Updated Zika and other Travel-associated Arboviral Diseases Screening Guidance

Summary
This HAN Advisory serves to inform healthcare providers across the state that new Zika screening and evaluation guidance has been implemented by the Oklahoma State Department of Health (OSDH) to reflect changes in guidance published by the Centers for Disease Control and Prevention (CDC).1,2 For this reason, the OSDH Acute Disease Service (ADS) has updated our Zika clinician packet and laboratory guidance documents. Clinicians should use the updated forms during patient evaluation to determine if the clinical and travel criteria are met to access diagnostic testing for Zika virus infection.

Updated Testing Recommendations

Symptomatic Patients with Zika Exposure
It is still recommended to test symptomatic patients with at least two Zika-compatible symptoms (fever, rash, arthralgia, conjunctivitis) who report travel to or sexual contact with a person who resides/visited a Zika outbreak-affected country.

Asymptomatic Pregnant Women
New changes have been implemented for asymptomatic pregnant women. CDC has established two risk levels for asymptomatic, pregnant females: (1) Pregnant women with ongoing exposure, and (2) those without ongoing exposure. Ongoing exposure is defined as those who have had foreign residence in a Zika-affected country during pregnancy or the eight weeks prior to conception, as well as those patients who report frequent (at least monthly) travel to a Zika-affected region.

1. Asymptomatic, Pregnant Women With Ongoing Exposure
It has now been established that previous residence in a Zika-affected country or frequent travel to a Zika-affected region places a pregnant women and her fetus at higher risk of both infection and adverse outcomes.

It is recommended to continue to test women in this category for Zika virus infection. It is important to understand there has been a change in the frequency and testing type. The Zika IgM test has proven to be unreliable for asymptomatic, pregnant women as CDC studies have now shown that IgM levels can actually remain elevated well beyond 200 days post-exposure making it impossible to determine if positive IgM results reflects exposure that occurred prior to conception or is actually reflective of recent travel or sexual exposure. This makes follow-up difficult and confusing for both clinicians and patients. For this reason, CDC is now recommending asymptomatic, pregnant women with ongoing Zika exposure to be only tested by PCR three times during pregnancy. Testing should occur at initial prenatal visit and then two additional times, preferably once per trimester.

2. Asymptomatic, Pregnant Women Without Ongoing Exposure
CDC’s new guidance states that Zika testing for this category of women is no longer recommended for the majority of states. Oklahoma is not a border or high risk state with documented local mosquito transmission of Zika virus. Furthermore, both state and national data support the notion that the risk of Zika virus infection in pregnant women who only travel out of the US for vacation or short stays are at a low risk of developing Zika virus disease, thus low risk to the fetus acquiring infection.
Asymptomatic, pregnant females comprise approximately 75% of consultations and testing requests done by the Oklahoma State Department of Health. Since February 2016, OSDH has tested 544 asymptomatic, pregnant females with either travel to Zika-affected region or reported sexual exposure with a partner who traveled to high risk area; one (0.18%) tested positive for Zika virus infection.

Given the strong state and national data supporting the low risk of Zika virus in this group, the OSDH will no longer be testing women in this category or their sexual partners. Women (or partners) who still desire testing outside of CDC guidelines may elect to pursue testing through a commercial reference laboratory.

Infant and Placental Testing
The OSDH will continue to evaluate and test infants who have suspected or confirmed microcephaly or other neurologic birth defects (diagnosed prenatally or at birth) whose mother was potentially exposed to Zika virus, as well as infants born to mothers with laboratory evidence of Zika virus infection during pregnancy.

Summary
If the completed screening process indicates the patient is at risk for Zika virus infection, notify the ADS epidemiologist-on-call at (405) 271-4060 for consultation, to confirm all criteria for testing are met, and to coordinate specimen collection and submission. Once the patient has been approved for testing, clinicians should follow the attached specimen collection guidance to submit the required specimen(s) to the OSDH Public Health Laboratory (PHL). The epidemiologist-on-call will work with clinicians to coordinate specimen transport to the PHL. Guidance related to appropriate specimen collection, handling, and shipping can be found in the attached “Laboratory Testing Guidance” document.

