup>rd</sup>			

**Questions? Call Maria Salas at (510) 307-8606**

Submitting Physician \_\_\_\_\_ Phone Number (\_\_\_\_) \_\_\_\_\_  
 Submitting Facility \_\_\_\_\_ Phone Number (\_\_\_\_) \_\_\_\_\_



## **Appendix D: West Nile Virus Laboratory Testing at California Department of Public Health, Viral and Rickettsial Disease Laboratory**

Laboratory diagnosis of human West Nile virus (WNV) infection is a multi-step process. In some cases, physicians send specimens to private commercial laboratories for WNV diagnostic testing. More commonly, specimens are sent to the local or state health department for diagnostic laboratory testing.

Testing available at the California Department of Public Health Viral and Rickettsial Disease Laboratory includes:

### **Serologic tests**

**Enzyme Immunoassay (EIA) testing:** The immunoglobulin M (IgM) antibody-capture enzyme immunoassay (EIA) is the frontline test for WNV diagnosis. The EIA is the ideal test because it is both simple and sensitive (i.e., highly likely to find true positives). EIA testing can be completed in 14 calendar days from the time samples arrive at the laboratory. Generally several specimens are tested in each EIA run.

The immunoglobulin G (IgG) EIA test is used as an adjunct test—a single IgG result cannot differentiate between old and new infection; however, paired sera showing significant change in IgG antibody levels can be helpful.

**Immunofluorescence Assay (IFA) testing:** IFA tests for WNV can also test for IgM and IgG antibodies. The advantages of these tests are that they are rapid and amenable to just a few samples. However, the IFA is a more subjective assay than the EIA.

### **Molecular tests**

Molecular methods for WNV testing can be used as an adjunct to the serologic tests. For diagnosis of clinical disease, serological tests are more accurate than molecular tests. Reverse Transcriptase - Polymerase Chain Reaction (RT-PCR) is a process that uses nucleic acid amplification techniques. While these tests can be useful in diagnosis, they have low sensitivity for a variety of reasons for WNV, making them inappropriate as the sole test for laboratory diagnostic testing of possible human WNV infections. An advantage of this method is the relatively rapid turn around time. RT-PCRs may be useful for immunocompromised individuals that have a delay in antibody response and prolonged viremia. Additionally, VRDL uses molecular methods to rule out enterovirus.

### **Confirmation of results**

#### **Plaque reduction neutralization test (PRNT)**

Once VRDL has an initial positive result, further testing may be done to confirm that the infection detected is West Nile virus. WNV is a flavivirus, which can be problematic as far as cross-reactivity with other flaviviruses. The flaviviruses include St. Louis encephalitis (SLE) and Japanese encephalitis (JE) viruses, both of which are closely related to WNV, as well as yellow fever (YF) and dengue (DEN) viruses. People who have been recently vaccinated for JE or YF, or who have a recent exposure to JE, YF, SLE, or DEN viruses, may have a positive IgM for WNV, even though they have not actually been exposed to WNV.

Additional laboratory testing may be required to rule out the false-positive reactions that result from an exposure to a related flavivirus. The PRNT is the most specific test available for distinguishing between and among the arthropod-borne flaviviruses. Because exposure to other flaviviruses is possible in many areas of WNV activity, initial IgM positive results may need to be confirmed by PRNT. The PRNT usually takes up to 8 days if testing for both WNV and SLE viruses is required. The process may take even longer if testing with YF or Dengue viruses is necessary. This additional testing (e.g., the PRNT) may require growth of the virus and may take a week or more (plus shipping time) to conduct. Since PRNT testing is not currently validated for diagnostic purposes at the VRDL, PRNT results are reported out separately and should be used for surveillance purposes only.

### **Tests in development**

The VRDL is in the process of developing tests for more rapid confirmation of WNV, e.g. the Western Blot.

## Appendix E: Surveillance Case Definition for West Nile Virus Infection in Humans

West Nile virus infection is reportable to local health departments under Title 17 of the California Code of Regulations. Below is the case definition for West Nile virus disease as summarized by the Centers for Disease Control and Prevention (CDC) [available at <http://www.cdc.gov/ncidod/dvbid/westnile/clinicians/surveillance.htm#casedef>]. Blood donors that test positive for West Nile virus through blood bank screening should also be reported to CDPH, regardless of clinical presentation.

