SIEMENS

ADVIA Centaur® XP
ADVIA Centaur® XPT
Immunoassay Systems

Zika Test

Note: The ADVIA Centaur® Zika test requires the use of two assays sold separately. All Zika samples must be tested initially with the ADVIA Centaur Zika Ab assay. All ADVIA Centaur Zika Ab equivocal samples must be tested with the ADVIA Centaur Zika IgM assay before results are reported. Due to the need to test all ADVIA Centaur Zika Ab equivocal samples with the ADVIA Centaur Zika IgM assay, both assays share a common Instructions for Use (IFU).

For Use Under Emergency Use Authorization (EUA) Only

For *in vitro* diagnostic use

RxOnly

Current revision and date[a]	Rev. D, 2017-12	
Product Name	ADVIA Centaur® Zika Ab (ZikaAb) (100 tests)	REF 11200700
	ADVIA Centaur Zika IgM (ZikaM) (50 tests)	REF 11200103
Systems	ADVIA Centaur XP system ADVIA Centaur XPT system	
Materials Required but Not Provided	ADVIA Centaur Wash 1 (2 x 1500 mL)	REF 01137199
	ADVIA Centaur Wash 1 (2 x 2500 mL)	REF 03773025
	ADVIA Centaur ZikaAb Quality Control	REF 11200712
	ADVIA Centaur ZikaM Quality Control	REF 11200111
Specimen Types	Human serum, plasma (EDTA, lithium heparin)	
Measuring Interval	0.00–10.00 Index	
Reagent Storage	2–8°C	
Reagent On-System Stability	28 days	

[a] In Rev. B or later, a vertical bar in the margin indicates a technical update to the previous version.

Intended Use

The ADVIA Centaur® Zika test is intended for in vitro diagnostic use in the presumptive qualitative detection of IgM antibodies to the Zika virus in human serum and plasma (potassium EDTA or lithium heparin, each collected alongside a patient-matched serum specimen) specimens collected from individuals meeting CDC Zika virus clinical criteria (e.g. a history of clinical signs and symptoms associated with Zika virus infection) and/or CDC Zika virus epidemiological criteria (for instance, history of residence in or travel to a geographic region with active Zika transmission at the time of travel, or other epidemiological criteria for which Zika virus testing may be indicated). Specimens from symptomatic patients or returning travelers from endemic areas should not be collected prior to 8 days after onset of symptoms or risk of exposure, respectively. The assay is intended for use in laboratories in the United States

that are certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA), 42 U.S.C. §263a, to perform high or moderate complexity tests, or by similarly qualified non-U.S. laboratories, consistent with the latest CDC guideline for the diagnosis of Zika virus infection.

Specimens are tested using the ADVIA Centaur XP and ADVIA Centaur XPT systems. Assay results are for the presumptive detection of IgM antibodies to Zika Virus (ZIKV). The detection of IgM antibodies to the Zika virus is determined by combining in an algorithm the measurements of the ADVIA Centaur Zika Ab (ZikaAb) assay and, as applicable, the ADVIA Centaur Zika IgM (ZikaM) assay. Positive results are not definitive for the diagnosis of Zika virus infection. False positive results are possible in patients with a history of infection with other Flaviviruses. Confirmation of the presence of anti-Zika IgM antibodies in presumptive positive specimens requires additional testing according to the latest CDC guideline for the diagnosis of Zika virus infection. Within the United States and its territories, laboratories are required to report presumptive positive IgM results to the appropriate public health authorities.

Results of this test cannot be used as the sole basis of patient management decisions and must be combined with clinical observations, patient history, epidemiological information, and other laboratory evidences. Zika IgM levels over the course of illness are not well characterized. IgM levels are variable, may be detectable near day four post onset of symptoms and persist up to approximately 12 weeks following initial infection.

Negative results do not preclude the possibility of Zika virus infection, past or present. Negative results may be seen in specimens collected before day four post onset of symptoms or after the window of detectable IgM closes.

The ADVIA Centaur Zika test is intended for use by trained laboratory personnel who have received training in the use of and interpretation of the ADVIA Centaur Zika test. The assay is only for use under the Food and Drug Administration's Emergency Use Authorization.

Summary and Explanation

Zika Virus (ZIKV) is a single-stranded, positive-sense RNA virus.[1] ZIKV belongs to the family Flaviviridae which includes closely related dengue, West Nile, Japanese encephalitis, and yellow fever viruses.[2] ZIKV was first isolated from rhesus monkey in Zika forest of Uganda in 1947.1 In humans, ZIKV infection was first reported in Nigeria in 1954 and the first ZIKV epidemic was reported on Western Pacific Island of Yap in 2007 and later in French Polynesia in 2013 and 2014. In the Americas, ZIKV outbreak first emerged in Brazil in March 2015 and spread to several countries and territories by March 2016.[3]

ZIKV infection is mainly transmitted by bite of infected mosquito *Aedes aegypti*. However, ZIKV transmission from mother to fetus during pregnancy and through sexual contact with infected partners has been reported.[3] Potential transmission through blood transfusion has been documented.[1] Most people infected with ZIKV exhibit mild symptoms or are asymptomatic (do not develop symptoms).[4] Common symptoms include fever, rash, joint pain and red eyes and these symptoms can be observed up to a week.[3, 4] ZIKV infection in pregnant women may cause microcephaly (where the baby's head is smaller than expected, a sign of incomplete brain development) in fetuses, which is a major public health concern.[1, 3, 4] The association of ZIKV infection with Guillain-Barre syndrome, a neurological illness that can cause temporary paralysis, has been reported.[1, 3, 4]

During ZIKV infection, viremia is expected for a week after onset of symptoms.[2] IgM antibodies specific to ZIKV is reported to develop during the first week after development of symptoms.[2] No data is available for duration of IgM antibody persistence but it is expected to be present for 12 weeks.[2] The detection of ZIKV specific IgM antibodies is used for diagnosis and appropriate clinical management of the suspected Zika virus infected patient.[2]

Principles of the Procedure

The ADVIA Centaur Zika Ab assay is an antibody capture immunoassay using a 2-pass format. In the first pass, coated microparticles (Solid Phase) are added to the cuvette, binding antibodies from the patient sample. The captured antibodies are washed and resuspended. In the second pass, the anti-Zika antibodies captured on the Solid Phase are detected by the addition of NS1 antigen labeled with acridinium ester (Lite Reagent) for chemiluminescent detection.

The ADVIA Centaur Zika IgM assay is an IgM capture immunoassay using a 2-pass format. In the first pass the microparticles, coated with anti-human IgM monoclonal antibody (Solid Phase), are added to the cuvette, binding IgM from the patient sample. The captured IgM antibodies are washed and resuspended. In the second pass the anti-Zika IgM captured on the Solid Phase is detected by the addition of NS1 antigen labeled with acridinium ester (Lite Reagent) for chemiluminescent detection.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur ZikaAb ReadyPack® primary reagent pack; Lite Reagent	5.0 mL/reagent pack NS1 Antigen labeled with acridinium ester (0.4 µg/mL) in buffered saline with surfactant, blockers, sodium azide (< 0.1%) and preservatives	2–8°C	* On-system: 28 days
ADVIA Centaur ZikaAb ReadyPack primary reagent pack; Solid Phase Reagent	25.0 mL/reagent pack Streptavidin-coated paramagnetic microparticles preformed with biotinylated anti-human IgM antibody (~0.1 mg/mL) in buffered saline with surfactant, blockers, sodium azide (< 0.1%) and preservatives	2–8°C	* On-system: 28 days
ADVIA Centaur ZikaAb ReadyPack primary reagent pack; Ancillary Well Reagent	5.0 mL/reagent pack Buffered saline with surfactant, blockers, sodium azide (< 0.1%) and preservatives	2–8°C	* On-system: 28 days
ADVIA Centaur ZikaAb Calibrators High Low	1.0 mL/vial Processed human plasma negative or positive for Zika IgM antibodies with sodium azide (< 0.1%) and preservatives.	2–8°C	* Opened: 60 days On-system: 8 hours
ADVIA Centaur ZikaM ReadyPack primary reagent pack; Lite Reagent	2.5 mL/reagent pack NS1 Antigen labeled with acridinium ester (0.4 µg/mL) in buffered saline with surfactant, blockers, sodium azide (< 0.1%) and preservatives	2–8°C	* On-system: 28 days
ADVIA Centaur ZikaM ReadyPack primary reagent pack; Solid Phase Reagent	12.5 mL/reagent pack Streptavidin-coated paramagnetic microparticles preformed with biotinylated anti-human IgM antibody (~0.1 mg/mL) in buffered saline with surfactant, blockers, sodium azide (< 0.1%) and preservatives	2–8°C	* On-system: 28 days
ADVIA Centaur ZikaM ReadyPack primary reagent pack; Ancillary Well Reagent	2.5 mL/reagent pack Buffered saline with surfactant, blockers, sodium azide (< 0.1%) and preservatives	2–8°C	* On-system: 28 days

