COMPAC
www.com-pac.com

ZIKA VIRUS SHIPPING SOLUTIONS

Com-Pac International has manufactured Laboratory specimen handling, storage and shipping products for over 25 years. Due to the recent Zika Virus outbreaks, Com-Pac has added two new specimen handling products designed specifically around the recently provided guidance from the Centers for Disease Control and Prevention (CDC) relating to packaging and shipping this virus. We have attached the two documents from the CDC which provide this guidance with the appropriate sections highlighted.

Per the CDC guidance:

- Zika or suspected Zika Virus specimens must be shipped as **"Biological Substance, Category B,"** and is assigned **UN 3373**. Shipment of Category B substances must be packaged in accordance with Department of Transportation Hazardous Materials Regulations 49 CFR, Parts171-180.

- For serology testing, specimens should be shipped either frozen (-70^0 C) on dry ice or refrigerated (4ºC) on blue gel packs.

- For virus isolation and/or nucleic acid amplification testing of tissue specimens, specimens should be frozen as son as possible and shipped on sufficient dry ice to remain frozen until received.

- At least 0.5 mL of serum and/or 1.0 mL of CSF is required for serology testing. Serum samples may be shipped in red top, tiger top or serum separator tubes, measuring no more than 5 cm tall and approximately 13 mm in diameter (e.g. 1.8 mL cryotube or 2.0 mL microtube).

As specified above, the packaging requirements for shipment of Category B substances is regulated by the D.O.T. in the U.S. and the International Air Transport Association (IATA) internationally. You and your employer can be subject to fines and penalties if the packaging regulations are not followed.

- All of Com-Pac's shippers designated for use with Category B specimens have been tested and certified to comply with the UN 6.2 Dangerous Goods Regulations, 49 CFR D.O.T. regulations for air and ground shipments and IATA Packaging Instructions 650 for international shipment. Each of our shippers comes complete with all required absorbents, labels and labeling instructions, and shipping declarations.

- It should be noted that if you are shipping Zika specimens on dry ice, in addition to the labels required for the package containing the specimen, you must affix the dry ice label to the outside of the cooler.

Be sure to check out Com-Pac's new **INFECON® 6200** and **INFECON® 6300** UN certified specimen shippers which are specifically designed to ship the Zika virus as specified by the CDC Guidelines.

800 Industrial Park Road
Carbondale, Illinois 62901
Tel 618.529.2421
Fax 618.549.4408

Zika Virus Shipping Solutions

The CDC has provided the following guidance:

"Zika Virus samples may be shipped as <u>BIOLOGICAL SUBSTANCE, CATEGORY B</u> (UN 3373)."
[CDC Division of Vector-Bone Diseases Memorandum, dated February 07, 2016]

Recommended shipping temperature: Either refrigerated (4° C) on blue Gel Packs, or frozen (-70° C) on dry ice.

Complete Shipping Kits Designed Specifically For Use With the Zika Virus

INFECON® 6200 (½ Liter Vessel)
72 Hours @ -70°C with 22 lbs. Dry Ice
72 Hours @ 4°C with Gel Packs
Up to 6 Standard Tubes
Cat. No. INF-6200

INFECON® 6300 (1 Liter Vessel)
72 Hours @ -70°C with 22 lbs. Dry Ice
72 Hours @ 4°C with Gel Packs
Up to 20 Standard Tubes
Cat. No. INF-6300

Components May be Purchased Separately

INFECON® 2000
½ Liter Vessel, Carton, Bubble Pouch and Labels
Cat. No. INF-2000

INFECON® 3000
1 Liter Vessel, Carton, Bubble Pouch and Labels
Cat. No. INF-3000

INFECON® 6000
Overpack Cooler & Labels Only
76 Hours With 22 lbs. Dry Ice
Cat. No. INF-6000

INFECON® 5000
Dry Ice or Gel Pack Shipper
½ Liter Vessel - 60 Hrs With 5.6 lbs. Dry Ice
Cat. No. INF-5000