### **CASE DEFINITION: West Nile Virus**

*NOTE: This definition is for public health surveillance purposes only. It is not intended for use in clinical diagnosis.*

#### **Clinical description**

Arboviral infections may be asymptomatic or may result in illnesses of variable severity sometimes associated with central nervous system (CNS) involvement. When the CNS is affected, clinical syndromes ranging from febrile headache to aseptic meningitis to encephalitis may occur, and these are usually indistinguishable from similar syndromes caused by other viruses. Arboviral meningitis is characterized by fever, headache, stiff neck, and pleocytosis. Arboviral encephalitis is characterized by fever, headache, and altered mental status ranging from confusion to coma with or without additional signs of brain dysfunction (e.g., paresis or paralysis, cranial nerve palsies, sensory deficits, abnormal reflexes, generalized convulsions, and abnormal movements). West Nile fever syndrome can be variable and often includes headache and fever ( $T \geq 38^{\circ}\text{C}$  or  $100.4^{\circ}\text{F}$ ). Other symptoms include rash, swollen lymph nodes, eye pain, nausea or vomiting. After initial symptoms, the patient may experience several days of fatigue and lethargy.

#### **Laboratory Criteria for Diagnosis**

- **Fourfold or greater change in virus-specific serum antibody titer, or**
- **Isolation of virus from or demonstration of specific viral antigen or genomic sequences in tissue, blood, cerebrospinal fluid (CSF), or other body fluid, or**
- **Virus-specific immunoglobulin M (IgM) antibodies demonstrated in CSF by antibody-capture enzyme immunoassay (EIA), or**
- **Virus-specific IgM antibodies demonstrated in serum by antibody-capture EIA and confirmed by demonstration of virus-specific serum immunoglobulin G (IgG) antibodies in the same or a later specimen by another serologic assay (e.g., neutralization or hemagglutination inhibition).**

#### **Case Classification**

- ***Probable:* A case occurring during a period when arboviral transmission is likely and with the following supportive serology: 1) a single or stable (less than or equal to twofold change) but elevated titer of virus-specific serum antibodies; or 2) serum IgM antibodies detected by antibody-capture EIA but with no available results of a confirmatory test for virus-specific serum IgG antibodies in the same or a later specimen.**
- ***Confirmed:* An encephalitis or meningitis case that is laboratory confirmed.**

#### **Comment**

Because closely related arboviruses exhibit serologic cross-reactivity, positive results of serologic tests using antigens from a single arbovirus can be misleading. In some circumstances (e.g., in areas where two or more closely related arboviruses occur, or in imported arboviral disease cases), it may be epidemiologically important to attempt to pinpoint the infecting virus by conducting cross-neutralization

## Appendix E: Surveillance Case Definition for West Nile Virus Infection in Humans

tests using an appropriate battery of closely related viruses. This is essential, for example, in determining that antibodies detected against St. Louis encephalitis virus are not the result of an infection with West Nile (or dengue) virus, or vice versa, in areas where both of these viruses occur. Because dengue fever and West Nile fever can be clinically indistinguishable, the importance of a recent travel history and appropriate serologic testing cannot be overemphasized. In some persons, West Nile virus-specific serum IgM antibody can wane slowly and be detectable for more than one year following infection. Therefore, in areas where West Nile virus has circulated in the recent past, the co-existence of West Nile virus-specific IgM antibody and illness in a given case may be coincidental and unrelated. In those areas, the testing of serially collected serum specimens assumes added importance.