Please note CDC is currently offering a free continuing education (CE) activity discussing recent updates regarding U.S. pregnant women and infants with recent Zika virus exposure. Interested clinicians can register at the following link: https://www.cdc.gov/mmwr/cme/medscape_cme.html

Healthcare providers can contact the ADS epidemiologist-on-call at (405) 271-4060 for questions or clarification regarding this guidance or Zika Virus testing.

2. **The Updated Interim Guidance for Healthcare Providers Caring for Pregnant Women with Possible Zika Virus Exposure – United States, July 2017**: https://www.cdc.gov/mmwr/volumes/66/wr/mm6629e1.htm?s_cid=mm6629e1_w
ZIKA AND OTHER TRAVEL-ASSOCIATED ARBOVIRAL DISEASES SCREENING AND EVALUATION GUIDANCE

ACTIONS REQUESTED OF CLINICIANS: If patient meets one of the criteria below, please:

1. Fill out the screening form.
2. Fax it to Oklahoma State Department of Health (OSDH), Acute Disease Service (ADS) at (405) 271-6680.
3. Call the epidemiologist-on-call at (405) 271-4060 to consult and obtain the required pre-approval for testing.
4. If patient is approved for testing, complete the attached OSDH Public Health Lab requisition form for each specimen. This form is required to be submitted with each specimen collected for testing at the Public Health Lab.

If a patient meeting the criteria below is seen during non-business hours, specimens can be collected and held refrigerated until the next business day when an OSDH ADS epidemiologist is available for consultation and submission approval. If the patient is part of a suspected outbreak, or suspected local transmission event, please contact the ADS epi-on-call immediately at (405) 271-4060 (available 24/7/365).

- Symptomatic Individuals with Travel History or Concern for Sexual Transmission:
  - Two or more of the following symptoms: Acute fever, rash, arthralgia, conjunctivitis;
  - Travel to a Zika-affected area within 2 weeks prior to symptom onset. Countries or areas within the continental U.S. at risk for Zika transmission can be determined by accessing the following website: [http://wwwnc.cdc.gov/travel/page/zika-travel-information](http://wwwnc.cdc.gov/travel/page/zika-travel-information);
  - Concern for sexual transmission: Reports unprotected sex with partner(s) who traveled to a Zika-affected area. Specimen must be collected within 12 weeks after partner’s departure from a Zika-affected country in order to be eligible for testing;
  - Ability to collect urine and serum specimens within 12 weeks of symptom onset. Additional specimens may be requested during consultation with an ADS epidemiologist.

- Asymptomatic, Pregnant Women:
  - Those with ONGOING* possible Zika exposure:
    - Should be tested three times during pregnancy.
    - At initial prenatal visit and then two more times, preferably each trimester.
    - Collect urine and serum samples for Zika virus RT-PCR testing.
  - Those without ONGOING* possible Zika exposure:
    - Testing is no longer recommended (i.e., vacation travel, unprotected sexual exposure following vacation travel).

*Ongoing possible exposure to Zika virus includes frequent (at least monthly) travel to a Zika-affected area or frequent (at least monthly) unprotected sex with a partner who either resides in or frequently travels to a Zika-affected area. Travelers with short stays overseas (e.g., vacations, short mission trips) regardless of pregnancy status are no longer eligible for testing at the Oklahoma State Department of Health. Patients interested in Zika testing that don’t qualify for testing at OSDH can access testing through major reference laboratories at the patient’s expense.

- Infant and Placental Testing:
  - Infants who have suspected or confirmed microcephaly or other neurologic abnormality (diagnosed prenatally or at birth) and mother was potentially exposed to Zika virus.
  - Infants who were born to mother with laboratory evidence of Zika virus infection during pregnancy.