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur ZikaM Calibrators High Low	1.0 mL/vial Processed human plasma negative or positive for Zika IgM antibodies with sodium azide (< 0.1%) and preservatives.	2–8°C	* Opened: 60 days On-system: 8 hours
ADVIA Centaur Wash 1[a] WASH 1	1500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	* On-system: 1 month
ADVIA Centaur Wash 1[a] WASH 1	2500 mL/pack Phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	* On-system: 1 month

[a] Refer to *Materials Required but Not Provided*.
* All unopened reagents are stable until the expiration date on the product at the storage conditions indicated.

Warnings and Precautions

Safety data sheets (MSDS/SDS) are available on siemens.com/healthcare.

CAUTION! POTENTIAL BIOHAZARD

Contains human source material. Each donation of human blood or blood component was tested by FDA-approved methods for the presence of antibodies to human immunodeficiency virus type 1 (HIV-1) and type 2 (HIV-2) as well as for hepatitis B surface antigen (HBsAg) and antibody to hepatitis C virus (HCV). The test results were negative (not repeatedly reactive). No test offers complete assurance that these or other infectious agents are absent; this material should be handled using good laboratory practices and universal precautions.[5–7]

Laboratory biosafety guidance for working with Zika virus specimens is provided at http://www.cdc.gov/zika/statelabs/index.html. It is recommended that laboratories perform a risk assessment when conducting new tests and safety precautions should be based on the laboratory's risk assessment. The Zika virus is considered a pathogen that can be safely worked with in a biosafety level 2 (BSL-2) laboratory.

CAUTION

This device contains material of human and animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirement.

H317	**Warning**
P272, P280, P302+P352, P333+P313, P363, P501	May cause an allergic skin reaction. Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/protective clothing/eye protection/face protection. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Wash contaminated clothing before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations. **Contains:** reaction mass of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1); ADVIA Centaur Zika Ab Calibrators; ADVIA Centaur Zika IgM Calibrators

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For professional use.

For *in vitro* diagnostic use.

For Use Under Emergency Use Authorization (EUA) Only

Use routine laboratory precautions. Do not eat, drink, smoke or apply cosmetics in the area where samples and assay materials are handled. Avoid any contact between skin, eyes or mucous membranes.

Wear protective clothing such as laboratory coats, disposable gloves and eye protection when handling patient specimens. Wash hands thoroughly after handling samples and assay materials.

Avoid splashing or forming aerosols when handling or transferring samples, calibrators and controls. Any spill should be decontaminated with 10% bleach (0.5% sodium hypochlorite) and disposed of as though potentially infectious.

Preparing Reagents

All reagents are liquid and ready to use.

Note

- Discard the primary reagent packs at the end of the on-system stability interval.
- Do not use reagents beyond the expiration date.

Storing and Stability

Store unopened reagents upright at 2–8°C.

Protect unopened reagent packs from all heat and light sources. Reagent packs loaded on the system are protected from light.

All reagents are stable at 2–8°C until the expiration date on the product.

Specimen Collection and Handling

The ADVIA Centaur Zika test has been authorized for use with human serum and plasma (EDTA or lithium heparin) specimen types. However, confirmatory testing requires the use of serum samples. Therefore, serum is the primary diagnostic specimen for Zika virus RNA and serologic testing, and should be the priority specimen for collection and testing with the ADVIA Centaur Zika test. If plasma specimens are used with the ADVIA Centaur Zika test, a patient-matched serum specimen should also be collected, or if this is not possible, an additional serum specimen should be collected soon after the original specimen.

Collecting the Specimen

- Collect serum and plasma using recommended procedures for collection of diagnostic blood specimens by venipuncture.[8]
- Follow the instructions provided with your specimen collection device for use and processing.[9]
- Observe universal precautions for venipuncture when collecting blood samples. Handle all samples as if capable of transmitting disease.
- Complete clot formation should take place before centrifugation. Serum should be physically separated from cells as soon as possible.[10]
- Keep tubes stoppered and upright at all times.
- Do not use specimens with obvious microbial contamination.
- Test specimens as soon as possible after collecting.

Storing the Specimen

- Store samples capped and upright at all times at 2–8°C for up to 5 days.
- Do not use samples that have been stored at room temperature for longer than 24 hours.
- Specimens may be stored on the system for up to 8 hours.
- Separated specimens are stable for up to 24 hours at room temperature, and for up to 5 days at 2–8°C. For longer storage, specimens may be frozen for up to 40 days at ≤ -20°C. Avoid more than 3 freeze-thaw cycles. Do not store in a frost-free freezer.

The purpose of handling and storage information is to provide guidance to users. It is the responsibility of the individual laboratory to use all available references and/or its own studies when establishing alternate stability criteria to meet specific needs.

Transporting the Specimen

- Package and label samples for shipment in compliance with applicable federal regulations covering the transport of clinical samples and etiological agents.
- Store samples stoppered and upright at 2–8°C upon arrival. If shipment is expected to exceed 2 days, ship specimens frozen.

Procedure

Materials Provided

The following materials are provided with ADVIA Centaur Zika Ab:

REF	Contents	Number of Tests
11200700	1 ReadyPack primary reagent pack containing ADVIA Centaur ZikaAb Lite Reagent, Ancillary Well Reagent, and Solid Phase Reagent	100
	1 vial ADVIA Centaur ZikaAb low calibrator CAL L	
	1 vial ADVIA Centaur ZikaAb high calibrator CAL H	
	ADVIA Centaur ZikaAb Calibrator Assigned Value Card and barcode labels	
	ADVIA Centaur ZikaAb Master Curve Card	

The following materials are provided with ADVIA Centaur Zika IgM:

REF	Contents	Number of Tests
11200103	1 ReadyPack primary reagent pack containing ADVIA Centaur ZikaM Lite Reagent, Ancillary Well Reagent, and Solid Phase Reagent	50
	1 vial ADVIA Centaur ZikaM low calibrator CAL L	
	1 vial ADVIA Centaur ZikaM high calibrator CAL H	
	ADVIA Centaur ZikaM Calibrator Assigned Value Card and barcode labels	
	ADVIA Centaur ZikaM Master Curve Card	

Materials Required but Not Provided

The following materials are needed to perform this test, but are not provided:

Item		Description	
REF	01137199 (112351)	ADVIA Centaur Wash 1 WASH 1	2 x 1500 mL/pack
REF	03773025	ADVIA Centaur Wash 1 WASH 1	2 x 2500 mL/pack
REF	11200111	ADVIA Centaur ZikaM Quality Control	2 x 2 mL negative control CONTROL –
			2 x 2 mL positive control CONTROL +
		Lot-specific assigned value card and barcode labels	
REF	11200712	ADVIA Centaur ZikaAb Quality Control	2 x 2 mL negative control CONTROL –
			2 x 2 mL positive control CONTROL +
		Lot-specific assigned value card and barcode labels	

Assay Procedure

All patient samples must be tested initially with the ADVIA Centaur Zika Ab assay.

All ADVIA Centaur Zika Ab equivocal samples must be tested with the ADVIA Centaur Zika IgM assay.

Note When using the ADVIA Centaur Zika Ab assay on the ADVIA Centaur XP system, some samples that are > 10.00 Index will be reported as reactive. These samples must be treated as equivocal and undergo reflex testing with the ADVIA Centaur Zika IgM assay.