The seasonality of arboviral transmission is variable and depends on the geographic location of exposure, the specific cycles of viral transmission, and local climatic conditions. Reporting should be etiology-specific (see below; the six diseases printed in bold are nationally reportable to CDC):

- **St. Louis encephalitis virus disease**
- **West Nile virus disease**
- **Powassan virus disease**
- **Eastern equine encephalitis virus disease**
- **Western equine virus disease**
- **California serogroup virus disease** (includes infections with the following viruses: La Crosse, Jamestown Canyon, snowshoe hare, trivittatus, Keystone, and California encephalitis viruses)

**Asymptomatic West Nile Virus Infection:** Asymptomatic infection with WNV, which is generally identified in blood donors, is also reportable. WNV-positive blood donors detected by blood banks are reported directly to local health departments. Blood donors who test positive for WNV may not necessarily be ill, nor will they initially have positive IgM or IgG antibody test results. Local health departments should report blood donors who meet the following criteria for being a presumptively viremic donor to CDPH-CDER:

A presumptively viremic donor (PVD) is a person with a blood donation that meets at least one of the following criteria:

- a) One reactive nucleic acid-amplification (NAT) test with signal-to-cutoff (S/CO)  $\geq 17$
- b) Two reactive NATs

Additional serological testing is not required. Local health departments should follow up with the donor after two weeks of the date of donation to assess if the patient subsequently became ill. If the donor did become ill as a result of WNV infection, an updated case report form should be sent to CDER so that the blood donor may be reclassified as a clinical case.

---

Note: Due to the continued risk of unintentional or intentional introduction of exotic arboviruses into the United States (e.g., Venezuelan equine encephalitis virus), or the reemergence of indigenous epidemic arboviruses (e.g., St. Louis encephalitis and western equine encephalitis viruses), physicians and local public health officials should maintain a high index of clinical suspicion for cases of potential exotic or unusual arboviral etiology, and consider early consultation with arboviral disease experts at state health departments and CDC.

## Appendix F: West Nile Virus (WNV) Infection Case Report

### Patient Information:

**Last Name:** \_\_\_\_\_ **First Name:** \_\_\_\_\_ **DOB:** \_\_\_/\_\_\_/\_\_\_ **Age:** \_\_\_ **Med Rec #:** \_\_\_\_\_  
**Address:** \_\_\_\_\_ **City:** \_\_\_\_\_ **Zip Code:** \_\_\_\_\_  
**Phone:** Home (\_\_\_\_\_) \_\_\_\_\_ Work (\_\_\_\_\_) \_\_\_\_\_ **Occupation:** \_\_\_\_\_  
**Sex:**  Male  Female  Unknown **Ethnicity:**  Hispanic  Non-Hispanic  Unknown **Race:**  White  Black  Unknown  Asian/ Pacific Islander  American Indian/Alaskan Native  Other: \_\_\_\_\_

### Physician Information (Mandatory):

**Name:** \_\_\_\_\_ **Facility:** \_\_\_\_\_  
**Pager/Phone:** (\_\_\_\_\_) \_\_\_\_\_ **Fax:** (\_\_\_\_\_) \_\_\_\_\_ **Email:** \_\_\_\_\_  
**Date of first symptom(s):** \_\_\_/\_\_\_/\_\_\_  Hospitalized or  ER / Outpatient  
**If hospitalized, admit date:** \_\_\_/\_\_\_/\_\_\_ **Discharge date:** \_\_\_/\_\_\_/\_\_\_ **If patient died, date of death:** \_\_\_/\_\_\_/\_\_\_

#### Clinical syndrome:

Encephalitis .....  Yes  No  Unk  
 Aseptic meningitis .....  Yes  No  Unk  
 Acute flaccid paralysis ....  Yes  No  Unk  
 Febrile illness .....  Yes  No  Unk  
 Asymptomatic .....  Yes  No  Unk  
 Other \_\_\_\_\_

#### Do the following apply anytime during current illness:

In ICU .....  Yes  No  Unk  
 Fever ≥38°C.....  Yes  No  Unk  
 Headache .....  Yes  No  Unk  
 Rash .....  Yes  No  Unk  
 Stiff neck .....  Yes  No  Unk  
 Muscle pain/weakness ....  Yes  No  Unk  
 Altered consciousness ....  Yes  No  Unk  
 Seizures .....  Yes  No  Unk