Acute Disease Service
Oklahoma State Department of Health

Phone: (405) 271-4060
Fax: (405) 271-6680
Website: [http://ads.health.ok.gov](http://ads.health.ok.gov)
Zika and Other Travel-Associated Arboviral Diseases
Laboratory Testing Guidance

Zika virus testing is performed by the Oklahoma State Department of Health (OSDH) Public Health Laboratory (PHL). However, prior to specimen collection/submission, an epidemiologist from the OSDH Acute Disease Service (ADS) must gather pertinent clinical signs and symptoms, travel, and other epidemiologic information from the clinician to determine if a patient meets the required criteria for Zika virus testing as indicated by the Centers for Disease Control and Prevention (CDC). All specimens must be approved by the ADS prior to shipping to the OSDH PHL for testing.

The OSDH PHL is a CDC-designated laboratory that performs Zika virus testing by Emergency Use Authorization using the CDC Zika IgM Antibody Capture (MAC) ELISA and the CDC Trioplex Real-time RT-PCR Assay. Specimens may be referred by the OSDH PHL to the CDC or other laboratories for additional testing, as indicated.

For questions concerning Zika testing criteria, contact the OSDH ADS epidemiologist-on-call at (405) 271-4060. For questions regarding specimen collection, storage, transport, and lab requisition forms, contact the OSDH PHL Client Services at (405) 271-5070.

Please, note that an OSDH PHL Test Requisition Form must be submitted with each specimen. If the form is not completed appropriately, or is not received, testing may be canceled or significantly delayed.

- Urine and serum are the preferred specimen types and are required for each individual approved for testing. Additional specimens may be recommended during consultation with an ADS epidemiologist.

**Specimen Collection, Storage, and Shipping:**
- **Whole blood** in serum separator tube (SST) (a.k.a., tiger-top tube)
  - Following collection, gently invert SST no more than 8 times then allow blood to clot in upright position for at least 30 mins and no more than 60 mins then centrifuge at 3000 rpm for 10 mins.
  - ≥ 2.0 mL (minimum) required; collect additional tubes to meet volume requirements, as needed.
  - Store refrigerated (2-8 °C) and ship using ice packs.
  - If transit time will be > 7 days post-collection, pour serum into a sterile, leak-proof, screw-cap tube and store/shipped frozen (-20°C or colder).
- **Urine** in sterile container with sterile screw-cap container
  - Following collection, transfer urine to a sterile screw-cap container. To prevent leakage during shipping, secure parafilm around container cap. Do not ship urine cups.
  - ≥ 1.0 mL (minimum) required; must be submitted together with a patient-matched serum specimen.
  - Store refrigerated (2-8 °C) and ship using ice packs; prefer specimen frozen (-20°C or colder), then shipped on dry ice, if possible.
- **CSF and amniotic fluid** in sterile screw-cap container
  - ≥ 1.0 mL (minimum) required; must be submitted together with a patient-matched serum specimen.
  - Store refrigerated (2-8 °C) and ship using ice packs; prefer specimen frozen (-20°C or colder), then shipped on dry ice, if possible.
- **Other specimens types**
  - For submission of other specimen types, such as placenta tissue or umbilical cord, coordinate with the OSDH ADS epidemiologist-on-call at (405) 271-4060.
Completing the Test Requisition Form

- An OSDH PHL Test Requisition Form must be completed and submitted with each specimen type.
- The OSDH PHL Test Requisition Form can be downloaded/electronically completed at the OSDH PHL website (“Forms”) or a hard copy can be provided by the OSDH ADS epidemiologist-on-call.
  - Include patient’s name or unique patient identifier (e.g., MR#), DOB, sex, specimen type, date of specimen collection, name and address of submitter, and test requested.
  - Indicate specimen source; a separate test requisition form is required for each specimen type, e.g., if submitting a serum and urine specimen on the same patient, then two test requisition forms will be required.
  - Under the Virology section of the form, mark ‘Zika virus, IgM antibodies and/or Zika virus, chikungunya virus, dengue virus, PCR’.

Shipping to the OSDH PHL

- Ship to the OSDH PHL Monday through Thursday using the following address:
  OSDH Public Health Laboratory
  1000 NE 10th Street
  Oklahoma City, OK 73117-1299
- For specimens that cannot be shipped immediately, store according to specimen storage guidelines above.
- Specimens must be packaged and shipped in accordance with Category B agent guidelines.
- Courier service to the OSDH PHL may be available through your local hospital; contact the PHL Client Services.