ADVIA Centaur Zika Ab

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following actions:

1. Dispenses 15 µL of sample into a cuvette.
2. Dispenses 250 µL of Solid Phase, and incubates for 18.25 minutes at 37°C.
3. Separates, aspirates, and washes the cuvettes with ADVIA Centaur Wash 1.
4. Dispenses 50 µL each of Ancillary Well Reagent and Lite Reagent and incubates for 18 minutes at 37°C.
5. Separates, aspirates, and washes the cuvettes with ADVIA Centaur Wash 1.
6. Dispenses 300 µL of ADVIA Centaur Acid Reagent and 300 µL of ADVIA Centaur Base Reagent to initiate the chemiluminescent reaction.
7. Reports results according to the selected option, as described in the system operating instructions.

A direct relationship exists between the level of Zika antibodies present in the patient sample and the amount of relative light units (RLUs) detected by the system.

ADVIA Centaur Zika IgM

For detailed instructions on performing the procedure, refer to the system operating instructions.

The system automatically performs the following actions:

1. Dispenses 15 µL of sample into a cuvette.
2. Dispenses 250 µL of Solid Phase, and incubates for 18.25 minutes at 37°C.
3. Separates, aspirates, and washes the cuvettes with ADVIA Centaur Wash 1.

4. Dispenses 50 µL each of Ancillary Well Reagent and Lite Reagent and incubates for 18 minutes at 37°C.
5. Separates, aspirates, and washes the cuvettes with ADVIA Centaur Wash 1.
6. Dispenses 300 µL of ADVIA Centaur Acid Reagent and 300 µL of ADVIA Centaur Base Reagent to initiate the chemiluminescent reaction.
7. Reports results according to the selected option, as described in the system operating instructions.

A direct relationship exists between the level of Zika antibodies present in the patient sample and the amount of relative light units (RLUs) detected by the system.

Defining Reflex Testing

All samples that are ≥ 0.80 Index with the ADVIA Centaur Zika Ab assay must be reflex tested using the ADVIA Centaur Zika IgM assay.

The ADVIA Centaur system automatically calculates an Index value for each of the Zika Ab and Zika IgM assays based on each assay's calibrations.

ADVIA Centaur XP

Refer to *Section 8 - Defining Reference Ranges, Results Interpretations and Reflex Tests* in the ADVIA Centaur XP operator's guide for additional information.

Automatic reflex testing of the ADVIA Centaur Zika test is predefined in the test definition of the ADVIA Centaur XP system.

Note In some instances of highly reactive samples, the system will not automatically perform reflex testing. In these instances, the operator must manually schedule reflex testing with the ADVIA Centaur Zika IgM assay.

ADVIA Centaur XPT

Refer to *Chapter 10 - Defining Reference Ranges, Results Interpretations and Reflex Tests* in the ADVIA Centaur XPT operator's guide for additional information.

Automatic reflex testing of the ADVIA Centaur Zika test is **not** predefined in the test definition of the ADVIA Centaur XPT system.

To set up automatic reflex testing of the ADVIA Centaur Zika test on your system, follow these steps.

1. On the command bar, select **Setup** and then select **Test Definition**.
2. Select **ZikaAb** and then select **Ranges**.
3. On the **Interpretation** tab, select **Edit**.
4. In the **Equivocal** box, select **ZikaM** from the **Reflex** drop-down list.
5. Select **Save**.
6. On the **Index** tab, select **Edit**.
7. In the **Above Range** box, select **ZikaM** from the **Reflex** drop-down list.
8. Select **Save**.

Defining Result Interpretations

A result interpretation is a label that the system must use for results within a certain range. The default result interpretations for the ADVIA Centaur Zika Ab assay are nonreactive and equivocal. The result interpretations for the ADVIA Centaur Zika IgM assay are nonreactive and reactive.

An additional result of "Reflex to ZikaM" must be added to samples that are ≥ 0.80 Index (equivocal) with the ADVIA Centaur Zika Ab assay.

Follow these steps for the appropriate system type.

ADVIA Centaur XP

Refer to *Section 8 - Defining Reference Ranges, Results Interpretations and Reflex Tests* in the ADVIA Centaur XP operator's guide for additional information.

1. Enable ZikaAb Test Definition.
2. Select **Definition**.
3. Select **Edit** then **Calculate Results**.
4. Select **Add New**.
5. Add "**Reflex to ZikaM**" in the interpretation box and "**0.8**" in the low range box.
6. Select **Add New**.
7. Select **Continue**.
8. Select **Save**.

ADVIA Centaur XPT

Refer to *Chapter 10 - Defining Reference Ranges, Results Interpretations and Reflex Tests* in the ADVIA Centaur XPT operator's guide for additional information.

1. On the command bar, select **Setup** and then select **Test Definition**.
2. Select **ZikaAb** and then select **Ranges**.
3. On the **Interpretation** tab, select **Add Range**.
4. In the **Interpretation Type: Operator** (yellow) box, replace the default text ("Interpretation") with "**Reflex to ZikaM**".
5. In the **Reflex to ZikaM** box, set limits as 0.8 (low) and 9999 (high).
6. Select **Save**.

The range values must be absolute values. The system does not validate these values against any defined interpretations.

Preparing the System

A daily cleaning procedure must be completed prior to and after your laboratory's batched manually scheduled consolidated testing for the ADVIA Centaur Zika test.

Ensure that the system has sufficient primary reagent packs. For detailed information about preparing the system, refer to the system operating instructions.

Mix the primary reagents by hand (refer to *Preparing Reagents*). Load the ReadyPack primary reagent packs in the primary reagent area using the arrows as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. For detailed information about loading reagents, refer to the system operating instructions.

Important Information for Scheduling the ADVIA Centaur Zika Test

The ADVIA Centaur Zika Ab assay and Zika IgM assay may be run together, but must not be run with other ADVIA Centaur commercial assays.

It is recommended that the ADVIA Centaur Zika test be run in a manually scheduled assay consolidated worklist.

- See *Manually Scheduling Samples, Scheduling Batches* in the ADVIA Centaur XP System Operators Guide.
- See *Manually Creating Orders, Creating a Batch Order* in the ADVIA Centaur XPT Operators Guide.

Preparing the Samples

The ADVIA Centaur Zika test assay requires 15 µL of sample for a single determination of Zika Ab and 15 µL for a single determination of Zika IgM. This volume does not include the unusable volume in the sample container or the additional volume required when performing duplicates or other tests on the same sample. The minimum required volume to run 1 replicate of the ADVIA Centaur Zika Ab assay and 3 replicates of the ADVIA Centaur Zika IgM assay will typically vary between 150 µL to 250 µL, depending on the type of sample container used. For detailed information about determining the minimum required volume, refer to the system operating instructions.

Test samples as soon as possible after collecting. If samples are not tested immediately, follow the storage instructions provided (refer to *Storing the Specimen*).

Before placing samples on the system, ensure that samples have the following characteristics:

- Samples are free of fibrin or other particulate matter.
- Samples are free of bubbles or foam.

Note Remove particulates by centrifugation according to CLSI guidance and the collection device manufacturer's recommendations.[11]

Note If frozen samples are used, it is recommended that they are thawed at room temperature while gently rocking for 30 minutes prior to testing.

On-System Stability

The ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assay reagents are stable onboard the system for 28 days and are stable unopened until the expiration date on the product. Discard reagent packs at the end of the on-system stability interval. Do not use products beyond the expiration date printed on the product labeling.

ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM Calibrators are stable on the system for 8 hours. Dispose of any calibrator that remains in the sample cups after 8 hours on the system.

Defining Master Curve Values

The ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays require that you define the Master Curve when using a new reagent lot number. Use the barcode reader or keyboard to enter the Master Curve values on the system. The Master Curve Card contains the Master Curve values. For detailed information about defining the Master Curve, refer to the system operating instructions.

Performing Calibration

For calibration of the ADVIA Centaur Zika Ab assay, use ADVIA Centaur Zika Ab Calibrators provided with each kit. For calibration of the ADVIA Centaur Zika IgM assay, use ADVIA Centaur Zika IgM Calibrators provided with each kit. The calibrators provided in these kits are matched to the ReadyPack primary reagent pack; they are not interchangeable between the ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays.

Note The Low and High Calibrators provided in this kit are matched to the ReadyPack primary reagent pack. Do not mix calibrator lots with different lots of reagent packs.

Each lot of calibrators contains a Calibrator Assigned Value Card to facilitate entering the calibration values on the system. Enter the values using the barcode scanner or the keyboard. For detailed information about entering calibrator values, refer to the system operating instructions.