#### CSF Results

Date: \_\_\_/\_\_\_/\_\_\_  
 RBC: \_\_\_\_\_  
 WBC: \_\_\_\_\_  
 %Diff: \_\_\_\_\_  
 Protein: \_\_\_\_\_  
 Glucose: \_\_\_\_\_

#### CBC Results

Date: \_\_\_/\_\_\_/\_\_\_  
 WBC: \_\_\_\_\_  
 %Diff: \_\_\_\_\_  
 HCT: \_\_\_\_\_  
 Plt: \_\_\_\_\_

**Other lab results (MRI/CT, LFTs, etc.):** \_\_\_\_\_

#### Past medical history:

Hypertension:  Yes  No  Unk  
 Diabetes Type \_\_\_\_\_  Yes  No  Unk  
 Other: \_\_\_\_\_

#### Travel/Exposures within 4 wks of onset (specify details):

Mosquito bites/exposure .....  Yes  No  Unk  
*Dates/Locations:* \_\_\_\_\_  
 Travel outside of California .....  Yes  No  Unk  
*Dates/Locations:* \_\_\_\_\_  
 Travel outside the U.S. ....  Yes  No  Unk  
*Dates/Locations:* \_\_\_\_\_  
 Donated blood .....  Yes  No  Unk  
*Date:* \_\_\_/\_\_\_/\_\_\_  
 Donated organ .....  Yes  No  Unk  
*Date:* \_\_\_/\_\_\_/\_\_\_  
 Received blood transfusion .....  Yes  No  Unk  
*Date:* \_\_\_/\_\_\_/\_\_\_  
 Received organ transplant: .....  Yes  No  Unk  
*Date:* \_\_\_/\_\_\_/\_\_\_  
 Currently pregnant .....  Yes  No  Unk  
*Week of gestation:* \_\_\_\_  
 Ever traveled outside the U.S. ....  Yes  No  Unk  
*Dates/Locations:* \_\_\_\_\_  
 Ever rec'd yellow fever vaccine.....  Yes  No  Unk  
*Date:* \_\_\_/\_\_\_/\_\_\_

#### Knowledge of WNV prior to illness:

Did patient do anything to avoid mosquito bites?  
*If yes,*  Yes  No  Unk  
 - used insect repellent?  Yes  No  Unk  
 - drained standing water near home?  Yes  No  Unk

**Other significant history/exposures:** \_\_\_\_\_

**Other lab results (MRI/CT, etc.):** \_\_\_\_\_

#### West Nile Virus Test Results:

Testing Laboratory	Specimen Type	Coll Date	Test Type	Result

FAX this form: (510) 620-5896 or MAIL to: CDPH–West Nile Virus, 850 Marina Bay Parkway, Richmond CA 94804

# Appendix G: West Nile Virus (WNV) Infection Case Report- Supplemental Form

California Department of Public Health  
 Communicable Disease Emergency Response Branch  
 850 Marina Bay Parkway  
 Richmond, CA 94804

Date Form Completed: \_\_\_/\_\_\_/\_\_\_

*Beginning in 2008, the Centers for Disease Control and Prevention (CDC) will collect surveillance data on selected underlying medical conditions and therapies that have previously been identified as risk factors for severe illness, hospitalization, and/or death among persons with WNV disease. Initial reports of WNV infections should be sent to the California Department of Public Health immediately after they have been confirmed. However, this supplemental investigation form is not time-sensitive and can be submitted at any time after a case has been reported.*

## **Questions to Assess Underlying Medical Conditions and Medication Use**

**Patient Name (Last, First):** \_\_\_\_\_ **DOB:** \_\_\_/\_\_\_/\_\_\_

**Clinical syndrome:**    Neuroinvasive disease    West Nile fever    Other clinical    Asymptomatic infection

**1. Before your West Nile virus infection, did a health care provider ever tell you that you had any of the following medical conditions?**

- |   |                              |                             |                                  |
|---|------------------------------|-----------------------------|----------------------------------|
| Diabetes .....                                  | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| High blood pressure (hypertension) .....        | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Heart attack (myocardial infarction) .....      | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Angina or coronary artery disease .....         | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Congestive heart failure (CHF) .....            | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Stroke .....                                    | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Chronic obstructive pulmonary disease (COPD) .. | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Chronic liver disease .....                     | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Kidney failure or chronic kidney disease .....  | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Alcoholism .....                                | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Bone marrow transplant .....                    | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Solid organ transplant .....                    | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |

If yes: What organ was transplanted?: \_\_\_\_\_

What year was the transplant?: \_\_\_\_\_

Cancer .....