Cautionary Note Regarding Alternative Commercial Testing

Currently, several commercial laboratories in the US offer Zika virus testing using real-time RT-PCR. However, these laboratories do not provide Zika IgM ELISA testing with PRNT confirmation, and have no routine process to forward specimens to another laboratory when test results are negative. Therefore, if requesting Zika rRT-PCR testing from a commercial laboratory, providers should request the draw site/laboratory to retain an aliquot of the serum for Zika IgM testing if the rRT-PCR testing is negative.

Whole blood should be collected and processed per guidelines of the commercial testing laboratory but serum from an additional serum separator tube should be transferred to a polypropylene tube and stored refrigerated (2-8°C) until it is known if additional IgM testing is indicated. If a serum aliquot cannot be stored or is not available, but further testing is indicated, a new blood sample should be collected.
ZIKA AND OTHER TRAVEL-ASSOCIATED ARBOVIRAL DISEASES SCREENING FORM

Please complete all sections of the form, fax to the Acute Disease Service (ADS), F:(405) 271-6680, and then call the ADS epidemiologist-on-call at (405) 271-4060 prior to specimen collection and submission. Please complete all fields.

Patient Information

Last Name: ____________________________ First Name: ____________________________ MI: ____________ Date of Birth: _____/_____/______ Sex: □ Male □ Female Address: _____________________________________ City: _____________ County: ________ State: ___ Zip: ________

Primary contact number: ____________________________ Secondary contact number: ____________________________

Race: □ White □ Black □ Native America □ Asian □ Native Hawaiian/Pacific Islander □ Asian □ Unknown □ Other ______________________

Ethnicity: □ Hispanic □ Non-Hispanic □ Unknown Preferred Language: __________________ □ Interpreter needed

Healthcare Provider Information

Name of Reporting Person: ____________________________

Ordering Physician: _____________________________________

Work Phone: ____________________________ Fax Number: ____________________________ Organization: ____________________________

Address: ____________________________ City: ____________________________ State: ____________________________ Zip Code: ____________________________

Symptom Information

Did patient have two or more of the symptoms below? □ Yes □ No (If yes, complete symptom information below. If no, go to next question.)

- Is the patient pregnant? □ Yes □ No (If yes, go to next question. If no, testing not indicated.)
- If patient is pregnant, does the patient report having at least monthly travel to a Zika-affected area or monthly sexual contact with partner who resides in/travels to a Zika affected area? (If no, testing not indicated. If yes, skip to exposure assessment.)

Symptom Onset date: ___/___/______

Fever (subjective OR measured) □ Yes □ No □ Unknown If yes, max temp: ____________

Rash □ Yes □ No □ Unknown Rash description: □ Petechial □ Macular □ Vesicular

Conjunctivitis □ Yes □ No □ Unknown

Arthralgia □ Yes □ No □ Unknown

Was the patient hospitalized? □ Yes □ No □ Unknown

Hospital name: ____________________________ Admit Date: _____/_____/______ Discharge Date: _____/_____/______

Exposure Assessment

If symptomatic:

Within 14 days before symptom onset, did the patient travel in an area in which Zika virus is present? □ Yes □ No (If yes, please list patient’s travel details on the following page.)

- If no, did the patient report unprotected sex with their sexual partner following their return from a Zika-affected country? □ Yes □ No (If yes, please list partner’s travel details on the following page. If no, testing not indicated.)

If asymptomatic and pregnant:

Did the patient live in a foreign country in the eight weeks prior to conception or anytime during pregnancy? □ Yes □ No

If yes, please list country of foreign residence and dates of residence.

Country: ____________________________ Dates of residence: _____/_____/______ - _____/_____/______

Does the pregnant patient report frequent (at least monthly) travel to a Zika outbreak-affected region during pregnancy?
ZIKA AND OTHER TRAVEL-ASSOCIATED ARBOVIRAL DISEASES SCREENING FORM

☐ Yes ☐ No
☒ If yes, how often does the patient report travel during pregnancy?