INFECON® 5500
Dry Ice or Gel Pack Shipper
1 Liter Vessel - 100 Hrs. With 16 lbs. Dry Ice
Cat. No. INF-5500

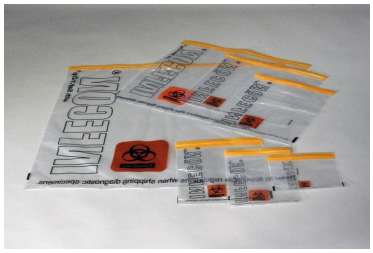
INFECON® Gel Packs
16 Oz. Reusable
Cat. No. INF-900

Com-Pac Shippers - Compliance, Convenience, Cost Effectiveness

- ✓ **Items Designated "For Category B Specimens" are UN Certified, Meet 49 CFR D.O.T. Regulations for Air & Ground Shipments, and Meet ICAO/IATA Packing Instruction 650.**
- ✓ **IItems Include All Accessories, Absorbents, Labels, Labeling Instructions and Shipping Declarations.**
- ✓ **Components Such As Boxes, Vessels, Labels and Absorbents May Be Purchased Separately for Refurbishment and Reuse.**

Check-Out Our Other Specimen Transport and Storage Products

BITRAN® LEAKPROOF SPECIMEN BAGS
3 Mil PE with No Printing
Leakproof Resealable Zipper
Cat. No. Based on Size



INFECON® LEAKPROOF SPECIMEN BAGS
3 Mil PE with Document Pouch
Leakproof Resealable Zipper
Biohazard Logo
Cat. No. Based on Size

INSPEX® TAMPER-EVIDENT ADHESIVE SPECIMEN BAGS
3 Mil PE with Biohazard Logo
Cat. No. 8022-XP 6.5" x 12"

BITRAN® BUBBLE POUCH BAG
Liquid-Tight Bitran Zipper Bag
With Document Pouch
6 Compartment Bubble Pouch
Cat. No. DA-1718 7" X 8"
Cat. No. DA-1912 9" X 12"

SAF-T-ZIP® SPECIMEN BAGS
6" X 9" 2.8 Mil PE Secondary Bag
Document Pouch, Resealable
Zipper & Biohazard Logo
Cat. No. Based on Zipper Color

New Product!

INSPEX® 95 kPa SPECIMEN BAG
6" X 9" Super-Tough Material
Tamper-Evident Adhesive Closure
Cat. No. XP-95-0609

Links to Helpful Websites on Specimen Packaging & Shipping

CDC Guidance for Revised Diagnostic Testing, Specimen Collection and Shipping for Zika Virus (Feb. 07, 2016):
Http://www.cdc.gov/zika/pdfs/denvchikvzikv-testing-algorithm.pdf

Diagram of a "Category B" Biological Substance Shipper:
http://com-pac.com/wp-content/uploads/2012/02/Com-Pac_CategoryBShipper.png

CDC Instructions for Submitting Diagnostic Specimens to the DVBV Arbovirus Diagnostic Lab:
Http://www.cdc.gov/ncezid/dvbd/specimensub/arboviral-shipping.html

CDC IDASH Form Which MUST be Completed Prior to Submitting Specimen Samples (CDC Form 50.34):
Http://www.cdc.gov/laboratory/specimen-submission/form.html

COMPAC
www.com-pac.com

Your Specimen Containment & Shipping Experts for Over 25 Years....