	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown
--	------------------------------	-----------------------------	----------------------------------

If yes: What type(s)?: \_\_\_\_\_

What year were you diagnosed?: \_\_\_\_\_

Are you currently being treated for cancer?:  Yes    No    Unknown

**2. Before your West Nile infection, did a health care provider ever tell you that you had a medical condition that limited your ability to fight an infection?**

	<input type="checkbox"/> Yes	<input type="checkbox"/> No	<input type="checkbox"/> Unknown
--	------------------------------	-----------------------------	----------------------------------

If yes: What condition(s)?: \_\_\_\_\_

**3. At the time you were diagnosed with West Nile virus infection, were you taking any of the following types of prescription medications or treatments?**

- |  |                              |                             |                                  |
|--|------------------------------|-----------------------------|----------------------------------|
| Chemotherapy .....                                     | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Other treatments for cancer .....                      | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Hemodialysis .....                                     | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Other treatments for kidney disease .....              | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Oral or injected steroids (not inhaled or topical) ... | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Insulin or other medications to treat diabetes .....   | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Medications to treat high blood pressure .....         | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Medications to treat coronary artery disease .....     | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Medications to treat congestive heart failure .....    | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |
| Medications that suppress the immune system .....      | <input type="checkbox"/> Yes | <input type="checkbox"/> No | <input type="checkbox"/> Unknown |

**4. Which of the following sources provided the information above? (check all that apply)**

- |          |                              |                             |                      |                              |                             |
|----------|------------------------------|-----------------------------|----------------------|------------------------------|-----------------------------|
| Patient  | <input type="checkbox"/> Yes | <input type="checkbox"/> No | Family member/friend | <input type="checkbox"/> Yes | <input type="checkbox"/> No |
| Provider | <input type="checkbox"/> Yes | <input type="checkbox"/> No | Medical record       | <input type="checkbox"/> Yes | <input type="checkbox"/> No |

California Department of Public Health  
Communicable Disease Emergency Response Branch  
850 Marina Bay Parkway, Richmond, CA 94804  
(510) 620-3987 Fax (510) 620-5896

## Report of West Nile Virus-Positive Blood Donor to the California Department of Public Health

1. Blood Collection Facility:
  - a. Name: \_\_\_\_\_
  - b. Address: \_\_\_\_\_ Zip Code \_\_\_\_\_
  - c. Telephone number: (\_\_\_\_) \_\_\_\_\_ - \_\_\_\_\_
  - d. Contact person: \_\_\_\_\_
  
2. Blood Unit Identification Number: \_\_\_\_\_
  
3. Date of Collection: \_\_\_\_/\_\_\_\_/\_\_\_\_
  
4. Donor's name: \_\_\_\_\_
  
5. Case identification number assigned by the blood center \_\_\_\_\_  
(This tracking code should be different from the index blood unit identification number or other operational identification numbers. It is to be used to track the case investigation)
  
6. Donor's date of birth: \_\_/\_\_/\_\_\_\_
  
7. Donor's gender: M/F
  
8. Donor's Address \_\_\_\_\_  
  
ZIP code: \_\_\_\_\_ Tel: (\_\_\_\_) \_\_\_\_\_
  
9. This test was confirmed: Y/N If Y, confirmatory test and result: \_\_\_\_\_
  
10. NAT #1 S/CO: \_\_\_\_\_
  
11. NAT #2 S/CO: \_\_\_\_\_ (if done)
  
12. Blood testing laboratory (optional): Name: \_\_\_\_\_  
Address: \_\_\_\_\_  
Phone: (\_\_\_\_) \_\_\_\_\_ - \_\_\_\_\_
  
13. Comments \_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_