_____________________________________________________________________________________________

Does the pregnant patient report repeated (at least monthly), unprotected sexual exposure to a partner who has continued to travel to a foreign country during client’s pregnancy? ☐ Yes ☐ No
☒ If yes, how often does the patient report unprotected sexual exposure during pregnancy?

_____________________________________________________________________________________________

Exposure Assessment (Continued)

Refer to CDC Zika Travelers Advisory page for list of countries: http://wwwnc.cdc.gov/travel/page/zika-travel-information

If yes, list which countries and regions/areas/cities visited, and dates of travel:

1) Country: ____________________________
   Date Arrived in Country: _____/_____/______
   Date Departed Country: _____/_____/______
   Regions/areas/cities visited: ____________________________

2) Country: ____________________________
   Date Arrived in Country: _____/_____/______
   Date Departed Country: _____/_____/______
   Regions/areas/cities visited: ____________________________

☒ Was the patient pregnant at the time of travel? ☐ Yes ☐ No
   If yes, number of gestational weeks at the time of travel: _____ weeks
   If yes, is the patient still pregnant? ☐ Yes ☐ No
   If the patient is no longer pregnant, indicate outcome of pregnancy: ☐ Live birth ☐ Fetal loss ☐ Elective termination
   If live birth, what was date of delivery and facility of delivery:

_________________________________________________________________________________________________

☒ Did the patient become pregnant within approx. 2 weeks after returning from a Zika affected country or region? ☐ Yes ☐ No

☒ Has the patient ever been vaccinated for Yellow Fever or Japanese encephalitis? ☐ Yes ☐ No ☐ Unknown

☒ Has the patient previously been diagnosed with Dengue, Chikungunya, Yellow Fever, or West Nile virus? ☐ Yes ☐ No ☐ Unknown
   If yes, specify disease and year: ____________________________

☒ Has the patient been tested for other etiologies for the current illness? ☐ Yes ☐ No ☐ Unknown
   ☐ Chikungunya Lab name: ___________ Date of test ___/___/___ Result:_______
   ☐ Dengue Lab name: ___________ Date of test ___/___/___ Result:_______
   ☐ West Nile Virus Lab name: ___________ Date of test ___/___/___ Result:_______
   ☐ Other Lab name: ___________ Date of test ___/___/___ Result:_______

FOR INTERNAL USE ONLY:

☐ Symptomatic ☐ Asymptomatic ☐ Pregnant ☐ Not Pregnant ☐ Ongoing Exposure ☐ No Ongoing Exposure ☐ Specimen < 14 days from symptom onset or exposure
☐ Specimen ≥ 14 days and < 12 weeks from symptom onset or exposure

Acute Disease Service
Oklahoma State Department of Health
Phone: (405) 271-4060
Fax: (405) 271-4680
Website: http://ads.health.ok.gov
Test Request

**Source/Type**
- Blood
- Serum
- Urine
- Stool
- CSF
- Pleural fluid
- Pericardial fluid
- Blood smears
- Sputum, expect.
- Sputum, induced
- Bronchial brush
- Bronchial wash
- Bronchoalveolar lavage
- Tracheal aspirate
- Nasopharynx
- Nasal
- Throat
- Eye
- Rectum/anus
- Tissue (specify):
  - Wound/lesion (specify):
  - Environmental (specify):
  - Other (specify):