800 Industrial Park Road
Carbondale, Illinois 62901 USA
Tel: 800-824-0817

Memorandum

Date: February 7, 2016

From: CDC, Division of Vector-Borne Diseases

Subject: Revised diagnostic testing for Zika, chikungunya, and dengue viruses in US Public Health Laboratories

Background

Many countries in the Americas now have local transmission of multiple arboviruses that can cause febrile illness with rash, myalgia, or arthralgia. Therefore, laboratory testing has become even more important to confirm the etiology of these diseases. Zika, chikungunya, and dengue virus infections should all be considered for patients with acute fever, rash, myalgia, or arthralgia who have traveled within the previous 2 weeks to an area with ongoing transmission or are living in an area with ongoing transmission. In accordance with the Updated Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age During Ongoing Zika Virus Transmission — United States, 2016 (http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2er.htm), this test algorithm now includes a recommendation to offer serologic testing to asymptomatic pregnant women with a history of travel to areas with local transmission of Zika virus or are living in an area with ongoing transmission. Laboratory evidence of recent chikungunya, dengue, or Zika virus infection is generally accomplished by testing serum to detect viral nucleic acid or virus-specific immunoglobulin (Ig) M and neutralizing antibodies. However, serological cross-reactivity may occur between Zika and other flaviviruses (e.g., dengue, yellow fever, St. Louis encephalitis, Japanese encephalitis, West Nile), so emphasis should be placed on molecular testing (RT-PCR) in acute specimens received from individuals with clinically compatible illness. Laboratory testing for Zika, chikungunya, and dengue viruses is currently available at CDC and several state and territory health departments.

Laboratory assays for acute specimens

During the first 7 days of these illnesses, viral RNA can often be identified in serum, and RT-PCR is the preferred test for Zika, chikungunya, and dengue viruses. In addition, for dengue viruses, NS1 antigen can be detected by ELISA in acute phase specimens but this assay is not widely available in the US. Because viremia decreases over time, a negative RT-PCR collected 5-7 days after symptom onset does not exclude flavivirus infection and serologic testing should be performed.

Virus-specific IgM antibodies may be detectable $\geq$4 days after onset of illness. However, serum collected within 7 days of illness onset may not have detectable virus-specific IgM antibodies. IgM antibodies against Zika virus, dengue viruses, and other flaviviruses have strong cross-reactivity which may generate false positive results in serological tests.

Laboratory assays for convalescent specimens
IgM antibodies typically persist for approximately 2-12 weeks. In patients with a compatible clinical syndrome, serum collected as early as 4 days after illness onset can be tested by Zika, chikungunya, and dengue virus-specific IgM ELISA and positive results confirmed by testing for neutralizing antibodies (Figure 1).

Due to serological cross-reactivity between flaviviruses, current IgM antibody assays cannot reliably distinguish between Zika and dengue virus infections. Therefore, an IgM positive result in a dengue or Zika IgM ELISA test should be considered indicative of a recent flavivirus infection. Plaque-reduction neutralization tests (PRNT) can be performed to measure virus-specific neutralizing antibodies and may be able to determine the cause of primary flavivirus infection. In patients who have received yellow fever or Japanese encephalitis vaccination or infected with another flavivirus in the past, cross-reactive antibodies in both the IgM and neutralizing antibody assays may make it difficult to identify which flavivirus is causing the patient's current illness.

Serologic testing for Zika virus infection may be performed on serum specimens from asymptomatic pregnant women (Figure 2). Serologic test interpretation is complex; a positive IgM result can be difficult to interpret since cross-reactivity can occur with related flaviviruses. PRNT may be able to discriminate between cross-reacting antibodies in primary flavivirus infections. In addition, a negative Zika IgM result obtained 2-12 weeks after travel suggests that infection did not occur. Based on experience with other flaviviruses, we expect that antibodies will be present at least 2 weeks after virus exposure and persist for at least 12 weeks. Information about the performance of serologic testing of asymptomatic individuals is limited.

As with any diagnostic test, while a negative Zika IgM or RT-PCR test would suggest that an infection has not occurred, a negative Zika IgM or RT-PCR test result does not rule out infection with Zika virus.

For additional information, please see Update: Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age with Possible Zika Virus Exposure — United States, 2016 (http://www.cdc.gov/mmwr/volumes/65/wr/mm6505e2er.htm).