Perform the calibration procedure using the following steps:

Note This procedure uses calibrator volumes sufficient to measure each calibrator in duplicate.

1. Schedule the calibrators to the worklist.
2. Label 2 sample cups with calibrator barcode labels: 1 for the low and another for the high.

3. Gently mix the calibrators and dispense 4–5 drops into the appropriate sample cups.

   Note Each drop from the calibrator vial is approximately 50 µL.
4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

Note Dispose of any calibrator remaining in the sample cups after 8 hours. Do not refill sample cups when the contents are depleted; if required, dispense fresh calibrators.

Calibration Frequency

Calibrate the assay at the end of the 14-day calibration interval.

Additionally, the ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays require a two-point calibration:

- When changing lot numbers of primary reagent packs.
- When replacing system components.
- When quality control results are repeatedly out of range.

Using Barcode Labels

Note Calibrator barcode labels are lot-number specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.

Use the ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM Calibrator barcode labels to identify the Low and High Calibrator sample cups when performing the ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays. Place the barcode label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

Performing Master Curve Calibration

The ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays require a Master Curve calibration when using a new lot number of Lite Reagent, Solid Phase, and Ancillary Well Reagent. For each new lot number of Lite Reagent, Solid Phase, and Ancillary Well Reagent, use the barcode reader or keyboard to enter the Master Curve values on the system. The Master Curve card contains the Master Curve values. For detailed information about entering calibration values, refer to the system operating instructions.

Calibration Procedure

Note This procedure uses calibrator volumes sufficient to measure each calibrator in duplicate. The required calibrator volume depends on the number of assays being calibrated using these calibrators, and the number of calibrator replicates. A separate calibration procedure must be performed for each of the ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays.

For detailed information about processing calibrators, refer to the system operating instructions.

Perform the calibration for ADVIA Centaur Zika Ab or ADVIA Centaur Zika IgM assays using the following steps:

1. Ensure that the appropriate master curve values are entered on the system. Refer to *Defining Master Curve Values*.
2. Enter the calibrator assigned values found on the ADVIA Centaur Zika Ab or ADVIA Centaur ZikaM Calibrator Assigned Value Card into the system.
3. Load the required reagents and other materials required for the assay.
4. Schedule the calibrators to the worklist.

5. Label 2 sample cups with ADVIA Centaur Zika Ab or ADVIA Centaur Zika IgM Calibrator barcode labels: 1 cup for the low calibrator and 1 cup for the high calibrator. Place the barcode label on each sample cup with the readable characters oriented vertically.

Note Calibrator barcode labels are lot-number-specific. Do not use barcode labels from one lot of calibrators with any other lot of calibrators.

6. Gently mix the calibrators and dispense 4–5 drops into the appropriate sample cups. Avoid bubbles.

Note The required volume for testing depends on the number of replicates. Each drop is approximately 50 µL.

7. Load the calibrator sample cups in a rack.
8. Place the rack in the sample entry queue.
9. Start the entry queue, if required.

Note Dispose of any calibrator that remains in the sample cups after 8 hours on the system. Do not refill sample cups when the contents are depleted; if required, dispense fresh calibrators.

Performing Quality Control

Siemens Healthcare Diagnostics recommends the use of ADVIA Centaur Zika Ab Quality Control (REF 11200712) with the ADVIA Centaur Zika Ab assay and ADVIA Centaur Zika IgM Quality Control (REF 11200111) with the ADVIA Centaur Zika IgM assay. Perform the quality control procedure according to the quality control instructions for use.

Quality control samples should be assayed at least once on each day that samples are analyzed to monitor system performance and chart trends. Quality control samples should also be assayed when performing a two-point calibration.

Follow local, state and federal government regulations or accreditation requirements for quality control frequency. Individual laboratory quality control programs may require more frequent quality control testing.

For detailed information about entering quality control values, refer to the system operating instructions.

A satisfactory level of performance is achieved when the analyte values obtained are within the acceptable control range for the system or within your range, as determined by an appropriate internal laboratory quality control scheme.

If the ADVIA Centaur Zika Ab controls are out of range, specimen results with the ADVIA Centaur Zika Ab assay are invalid and must be repeated.

If the ADVIA Centaur Zika IgM controls are out of range, specimen results with the ADVIA Centaur Zika IgM assay are invalid and must be repeated.

Taking Corrective Action

If the quality control results do not fall within the expected values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required system maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.
- If necessary, contact your local technical support provider or distributor for assistance.
- Repeat testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

The system reports ADVIA Centaur Zika Ab results in Index Values and as nonreactive or equivocal.

The system reports ADVIA Centaur Zika IgM results in Index Values and as nonreactive or reactive.

For detailed information about how the system calculates results, refer to the system operating instructions.

Note When using the ADVIA Centaur Zika Ab assay on the ADVIA Centaur XP system, some samples that are > 10.00 Index will be reported as reactive. These samples must be treated as equivocal and undergo reflex testing with the ADVIA Centaur Zika IgM assay.

Interpretation of Results

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings. Results must not be reported to the patient until all testing is completed per the ADVIA Centaur Zika test algorithm depicted below.

The ADVIA Centaur system reports ADVIA Centaur Zika Ab results as nonreactive or equivocal, based on index values established with the calibrators:

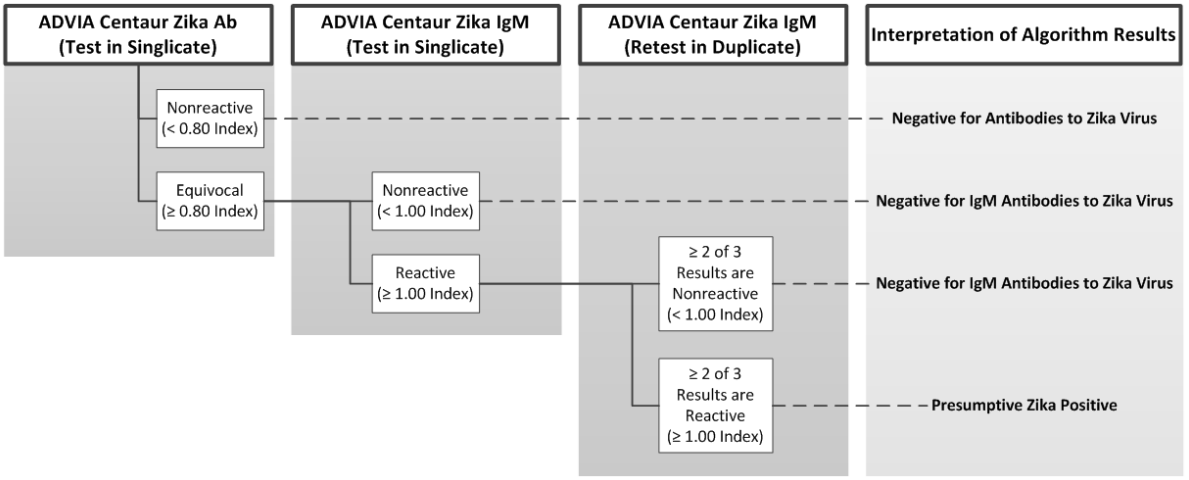
- Samples with a calculated value < 0.80 Index (nonreactive) using the ADVIA Centaur Zika Ab assay are Negative for antibodies to Zika virus, and must be reported accordingly.
- Samples with a calculated value ≥ 0.80 Index (equivocal) using the ADVIA Centaur Ab assay must be reflex tested using the ADVIA Centaur Zika IgM assay.

The ADVIA Centaur system reports ADVIA Centaur Zika IgM results as nonreactive or reactive, based on index values established with the calibrators:

- Samples with a calculated value < 1.00 Index (nonreactive) using the ADVIA Centaur Zika IgM assay are Negative for IgM antibodies to Zika virus, and must be reported accordingly.
- Samples with a calculated value ≥ 1.00 Index (reactive) using the ADVIA Centaur Zika IgM assay must be retested in duplicate:
    - If ≥ 2 out of 3 results using the ADVIA Centaur Zika IgM assay are < 1.00 Index (nonreactive), the sample is Negative for IgM antibodies to Zika virus, and must be reported accordingly.
    - If ≥ 2 out of 3 results using the ADVIA Centaur Zika IgM assay are ≥ 1.00 Index (reactive), the sample is Presumptive Zika Positive, and must be reported accordingly. The result must be confirmed according to the latest CDC guideline for the diagnosis of Zika virus infection. For information regarding the Zika testing algorithm, refer to CDC guidance for state and local public health laboratories at https:www.cdc.gov/zika/laboratories/index.html.