**Test Request**

<table>
<thead>
<tr>
<th>Category</th>
<th>Test Name</th>
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<tbody>
<tr>
<td><strong>Bacteriology</strong></td>
<td>Bacterial isolate, identification/serotyping/confirmation</td>
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<tr>
<td></td>
<td>Variable specimen according to source (contact lab)</td>
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<td></td>
<td>Bacteria, non-enteric, isolation and identification</td>
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<tr>
<td></td>
<td>Variable specimen according to source (contact lab); requires pre-approval</td>
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<tr>
<td></td>
<td>Enteric pathogens, isolation and identification</td>
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<tr>
<td></td>
<td>Feces, 2 g or 5-10 mL in Cary Blair or GN Broth (STE C only)</td>
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<td></td>
<td>Bordetella</td>
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<td>Nasopharynx, 1 or 2 swabs; isolate, confirm visible growth</td>
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<td></td>
<td>Chlamydia/Gonorrhea</td>
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<td></td>
<td>Urine, first 20-60 mL of void – transfer to UPT tube</td>
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<td></td>
<td>Group B streptococcus</td>
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<tr>
<td></td>
<td>Vaginal/anal swab in LI M broth (combined vaginal/anal collection preferred)</td>
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<tr>
<td></td>
<td>Syphilis, RPR w/ reflex to TP-PA</td>
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<td></td>
<td>Serum in SST, 2 mL</td>
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<td></td>
<td>Syphilis, RPR and TP-PA</td>
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<td></td>
<td>Serum in SST, 2 mL; (CHDs only, requires pre-approval by DIS)</td>
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<tr>
<td></td>
<td>Bacteria, environmental (contact lab)</td>
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<td></td>
<td>Mycobacteria, smear and culture w/ reflex to identification</td>
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<td>Respiratory sediments, 5-10 mL; Sterile fluid, ≥2 mL; Blood, 5-10 mL ACD or heparin; Tissue, 1 g; Urine, ≥5 mL</td>
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<tr>
<td></td>
<td>Mycobacteria, isolate identification</td>
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<td>Liquid culture, &gt;3 mL; Solid culture, visible growth</td>
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<td>M. tuberculosis complex PCR</td>
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<td></td>
<td>Respiratory sediments, 5-10 mL (CHDs require OSDH TB physician pre-approval)</td>
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<td>Hepatitis B surface antigen (HBsAg)</td>
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<td>Serum, 2 mL (approved submitters only)</td>
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<td>HIV-1/2 antigen/antibodies</td>
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<td>Serum in SST, 2 mL (approved submitters only)</td>
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<td></td>
<td>Human papillomavirus, high risk</td>
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<td>Residual ThinPrep, 1 mL</td>
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<td></td>
<td>Influenza virus A and B</td>
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<td>Nasopharyngeal (preferred), nasal or throat swabs, 1 or 2 in VTM</td>
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<tr>
<td></td>
<td>Rubella antibodies</td>
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<td></td>
<td>Serum in SST, 1 mL (female CHD patients only)</td>
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<td></td>
<td>Virus isolation and/or identification</td>
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<td></td>
<td>Throat, nasopharynx, rectum, eye, lesion, 1 swab in VTM; Blood, 5 mL heparin; Feces, 2 g or 5-10 mL; CSF, 1 mL; Eye scrapings in VTM; Urine, 20 mL (first morning void); Isolate; Other (contact lab)</td>
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<td></td>
<td>West Nile virus/St. Louis encephalitis virus, IgM antibodies</td>
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<td></td>
<td>Serum in SST, 2 mL; CSF, 1 mL (CSF must be accompanied by serum)</td>
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<td></td>
<td>Zika virus, IgM antibodies and/or Zika virus, chikungunya virus, dengue virus, PCR</td>
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<tr>
<td></td>
<td>Serum in SST, 2 mL; CSF, 1 mL; Urine 1 mL; Amniotic fluid 1 mL (CSF, urine and amniotic fluid must be accompanied by serum)</td>
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<td>Intestinal ova and parasites (O&amp;P)</td>
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<tr>
<td></td>
<td>Solid feces, 2 g or Liquid feces, 5-10 mL in PVA and 10% formalin</td>
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<tr>
<td></td>
<td>Parasites, blood</td>
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<tr>
<td></td>
<td>Babesia/trypansomes/filariae: Giemsa or Giemsa-Wright-stained blood smears, 1 thick and 1 thin</td>
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<td></td>
<td>Malaria: Giemsa or Giemsa-Wright-stained blood smears, 1 thick and 1 thin</td>
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<tr>
<td></td>
<td>AND 2-6 mL EDTA blood</td>
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<td></td>
<td>Parasites, tissue</td>
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<tr>
<td></td>
<td>Impression or biopsy; Other (contact lab; requires pre-approval)</td>
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