Laboratory safety
Zika and dengue viruses are classified as biological safety level (BSL) 2 pathogens while chikungunya virus is classified as a BSL-3 agent. All should be handled in accordance with Biosafety in Microbiological and Biomedical Laboratories (BMBL) guidelines and a risk assessment performed for each laboratory for the specific procedures utilized. Until the association between Zika virus infection and congenital microcephaly is better understood, pregnancy should be considered a significant factor in risk assessment for individuals working with Zika virus, and the involvement of pregnant workers in studies with Zika virus should be minimized. It is recommended that laboratories perform a risk assessment when bringing on new tests, and safety precautions should be based on each laboratory's risk assessment. In particular, because chikungunya virus produces such high levels of viremia, serum from suspected chikungunya virus cases should be treated as potentially infectious even for serological procedures. For further information, see: BMBL http://www.cdc.gov/biosafety/publications/bmbl5/index.htm, and

Healthcare Infection Control Practices Advisory Committee Standard Precautions Standard (http://www.cdc.gov/hicpac/2007IP/2007ip_part3.html)

Options for obtaining/conducting Zika, chikungunya, and dengue virus diagnostic testing

CDC
Zika, chikungunya, and dengue virus RT-PCR, IgM ELISA, and PRNT are performed at CDC. The specific tests performed will depend on the timing of the specimens relative to illness onset and clinical information as outlined in the algorithm figure. To determine the appropriate testing algorithm and interpret results, please provide the date of illness onset, dates of specimen collection, specimen type, description of clinical illness, travel history, flavivirus vaccination history, and contact information for the submitter. Testing will primarily be performed on serum or CSF but other specimen types, including urine, amniotic fluid, and tissues, can be submitted alongside a patient-matched serum specimen for evaluation of the utility of these specimen types.

Within Puerto Rico, please call 787-706-2399 for questions about testing. For submission of specimens, please submit a dengue case investigation report (DCIR) for each specimen which can be downloaded from: http://www.cdc.gov/dengue/clinicalLab/index.html

For all other states and territories, state health departments should contact the CDC Arboviral Diseases Branch at 970-221-6400. A completed DASH form should accompany submitted specimens. More information about submitting specimens to CDC is at: http://www.cdc.gov/ncezid/dvbd/specimensub/arboviral-shipping.html.

State and Territory Health Department Laboratories
RT-PCR: The CDC chikungunya virus and Zika virus RT-PCR protocols follow essentially the same protocol as the CDC West Nile virus RT-PCR assay. CDC will provide chikungunya and Zika virus primer/probe sequences, an RNA-positive control, and chikungunya and Zika virus RT-PCR proficiency panels to state and territory laboratories that have demonstrated proficiency at the CDC West Nile virus RT-PCR assay. Dengue virus RT-PCR kits can be ordered online using the following link:
http://www.cdc.gov/dengue/clinicalLab/realTime.html

Zika virus IgM ELISA: The CDC Zika virus IgM ELISA is similar to the CDC West Nile virus IgM ELISA assay. State and territory laboratories that have demonstrated proficiency in performing the CDC West Nile virus IgM ELISA during the 2015 evaluation can request Zika virus antigen, conjugated antibody, and positive control serum for use in the CDC Zika virus IgM ELISA.

The CDC is currently working on a regulatory pathway to manufacture and distribute assays to support laboratory response to Zika. Further details will be shared when information becomes available.

For state and territory health departments interested in obtaining the materials described above, please contact eocevent278@cdc.gov. If your state or territory health department laboratory does not perform the CDC West Nile virus RT-PCR assay or IgM ELISA assay, consider sending specimens to CDC or using one of the commercial options described below.

Commercially available testing
There are no commercially available FDA-cleared diagnostic assays or kits for Zika virus infection in the United States at this time.

The following commercial reference laboratories perform testing for chikungunya and dengue viruses but none of the assays are FDA-cleared.

- Focus Diagnostics (http://www.focusdx.com/) performs a chikungunya virus RT-PCR and IgM and IgG IFA assays as well as an anti-DENV IgM ELISA.
- ARUP Laboratories (http://www.aruplab.com/) performs chikungunya virus and dengue virus IgG and IgM ELISA testing.
- Quest Diagnostics (http://www.questdiagnostics.com) performs dengue virus IgG and IgM immunoassays.