The cutoff for the ADVIA Centaur Zika IgM assay was established and verified based on results of testing with characterized specimens.

Refer to the following testing algorithm for the interpretation of sample results:



Note When using the ADVIA Centaur Zika Ab assay on the ADVIA Centaur XP system, some samples that are > 10.00 Index will be reported as reactive. These samples must be treated as equivocal and undergo reflex testing with the ADVIA Centaur Zika IgM assay.

Testing of specimens collected prior to 8 days after onset of symptoms or risk of exposure, respectively, is not supported by the authorization. However, if specimens collected before 8 days after onset of symptoms are inadvertently tested and the system reports results as nonreactive, testing should be repeated with a later bleed taken at least 7 days from the first specimen.

In the case of pregnant women follow the latest CDC interim pregnancy guidance for healthcare providers regarding clinical management of negative results (http//www.cdc.gov/zika/hc-providers/index.html).

Limitations

The following information pertains to limitations of the ADVIA Centaur Zika test:

- Specimens from symptomatic patients or travelers to endemic areas should not be collected prior to 8 days after onset of symptoms or risk of exposure, respectively.
- Recent Zika virus infection cannot be ruled out if test results from specimens collected more than 12 weeks after symptom onset or risk of exposure are negative by the ADVIA Centaur Zika test.
- The ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays must not be run with other ADVIA Centaur commercial assays.
- It is recommended that the ADVIA Centaur Zika test be run in a manually scheduled assay consolidated worklist.
- Results must not be reported to the patient until all testing is completed per the ADVIA Centaur Zika test algorithm.
- Assay performance characteristics have not been established for immunocompromised or immunosuppressed patients.
- Do not use specimens with obvious microbial contamination.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[12] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous values may be observed. Additional information may be required for diagnosis.
- In patients receiving therapy with high doses of biotin (that is, more than 5 mg/day), ensure blood draw is taken at least 8 hours after the last biotin administration.

- The ADVIA Centaur Zika test is limited to the detection of IgM antibodies to the Zika virus in human serum or plasma (EDTA or lithium heparin).
- A reactive Zika test result does not exclude co-infection by another Flavivirus.
- A nonreactive test result does not exclude the possibility of exposure to or infection with the Zika virus. IgM antibodies to Zika virus may be undetectable in some stages of the infection and in some clinical conditions.
- Assay performance characteristics have not been established when the ADVIA Centaur Zika test is used in conjunction with other manufacturers' assays for specific Zika serological markers.
- The performance of the ADVIA Centaur Zika test has not been established with cord blood, neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum or plasma, such as saliva, urine, amniotic fluid, or pleural fluid.
- The ADVIA Centaur Zika test has not been evaluated in a pediatric population.
- The ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays have not been evaluated for testing pooled blood and plasma and products made from such pools.

For Use Under Emergency Use Authorization (EUA) Only

Conditions of Authorization for Laboratories

The ADVIA Centaur Zika test Letter of Authorization, along with the authorized Fact Sheet for Healthcare Providers, the authorized Fact Sheet for Patients and authorized labeling are available on the FDA website:

https://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm

Use of the ADVIA Centaur Zika test must follow the procedures outlined in these manufacturer's Instructions for Use and the conditions of authorization outlined in the Letter of Authorization. Deviations from the procedures outlined are not permitted under the Emergency Use Authorization. To assist clinical laboratories running the ADVIA Centaur Zika test, the relevant Conditions of Authorization are listed verbatim below.

- Authorized laboratories will include with reports of the results of the ADVIA Centaur Zika test the authorized Fact Sheet for Healthcare Providers and the authorized Fact Sheet for Patients, and any additional ADVIA Centaur Zika test Fact Sheets for Healthcare Providers and Patients that OCET/OCS/OC and DMD/OIR/CDRH may authorize.[a] Under exigent circumstances, other appropriate methods for disseminating these Fact Sheets may be used, which may include mass media.
- Authorized laboratories will perform the ADVIA Centaur Zika test on only human serum or plasma (potassium EDTA or lithium heparin, each collected alongside a patient-matched serum specimen) specimens or with other authorized specimen types.[b]
- If non-serum specimens are used with the ADVIA Centaur Zika test, authorized laboratories responsible for collecting the patient specimen must collect a patient-matched serum specimen, or if this is not possible, an additional serum specimen must be collected soon after the original specimen. This is to facilitate any additional testing that may be required, using the latest CDC testing algorithms for the diagnosis of Zika virus infection, to confirm Zika virus infection.[b]
- Authorized laboratories must read the results of the ADVIA Centaur Zika test on the ADVIA Centaur XP, ADVIA Centaur XPT, or on other authorized instruments.
- Within the United States and its territories, authorized laboratories will report all Presumptive Zika Positive results to Siemens Healthcare Diagnostics.

- Authorized laboratories will report only the final interpretation of algorithm test results (Presumptive Zika Positive, Negative for IgM Antibodies to Zika Virus, or Negative for Antibodies to Zika Virus), as described in the Instructions for Use document, to healthcare providers.[c]
- Authorized laboratories will have a process in place to assure that, for Presumptive Zika Positive results, additional testing (as described in the Instructions for Use document) is performed and/or test results for other patient-matched specimens, using the latest CDC testing algorithms for the diagnosis of Zika virus infection, are considered.[c]
- Authorized laboratories will have a process in place for reporting test results to healthcare providers and relevant public health authorities, as appropriate.
- Authorized laboratories will collect information on the performance of the ADVIA Centaur Zika test and report to DMD/OIR/CDRH (via email CDRH-EUA-Reporting@fda.hhs.gov) and Siemens Healthcare Diagnostics any suspected occurrence of false negative and false positive results and significant deviations from the established performance characteristics of which they become aware.[a]
- All laboratory personnel using the assay must be appropriately trained in performing and interpreting immunoassay techniques, use appropriate laboratory and personal protective equipment when handling this kit, and use the test in accordance with the authorized labeling. All laboratory personnel using the assay must also be trained in and be familiar with the interpretation of results of the ADVIA Centaur Zika test.[c]
- Siemens Healthcare Diagnostics, its authorized distributor(s), and authorized laboratories will ensure that any records associated with this EUA are maintained until notified by FDA. Such records will be made available to FDA for inspection upon request.

Notes

[a] The Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and Division of Microbiology Devices (DMD)/Office of In Vitro Diagnostics and Radiological Health (OIR)/Center for Devices and Radiological Health (CDRH) are agencies within FDA.

[b] Confirmatory testing requires the use of serum samples. Therefore, serum is the primary diagnostic specimen for Zika virus RNA and serologic testing, and should be the priority specimen for collection and testing with the ADVIA Centaur Zika test.

[c] Refer to *Interpretation of Results*.

Expected Values

The prevalence of Zika virus infection varies by geographic location.

In a population of 2018 volunteer blood donors, pregnant females and pediatric subjects from an area of low prevalence of Zika virus infection (mainland U.S.), 2016 (99.90%) samples were found to be nonreactive and 2 of these samples were Presumptive Zika Positive using the ADVIA Centaur Zika test.

In a population of 85 patients reactive for Zika IgM, 83 (97.65%) were found to be Presumptive Zika Positive using the ADVIA Centaur Zika test.

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.[13]

Performance Characteristics

Clinical Sensitivity and Specificity

Clinical Sensitivity

Single draws from 49 Zika PCR-positive patients from the Dominican Republic and mainland U.S. were prospectively collected and evaluated using the ADVIA Centaur Zika test and a

commercially-available Zika IgM assay. The positive percent agreement of the ADVIA Centaur Zika test in this population was 95.92% (47/49).

Eight (8) serial draws from 36 Zika PCR-positive patients from the Dominican Republic were prospectively collected and evaluated using the ADVIA Centaur Zika test and a commercially-available Zika IgM assay. The positive percent agreement of the ADVIA Centaur Zika test in this population for specimens collected at 8 days or later after symptom onset was 94.14% (225/239).