There is an FDA-cleared kit for anti-DENV IgM antibodies which can be purchased (InBios, USA).

The following chikungunya virus IgM antibody test kits are available for purchase in the United States and provide sensitivity and specificity comparable to that of the CDC assays but may not be FDA-cleared:

- Anti-CHIKV IgM human ELISA kit (Abcam, UK)
- Anti-CHIKV ELISA (IgM) (Euroimmun, Germany)
- Anti-CHIKV IIFT (IgM) (Euroimmun, Germany)

Specimen collection and shipping

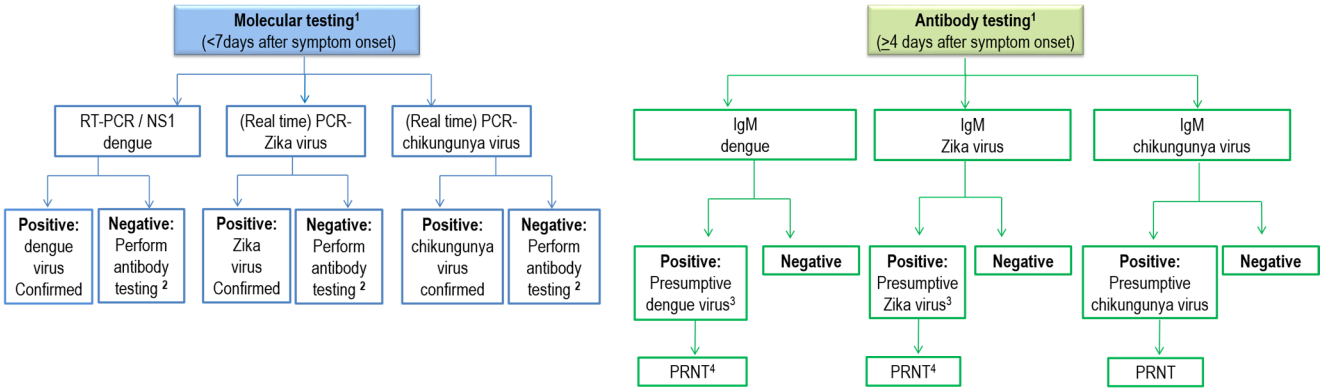
If a patient is suspected of having a Zika, chikungunya, or dengue infection, a serum specimen must be collected. Other specimens may also be collected for testing in addition to the serum specimen including CSF, urine, amniotic fluid and tissues. Information on the patient including the date of illness onset, description of clinical illness, travel history, and flavivirus vaccination history should be documented. Additional information on specimen collection can be found at: http://www.cdc.gov/ncezid/dvbd/specimensub/arboviral-shipping.html

Specimens collected from individuals for Zika virus studies may be transferred within the U.S. as Category B Biological substances in accordance with Department of Transportation Hazardous Materials Regulations (49 CFR Part 171-180). Guidance for packaging samples in accordance with Category B Biological substance requirements can be found in the CDC/NIH Publication Biosafety in Microbiological and Biomedical Laboratories, 5th edition. Additional information about the Department of Transportation Hazardous Materials Transport Regulations may be found at https://www.transportation.gov/pipelines-hazmat.

Reporting

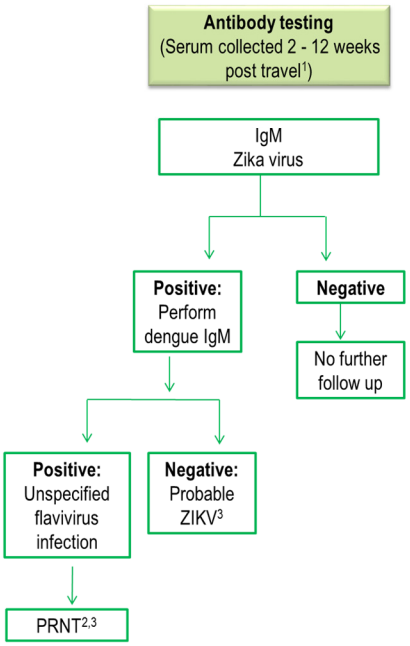
Zika, dengue, and chikungunya are all nationally notifiable conditions; state and territory health departments should report cases to CDC according to standard CSTE case definitions. State and territory health departments are requested to report laboratory-confirmed cases of any arbovirus to CDC through ArboNET, the national surveillance system for arboviral disease.