	Comparator Assay Negative			Comparator Assay Positive		
Days After Symptom Onset	**ADVIA Centaur Zika Test Reactive**	**ADVIA Centaur Zika Test Nonreactive**	**Negative % Agreement**	**ADVIA Centaur Zika Test Reactive**	**ADVIA Centaur Zika Test Nonreactive**	**Positive % Agreement**
0–7*	5	21	80.77%	7	4	63.64%
8–14	0	0	–––	26	0	100.00%
15–28	1	0	0.00%	56	1	98.25%
29–42	3	0	0.00%	61	2	96.83%
43–56	3	0	0.00%	59	4	93.65%
57–70	5	0	0.00%	18	4	81.82%
≥ 71	0	0	–––	5	3	62.50%
Total	**17**	**21**	**55.26%**	**232**	**18**	**92.80%**
Total (≥ Day 8)	**12**	**0**	**0.00%**	**225**	**14**	**94.14%**

* This timeframe is not supported by the authorization. IgM antibodies to Zika virus develop during the first week of illness.[2]

Seroconversion Sensitivity

Eight (8) serial draws from 36 Zika PCR-positive patients from the Dominican Republic were prospectively collected and evaluated using the ADVIA Centaur Zika test and a commercially-available Zika IgM assay. The following seroconversion sensitivity results were obtained:

	Reactive (Positive) Result from Initial Draw Date			Number of Reactive (Positive) Bleeds	
Series ID	**Comparator Assay**	**ADVIA Centaur Zika Test**	**Difference in Bleed Numbers***	**Comparator Assay**	**ADVIA Centaur Zika Test**
TDS0067	1 (Day 3)	2 (Day 27)	-1	8	4
TDS0123	3 (Day 13)	3 (Day 13)	0	6	6
TDS0173	2 (Day 10)	2 (Day 10)	0	7	7
TDS0220	1 (Day 6)	1 (Day 6)	0	8	8
TDS0246	2 (Day 19)	1 (Day 5)	+1	7	8
TDS0249	2 (Day 20)	1 (Day 5)	+1	7	8
TDS0257	2 (Day 19)	2 (Day 19)	0	6	7
TDS0263	2 (Day 18)	2 (Day 18)	0	7	7
TDS0271	1 (Day 4)	2 (Day 10)	-1	8	4
TDS0279	2 (Day 11)	2 (Day 11)	0	7	7
TDS0281	2 (Day 14)	2 (Day 14)	0	7	7
TDS0282	1 (Day 2)	2 (Day 13)	-1	8	7
TDS0284	2 (Day 17)	2 (Day 17)	0	7	7

	Reactive (Positive) Result from Initial Draw Date			Number of Reactive (Positive) Bleeds	
Series ID	Comparator Assay	ADVIA Centaur Zika Test	Difference in Bleed Numbers*	Comparator Assay	ADVIA Centaur Zika Test
TDS0292	2 (Day 13)	1 (Day 4)	+1	6	8
TDS0296	2 (Day 9)	2 (Day 9)	0	7	7
TDS0306	1 (Day 4)	1 (Day 4)	0	8	8
TDS0310	2 (Day 8)	2 (Day 8)	0	7	7
TDS0314	1 (Day 6)	1 (Day 6)	0	8	8
TDS0322	1 (Day 5)	1 (Day 5)	0	8	8
TDS0328	2 (Day 10)	2 (Day 10)	0	7	2
TDS0341	2 (Day 10)	2 (Day 10)	0	7	5
TDS0343	2 (Day 18)	2 (Day 18)	0	7	7
TDS0345	2 (Day 10)	2 (Day 10)	0	5	7
TDS0362	2 (Day 25)	2 (Day 25)	0	2	7
TDS0372	2 (Day 9)	2 (Day 9)	0	7	7
TDS0376	2 (Day 14)	2 (Day 14)	0	7	7
TDS0379	1 (Day 6)	1 (Day 6)	0	8	7
TDS0396	1 (Day 2)	1 (Day 2)	0	8	8
TDS0421	2 (Day 9)	1 (Day 2)	+1	7	8
TDS0422	1 (Day 8)	1 (Day 8)	0	7	8
TDS0437	2 (Day 12)	2 (Day 12)	0	7	7
TDS0440	2 (Day 12)	2 (Day 12)	0	7	7
TDS0458	2 (Day 12)	2 (Day 12)	0	7	7
TDS0468	2 (Day 14)	1 (Day 6)	+1	5	8
TDS0480	2 (Day 12)	2 (Day 12)	0	7	7
TDS0499	1 (Day 5)	2 (Day 12)	-1	8	7
	Total Reactive Bleeds			**250**	**249**

* The difference in bleed numbers is relative to the comparator assay. For example, a +1 means that the comparator assay required 1 additional bleed before reactivity was determined as compared to the time-point when the ADVIA Centaur assay confirmed positive.

Clinical Specificity (Populations from Areas of Low Zika Virus Prevalence)

A population of residents from an area of low prevalence of Zika virus infection (mainland U.S.) that were negative by a commercially-available Zika IgM assay were tested using the ADVIA Centaur Zika test. The categories included apparently healthy male and female blood donors (N = 1365), pregnant females (N = 485), and pediatric subjects 2 to 20 years of age (N = 128). The negative percent agreement of the ADVIA Centaur Zika test in this population was 99.90% (1976/1978).

	ADVIA Centaur Zika Test Result			
Category	Nonreactive	Reactive	Total	Specificity
Healthy Blood Donors	1365	0	1365	100.00% (1365/1365)
Pregnant Women	483	2	485	99.59% (483/485)
Pediatrics (2–20 years)	128	0	128	100.00% (128/128)
Total	**1976**	**2**	**1978**	**99.90% (1976/1978)**

Clinical Specificity (Populations from Areas of High Zika Virus Prevalence)

A population of residents and travelers to areas of high prevalence for Zika virus infection (Dominican Republic, Honduras and Puerto Rico) that were negative by a commercially-available Zika IgM assay were tested using the ADVIA Centaur Zika test. The categories included residents with symptoms associated with Zika infection but were PCR-negative for Zika virus (N = 46), asymptomatic residents (N = 262) and travelers (N = 47). The negative percent agreement of the ADVIA Centaur Zika test in this population was 94.37% (335/355).

	ADVIA Centaur Zika Test Result			
Category	**Nonreactive**	**Reactive**	**Total**	**Negative Percent Agreement**
Zika Endemic Area Travelers	47	0	47	100.00% (47/47)
Zika Endemic Area Symptomatic Residents	45	1	17	97.83% (45/46)
Zika Endemic Area Asymptomatic Residents	243	19	262	92.75% (243/262)
Total	**335**	**20**	**355**	**94.37% (335/355)**

Precision

The assay was designed to meet the following repeatability and within-laboratory precision requirements.

	Design Requirements	
Index Value	**Repeatability (Within-Run) %CV**	**Within-Lab (Total Precision) %CV**
< 0.80	N/A	N/A
0.80–2.00	≤ 12.0	≤ 15.0
> 2.00	≤ 8.0	≤ 10.0

Precision of the ADVIA Centaur Zika Ab assay was evaluated according to the CLSI protocol EP05-A3.[13] A two-member panel and controls were assayed in 2 replicates twice a day for 20 days (n = 80 for each sample).

The following results were obtained using 1 reagent lot and stored calibration curves.

		Repeatability		Within-Lab	
Sample	**Mean (Index)**	**SD (Index)**	**%CV**	**SD (Index)**	**%CV**
Negative Control	0.05	0.03	N/A	0.04	N/A
Positive Control	3.26	0.06	2.0	0.13	3.9
Plasma Pool 1	0.63	0.03	4.0	0.03	5.0
Plasma Pool 2	1.98	0.05	2.6	0.08	4.3

Precision of the ADVIA Centaur Zika IgM assay was evaluated according to the CLSI protocol EP05-A3.[13] A two-member panel and controls were assayed in 2 replicates twice a day for 20 days (n = 80 for each sample).

The following results were obtained using 1 reagent lot and stored calibration curves.

Sample	Mean (Index)	Repeatability		Within-Lab	
		SD (Index)	%CV	SD	%CV
Negative Control	0.00	0.02	N/A	0.02	N/A
Positive Control	2.92	0.06	1.9	0.13	4.6
Plasma Pool 1	0.82	0.04	4.4	0.06	7.9
Plasma Pool 2	2.11	0.05	2.5	0.10	4.6

Actual results obtained at individual laboratories may vary from the data provided.