Tiered algorithm for arbovirus detection for suspected cases of chikungunya, dengue, or Zika (Testing only performed if patient symptomatic and travel history indicates travel to affected area.)



- **[1] Due to extensive cross-reactivity in flavivirus serological assays, for samples collected <7 days post illness onset, molecular detection should be performed first.**
- [2] Perform if sample ≥4 days after symptom onset
- [3] Extensive cross-reactivity would be expected in samples from DENV/ZIKV circulation areas. A positive IgM assay with either antigen should be confirmed by using PRNT against both ZIKV and DENV as well as any other flavivirus (eg. SLEV, ZIKV, WNV, etc.) that might be found in that geographic area (including travel areas).
- [4]PRNT should include any flavivirus (eg. SLEV, ZIKV, WNV, etc.) that might be found in that geographic area (including travel areas).

Testing algorithm for Zika virus detection in asymptomatic, pregnant women



- [1] For women living in areas with ongoing transmission, refer to Updated Interim Guidelines for Health Care Providers Caring for Pregnant Women and Women of Reproductive Age During Ongoing Zika Virus Transmission — United States, 2016 for timing of sample collection.
- [2] Extensive cross-reactivity would be expected in samples from DENV/ZIKV circulation areas. A positive IgM assay with both antigens should be followed up by using PRNT against both ZIKV and DENV as well as any other flavivirus (eg. SLEV, ZIKV, WNV, etc.) that might be found in that geographic area (including travel areas). Depending on previous flavivirus exposure, resolution of infecting flavivirus may not be possible.
- [3] Follow up care should be undertaken as specified in the Interim Guidelines for Pregnant Women During a Zika Virus Outbreak – United States, 2016.

Instructions for Submitting Diagnostic Specimens to the DVBD Arbovirus Diagnostic Laboratory

CDC Submission Form

Please read these instructions for sending diagnostic specimens to CDC. Complete a CDC submission form (CDC 50.34) CDC Data and Specimen Handling (DASH) section form 50.34 for submission of laboratory specimens (http://www.cdc.gov/laboratory/specimen-submission/form.html) .

NOTE: Testing will not be initiated without the inclusion of:

1. **date of onset** of symptoms
2. **date of specimen** collection
   NOTE: If the specimen collection occurs within 8 days after the onset of symptoms, a convalescent specimen will be requested.
3. any **pertinent travel history** (3 months prior to the date of symptom onset)
4. the **patient's name** (**REQUIRED** for submitting specimens)

To enable printing of CDC submission form 50.34, each of the following fields must be completed, as directed:

i. Specimen Origin field (located on 1st page, top left corner), select “HUMAN” from the drop-down menu
ii. Test Order Name field (located on 1st page, top left), select “ARBOVIRUS SEROLOGY” from the drop-down menu
iii. Original Submitter e-mail field (located on 1st page, middle right box), type your e-mail address
iv. Brief clinical summary (located on 2nd page, top of page), include the name(s) of the arbovirus(es) for which you are requesting testing, if known. Also, if you would like to request testing other than serology, please note the type of test requested in this field

Shipping

For information regarding shipping packages and applicable regulations, please refer to the NCEZID Division of Scientific Resources' Specimen Management site (/ncezid/dsr/index.html) for specific information.