Crossreactivity

The ADVIA Centaur Zika test was evaluated for potential crossreactivity with specimens containing IgM antibodies against other flavivirus specimens and disease state specimens. The following results were obtained using the ADVIA Centaur Zika test.

Clinical Category	Number Tested	Number Reactive with ADVIA Centaur Zika Test
Anti-Nuclear Antibody (ANA)	19	0
Adenovirus	1	0
Borrelia sp. (Lyme disease)	11	0
Chikungunya virus	21	0
Cytomegalovirus (CMV)	12	0
Dengue virus	41	2
Epstein-Barr virus (EBV)	11	0
Human Anti-Mouse Antibody (HAMA)	15	0
Hepatitis (B) virus (HBV)	11	0
Hepatitis (C) virus (HCV)	15	0
Herpes Simplex Virus (HSV-1/2)	26	0
Leptospira	16	0
Malaria (*Plasmodium falciparum*)	10	2
Parvovirus B19	16	0
Rheumatoid Factor (RF)	21	0
Rubella Virus	10	0
Toxoplasma gondii	16	0
Treponema pallidum (Syphilis)	10	0
Varicella Zoster Virus (VZV)	15	0
West Nile Virus (VZV)	23	0
Yellow fever virus post-immunization	21	1
Total	**341**	**5**

Interferences

The ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays are designed to have ≤ 15% interference for substances at the levels indicated in the tables below. Testing was performed separately with both the ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays in accordance with CLSI Document EP07-A2.[14]

Specimens that are...	Demonstrate ≤ 10% change in results up to...
Hemolyzed	1000 mg/dL of hemoglobin
Lipemic	3000 mg/dL of triglycerides (Intralipid)
Proteinemic	12 g/dL of protein (human serum albumin)
Icteric	40 mg/dL of conjugated bilirubin
Icteric	60 mg/dL of unconjugated bilirubin

Specimens that contain...	Demonstrate ≤ 10% change in results up to...
Biotin	3500 ng/mL of biotin
Cholesterol	500 mg/dL of cholesterol

Assay results obtained at individual laboratories may vary from the data presented.

Standardization

The assay standardization for the ADVIA Centaur Zika Ab and ADVIA Centaur Zika IgM assays is based on agreement with known Zika positive samples. Assigned values of calibrators and controls are traceable to this standardization.

Technical Assistance

For customer support, please contact your local technical support provider or distributor.

siemens.com/healthcare

References

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7. Federal Occupational Safety and Health Administration. Bloodborne Pathogens Standard, 29 CFR 1910.1030.
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11. Boscato LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem.* 1988;34:27–33.
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Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition	Symbol	Definition
IVD	*In vitro* diagnostic medical device	REF	Catalog number
	Legal manufacturer	EC REP	Authorized Representative in the European Community
CE	CE Mark	CE 0088	CE Mark with identification number of notified body
	Consult instructions for use		Biological risk
	Do not freeze (> 0°C)		Temperature limitation
	Lower limit of temperature		Upper limit of temperature
	Keep away from sunlight and heat		Up
	Use by	Σ (n)	Contains sufficient for (n) tests
LOT	Batch code		Shake the reagent pack vigorously. Refer to *Preparing Reagents* in the assay-specific ADVIA Centaur product instructions for detailed information.
YYYY-MM-DD	Date format (year-month-day)	Rev.	Revision
MC DEF	Master Curve Definition	CHECKSUM	Variable hexadecimal number that ensures the Master Curve and Calibrator definition values entered are valid.
LOT DTL	Lot Details	DER GRÜNE PUNKT	Green dot
	Recycle	PRINTED WITH SOY INK	Printed with soy ink
RxOnly	Prescription device (US only)		

Trademarks

ADVIA Centaur and ReadyPack are trademarks of Siemens Healthcare Diagnostics.

Made in USA

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Zika Presumptive Positive Data Collection Form for Authorized Laboratories

Report for Presumptive Zika Positive Results on the ADVIA Centaur Zika Test under Emergency Use Authorization (EUA)

Laboratory Name: _____ Location: _____

Instrument ID: _____ Reporting Date: _____

Laboratory contact's name and phone number/email address (in case of inquiries): _____

Patient ID / Accession #	Sample ID	Result Date	Zika IgM Kit Lot #	Zika IgM Replicate	Relative Light Units (RLU)	Index Value	Interpretation
				Replicate (1)			
				Replicate (2)			
				Replicate (3)			

NOTE: Please submit this data collection form to Siemens Healthineers in accordance with the Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) to *Zika.Test.Team@Siemens-healthineers.com* This does NOT replace the requirements for reporting results to all relevant local and state health authorities. The Zika virus is considered to be a nationally notifiable disease. For guidelines on the Zika virus, please refer to www.cdc.gov/zika/hc-providers/index.html.

SIEMENS

ADVIA Centaur®

QC

Zika Ab (ZikaAb) Quality Control

For Use Under Emergency Use Authorization (EUA) Only

Contents

REF	Contents
11200712	2 vials of Negative Control CONTROL -
	2 vials of Positive Control CONTROL +
	Expected Values Card and barcode labels

Intended Use

The ADVIA Centaur® Zika Ab (ZikaAb) quality control is for *in vitro* diagnostic use to monitor the performance of the ADVIA Centaur Zika Ab assay using the ADVIA Centaur systems.

Control Description

Volume	Ingredients	Storage	Stability
2.0 mL/vial	Processed human plasma negative or positive for Zika antibodies with sodium azide (< 0.1%) and preservatives.	2–8°C	**Unopened:** Stable until the expiration date on the product **Opened:** 60 days **On-system:** 8 hours

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare.

CAUTION! POTENTIAL BIOHAZARD: Contains human source material. While each human serum or plasma donor unit used in the manufacture of this product was tested by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2, all products manufactured using human source material should be handled as potentially infectious. Because no test method can offer complete assurance that hepatitis B or C viruses, HIV, or other infectious agents are absent, these products should be handled according to established good laboratory practices.[1–3]

CAUTION
This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

H317 WARNING
P272, P280, P302+P352, P333+P313, P363, P501 May cause an allergic skin reaction. Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/protective clothing/eye protection/face protection. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Wash contaminated clothing before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1); ADVIA Centaur Zika Ab Controls

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For professional use.

For *in vitro* diagnostic use.

For Use Under Emergency Use Authorization (EUA) Only

Using the Barcode Labels

Note Control barcode labels are lot-number specific. Do not use barcode labels from one lot of controls with any other lot of controls.

Use the ADVIA Centaur ZikaAb Quality Control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur ZikaAb assay. Place the barcode label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

Performing Quality Control

For detailed information about entering quality control values, refer to the system operating instructions.

To monitor system performance and chart trends, as a minimum requirement, quality control samples should be assayed on each workshift that samples are analyzed. Quality control samples should also be assayed when performing a two-point calibration. Treat all quality control samples the same as patient samples.

Note This procedure uses control volumes sufficient to measure each control in duplicate.

1. Schedule the quality control samples to the worklist.
2. Label two sample cups with quality control barcode labels: one for the positive, and another for the negative.
3. Gently mix the quality control materials and dispense at least 4–5 drops into the appropriate sample cups.

Note Each drop from the control vial is approximately 50 µL.

4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

Dispose of any quality control that remains in the sample cups after 8 hours on the system. Do not refill sample cups when the contents are depleted; dispense fresh quality controls. Do not return any quality control materials back into the vials after testing because evaporation and contamination can occur, which may affect results.

Reviewing, Editing, and Printing Results

For detailed information about reviewing, editing, and printing quality control results, refer to the system operating instructions.

Expected Results

Refer to the lot-specific value card for the assigned values. A satisfactory level of performance is achieved when the analyte values obtained are within the expected control range for the lot number of ADVIA Centaur ZikaAb Quality Control, or within your laboratory's established range.

Taking Corrective Action

If the quality control results do not fall within the assigned values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.

If the quality control results are not within acceptable limits, recalibrate the assay and run the assay again. If necessary, contact your local technical support provided or distributor for assistance.

Perform corrective actions in accordance with your laboratory's established protocol. Retest patient samples before reporting results.

If necessary, contact your local technical support provider or distributor for assistance.

Limitations

Follow applicable government regulations for quality control. ADVIA Centaur ZikaAb Quality Control is for use only with the ADVIA Centaur ZikaAb assay. Assay values have not been established for assays other than the ADVIA Centaur ZikaAb assay.

The assigned values provided should be used as a guide in evaluating performance. Control intervals and ranges should be adapted to each laboratory's individual requirements. Values obtained should fall within the established range.

Each laboratory should establish corrective measures if individual values fall outside the range.

For Use Under Emergency Use Authorization (EUA) Only

Technical Assistance

For customer support, please contact your local technical support provider or distributor.

siemens.com/healthcare

References

1. Centers for Disease Control. Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in healthcare settings. *MMWR*, 1988;37:377–382, 387–388.
2. Clinical and Laboratory Standards Institute. *Protection of Laboratory Workers From Occupationally Acquired Infections; Approved Guideline—Fourth Edition*. CLSI Document M29-A4. Wayne, PA: Clinical and Laboratory Standards Institute; 2014.
3. Federal Occupational Safety and Health Administration. Bloodborne Pathogens Standard, 29 CFR 1910.1030.

Definition of Symbols

The following symbols may appear on the product labeling:

Symbol	Definition
IVD	*In vitro* diagnostic medical device
REF	Catalog number
	Legal manufacturer
EC REP	Authorized Representative in the European Community
CE	CE Mark
CE 0088	CE Mark with identification number of notified body
	Consult instructions for use
	Biological risk
	Temperature limitation
	Upper limit of temperature
	Lower limit of temperature
	Do not freeze (> 0°C)
	Keep away from sunlight and heat
	Up
	Use by
Σ (n)	Contains sufficient for (n) tests
LOT	Batch code
YYYY-MM-DD	Date format (year-month-day)
Rev.	Revision
DER GRÜNE PUNKT	Green dot
	Recycle
PRINTED WITH SOY INK	Printed with soy ink
RxOnly	Prescription Device (US only)

Made in USA

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SIEMENS

ADVIA Centaur®

QC

Zika IgM (ZikaM) Quality Control

For Use Under Emergency Use Authorization (EUA) Only

Contents

REF	Contents
11200111	2 vials of Negative Control CONTROL -
	2 vials of Positive Control CONTROL +
	Expected Values Card and barcode labels

Intended Use

The ADVIA Centaur® Zika IgM (ZikaM) quality control is for *in vitro* diagnostic use to monitor the performance of the ADVIA Centaur Zika IgM assay using the ADVIA Centaur systems.

Control Description

Volume	Ingredients	Storage	Stability
2.0 mL/vial	Processed human plasma negative or positive for Zika antibodies with sodium azide (< 0.1%) and preservatives.	2–8°C	**Unopened:** Stable until the expiration date on the product **Opened:** 60 days **On-system:** 8 hours

Warnings and Precautions

Safety data sheets (MSDS/SDS) available on siemens.com/healthcare.

CAUTION! POTENTIAL BIOHAZARD: Contains human source material. While each human serum or plasma donor unit used in the manufacture of this product was tested by FDA-approved methods and found nonreactive for hepatitis B surface antigen (HBsAg), antibody to hepatitis C (HCV), and antibody to HIV-1/2, all products manufactured using human source material should be handled as potentially infectious. Because no test method can offer complete assurance that hepatitis B or C viruses, HIV, or other infectious agents are absent, these products should be handled according to established good laboratory practices.[1–3]

CAUTION
This device contains material of animal origin and should be handled as a potential carrier and transmitter of disease.

Contains sodium azide as a preservative. Sodium azide can react with copper or lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent buildup of azides. Disposal into drain systems must be in compliance with prevailing regulatory requirements.

H317 WARNING
P272, P280, P302+P352, P333+P313, P363, P501 May cause an allergic skin reaction. Contaminated work clothing should not be allowed out of the workplace. Wear protective gloves/protective clothing/eye protection/face protection. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Wash contaminated clothing before reuse. Dispose of contents and container in accordance with all local, regional, and national regulations.
Contains: 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-2H-isothiazol-3-one (3:1); ADVIA Centaur Zika IgM Controls

Dispose of hazardous or biologically contaminated materials according to the practices of your institution. Discard all materials in a safe and acceptable manner and in compliance with prevailing regulatory requirements.

Caution: Federal (USA) law restricts this device to sale by or on the order of a licensed healthcare professional.

For professional use.

For *in vitro* diagnostic use.

For Use Under Emergency Use Authorization (EUA) Only

Using the Barcode Labels

Note Control barcode labels are lot-number specific. Do not use barcode labels from one lot of controls with any other lot of controls.

Use the ADVIA Centaur ZikaM Quality Control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur ZikaM assay. Place the barcode label on the sample cup so that the readable characters on the side of the label are vertical on the sample cup.

Performing Quality Control

For detailed information about entering quality control values, refer to the system operating instructions.

To monitor system performance and chart trends, as a minimum requirement, quality control samples should be assayed on each workshift that samples are analyzed. Quality control samples should also be assayed when performing a two-point calibration. Treat all quality control samples the same as patient samples.

Note This procedure uses control volumes sufficient to measure each control in duplicate.

1. Schedule the quality control samples to the worklist.
2. Label two sample cups with quality control barcode labels: one for the positive, and another for the negative.
3. Gently mix the quality control materials and dispense at least 4–5 drops into the appropriate sample cups.

Note Each drop from the control vial is approximately 50 µL.

4. Load the sample cups in a rack.
5. Place the rack in the sample entry queue.
6. Ensure that the assay reagents are loaded.
7. Start the entry queue, if required.

Dispose of any quality control that remains in the sample cups after 8 hours on the system. Do not refill sample cups when the contents are depleted; dispense fresh quality controls. Do not return any quality control materials back into the vials after testing because evaporation and contamination can occur, which may affect results.

Reviewing, Editing, and Printing Results

For detailed information about reviewing, editing, and printing quality control results, refer to the system operating instructions.

Expected Results

Refer to the lot-specific value card for the assigned values. A satisfactory level of performance is achieved when the analyte values obtained are within the expected control range for the lot number of ADVIA Centaur ZikaM Quality Control, or within your laboratory's established range.

Taking Corrective Action

If the quality control results do not fall within the assigned values or within the laboratory's established values, do not report results. Take the following actions:

- Verify that the materials are not expired.
- Verify that required maintenance was performed.
- Verify that the assay was performed according to the instructions for use.
- Rerun the assay with fresh quality control samples.

If the quality control results are not within acceptable limits, recalibrate the assay and run the assay again. If necessary, contact your local technical support provided or distributor for assistance.

Perform corrective actions in accordance with your laboratory's established protocol. Retest patient samples before reporting results.

If necessary, contact your local technical support provider or distributor for assistance.

Limitations

Follow applicable government regulations for quality control. ADVIA Centaur ZikaM Quality Control is for use only with the ADVIA Centaur ZikaM assay. Assay values have not been established for assays other than the ADVIA Centaur ZikaM assay.

The assigned values provided should be used as a guide in evaluating performance. Control intervals and ranges should be adapted to each laboratory's individual requirements. Values obtained should fall within the established range.

Each laboratory should establish corrective measures if individual values fall outside the range.

For Use Under Emergency Use Authorization (EUA) Only

Technical Assistance

For customer support, please contact your local technical support provider or distributor.

siemens.com/healthcare

References

1. Centers for Disease Control. Update: Universal precautions for prevention of transmission of human immunodeficiency virus, hepatitis B virus and other bloodborne pathogens in healthcare settings. *MMWR*, 1988;37:377–382, 387–388.
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Symbol	Definition
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REF	Catalog number
	Legal manufacturer
EC REP	Authorized Representative in the European Community
CE	CE Mark
CE 0088	CE Mark with identification number of notified body
	Consult instructions for use
	Biological risk
	Temperature limitation
	Upper limit of temperature
	Lower limit of temperature
	Do not freeze (> 0°C)
	Keep away from sunlight and heat
	Up
	Use by
Σ (n)	Contains sufficient for (n) tests
LOT	Batch code
YYYY-MM-DD	Date format (year-month-day)
Rev.	Revision
DER GRÜNE PUNKT	Green dot
	Recycle
PRINTED WITH SOY INK	Printed with soy ink
RxOnly	Prescription Device (US only)

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