Specimen Types and Amounts

a. Acute and convalescent specimens, if available, should be sent together.
b. Ideal timing of specimens for serology:

Specimen	Timing
Acute	3 to 10 days after onset of symptoms
Convalescent	2-3 weeks after acute sample

c. At least 0.5 mL of serum and/or 1.0 mL of CSF is required for serology testing. CSF specimens are routinely tested undiluted and therefore require larger amounts. Whole blood will not be accepted for serology testing. Please transfer serum or CSF to a plastic tube with screw cap measuring no more than 5 cm tall and approximately 13 mm in diameter (e.g. 1.8 mL cryotube or 2.0 mL microtube).
d. For serology testing, the specimen should be kept cold or frozen. The sample may be placed in an insulated container with blue ice packs. Additional blue ice packs should be used in the summer to ensure specimen integrity in hot weather.
e. For virus isolation and/or nucleic acid amplification testing, acceptable specimens are fresh frozen tissue, serum, or cerebrospinal fluid. Tissue specimens should be approximately 1 cm⊃3;, frozen as soon as possible at -70°C, and shipped on enough dry ice so that specimens remain frozen until received. Formalin-fixed specimens are not tested at DVBD and can be submitted to the Special Pathogens Laboratory in Atlanta, GA for immunohistochemistry:

   Infectious Disease Pathology Branch
   Centers for Disease Control and Prevention (MS-G32)
   1600 Clifton Rd, NE
   Atlanta, GA 30333

Testing Results

Test results are normally available 4 to 14 days after specimen receipt. Reporting times for test results may be longer during summer months when arbovirus activity increases. Receipt of a hard copy of the results will take at least 2 weeks after testing is completed. Initial serological testing will be performed using IgM capture ELISA and IgG ELISA. If the initial results are positive, further confirmatory testing may delay the reporting of final results. ALL RESULTS WILL BE SENT TO THE APPROPRIATE STATE HEALTH DEPARTMENT. Notify your state health department of any submissions to CDC.

Shipping Address

Send all specimens to:

CDC-DVBD
ATTN: Arbovirus Diagnostic Laboratory, DRA
CDC/DVBD/ADB
3156 Rampart Road
Fort Collins, CO 80521

Further Assistance

Additional assistance may be obtained from the DVBD Arbovirus Diagnostic and Reference Laboratory at 970-221-6400.

Page last reviewed: April 7, 2014
Page last updated: October 23, 2014
Content source: Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases (NCEZID)
Division of Vector-Borne Diseases (DVBD)

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives. Protecting People.™

Submitting Specimens to CDC

Specimen Submission Form

Submitters sending specimens to CDC for laboratory testing should supply all pertinent information associated with the specimen(s). This information will allow the laboratory to effectively review the test order and perform the appropriate test(s). The information supplied will be included in the laboratory report.

Specimens submitted for testing must be accompanied by CDC Form 50.34 [PDF - 2 pages] (/laboratory/specimen-submission/pdf/form-50-34.pdf).*

Features of the form:

- Pick-lists to select the correct form, order valid tests, enter accurate information
- Interactive Test Directory
- Easier data entry and printing using your computer
- Accurate data transfer using barcodes
- Download and save the form with your data

If you have any questions about the form or the submission process, check the "Help and FAQs (/laboratory/specimen-submission/help-faqs.html)" section or the "Training (/laboratory/specimen-submission/training.html)" Section to view a training webinar on the new submission form and view form specific training manuals.

* Persons with disabilities experiencing problems accessing this document should contact CDC-INFO by either completing the form at www.cdc.gov/cdc-info/requestform.html (http://www.cdc.gov/cdc-info/requestform.html) and use subject "508 Accommodation PR#31", or by calling 800-232-4636 (TTY number: 888-232-6348) and ask for 508 Accommodation PR#31.

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National Center for Emerging and Zoonotic Infectious Diseases (NCEZID)

Centers for Disease Control and Prevention 1600 Clifton Road Atlanta, GA 30329-4027, USA
800-CDC-INFO (800-232-4636) TTY: (888) 232-6348 - Contact CDC–INFO