SIEMENS

ADVIA Centaur®
ADVIA Centaur® XP
Immunoassay Systems

HIV Ag/Ab Combo (CHIV) Assay

Assay for the Detection of HIV p24 Antigen and Antibodies to Human Immunodeficiency Virus Type 1, Including Group O (HIV-1 + "O") and/or Type 2 (HIV-2)

Current Revision and Date[a]	Rev. B, 2016-DRAFT	
Product Name	ADVIA Centaur® CHIV assay (100 tests)	**REF** 10696880
Systems	ADVIA Centaur system ADVIA Centaur XP system	
Materials Required but Not Provided	ADVIA Centaur CHIV quality control material	**REF** 10697214
	ADVIA Centaur Probe Wash 3	**REF** 03333963
	ADVIA Centaur Wash 1 (2 x 1500 mL)	**REF** 01137199
	ADVIA Centaur Wash 1 (2 x 2500 mL)	**REF** 03773025
Specimen Types	Human serum and plasma (potassium-EDTA, lithium heparin, sodium heparin)	
Reagent Storage	2–8°C	
Reagent On-System Stability	42 days	

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

WARNING

This product is not intended for testing or screening pooled specimens from more than one individual, or for use in screening blood or plasma donors.

United States federal law restricts this device to sale by or on the order of a physician.

Intended Use

The ADVIA Centaur® HIV Ag/Ab Combo (CHIV) assay is an *in vitro* diagnostic immunoassay for the simultaneous qualitative detection of human immunodeficiency virus p24 antigen and antibodies to human immunodeficiency viruses type 1 (including group "O") and type 2, in serum and plasma (potassium EDTA, lithium heparin, sodium heparin) using the ADVIA Centaur and ADVIA Centaur XP systems. The ADVIA Centaur CHIV assay is intended to be used as an aid in the diagnosis of HIV infection in pediatric and adult populations, including pregnant women.

The ADVIA Centaur CHIV assay is not intended for the screening of blood or plasma donors. Although the effectiveness of the assay for screening blood or plasma donors has not been established, the assay can be used as a blood donor screening assay in urgent situations where traditional licensed blood donor screening tests are unavailable, or if their use is impractical.

A reactive result using the ADVIA Centaur CHIV assay does not distinguish HIV-1 p24 antigen, HIV-1 antibody, HIV-2 antibody, and HIV-1 group O antibody.

Summary and Explanation

Human immunodeficiency virus is the causative agent of acquired immunodeficiency syndrome (AIDS). AIDS was first described in the United States in 1981 and has become one of the leading causes of death worldwide. Despite educational efforts directed towards reducing the transmission of AIDS and increased advancements in treatment, the number of AIDS cases continues to increase.[1]

Human immunodeficiency virus type 1 (HIV-1) has been identified as the primary cause of acquired immunodeficiency syndrome (AIDS). This retrovirus, a member of the lentivirinae subfamily, is spread by sexual contact, exposure to infected blood or blood products, and perinatal transmission. In 1986, human immunodeficiency virus type 2 (HIV-2) was isolated from AIDS patients in West Africa. These viruses share epitopes of the core proteins, but exhibit little or no cross-reactivity between the envelope glycoproteins.[2,3]

Comparison of the nucleic acid sequences for HIV-1 and HIV-2 shows approximately 60% homology in the conserved genes, such as *gag* and *pol* (encoding core proteins), and 30 to 40% homology in less conserved regions (encoding envelope proteins). HIV-1 has been subdivided into group M (subtypes A-H) and group O.[4]

The routes of transmission of HIV-1 and HIV-2 are the same, however the transmission and the viral replication rate are much lower in HIV-2 infections. Clinical studies have shown that in HIV-2 infections there is a slower disease progression than in HIV-1 infections. In HIV-2 infections there is a slower rate in the decline of CD4 T cells and reduced viremia. Individuals infected with HIV-2 generally have a better clinical outcome.[2,5]

The ADVIA Centaur CHIV assay uses yeast-derived recombinant antigens corresponding to the viral envelope proteins. Recombinant antigens include an HIV-1 envelope protein (gp41/120) and an HIV-2 envelope protein (gp36). A synthetic peptide is added for the detection of antibodies to HIV-1 group O. The assay uses three monoclonal antibodies specific to HIV p24 antigen to capture and detect HIV p24 antigen in a sample.

The primary purpose of the ADVIA Centaur CHIV assay is to aid in the diagnosis of HIV infection and AIDS. Specimens that are initially reactive should be retested in duplicate. Repeat reactivity is highly predictive of the presence of antibody to HIV-1 and/or HIV-2 in specimens from people at risk for HIV infection. Therefore, these specimens should be followed-up with appropriate supplemental tests for HIV-1 and HIV-2 antibody and/or p24 antigen before making a diagnosis of HIV infection.

Principles of the Procedure

The ADVIA Centaur CHIV assay is a two-wash antigen/antibody sandwich immunoassay, in which antigens are bridged by antibody present in the patient sample, and antigen (p24) in the sample is bridged by antibody present in the reagents. The Solid Phase contains a preformed complex of streptavidin-coated paramagnetic microparticles and biotinylated HIV-1 and HIV-2 recombinant antigens, group O peptide antigen, and biotinylated anti-p24 antibody. This reagent is used to capture anti-HIV-1 and/or HIV-2 antibodies and/or HIV p24 antigen in the patient sample. The Ancillary Lite Reagent and Lite Reagent contain acridinium ester labeled HIV-1 and HIV-2 recombinant antigens, group O peptide antigen and acridinium ester labeled anti-p24 antibodies used to detect anti-HIV-1 and/or HIV-2 antibodies and/or p24 antigen bound to the Solid Phase in the sample.

A direct relationship exists between the amount of HIV antibody activity and/or HIV p24 antigen present in the specimen and the amount of relative light units (RLUs) detected by the system. A result of reactive or nonreactive is determined according to the Index Value established with the calibrators. Refer to *Interpretation of Results* for a description of the cut-off value calculation.

Reagents

Reagent	Description	Storage	Reagent Stability
ADVIA Centaur CHIV ReadyPack® primary reagent pack, Solid Phase	10.5 mL/reagent pack streptavidin-coated paramagnetic microparticles preformed with biotinylated HIV antigens (~1.5 µg/mL) and antibody (~4.5 µg/mL) in buffer with bovine serum albumin, mouse IgG, surfactant, and preservatives	2–8°C	**Unopened**: Stable until the expiration date on product. **On-system**: 42 days.
ADVIA Centaur CHIV ReadyPack primary reagent pack, Lite Reagent	5.5 mL/reagent pack recombinant HIV antigens (~0.12 µg/mL) and antibodies (~0.004 µg/mL) labeled with acridinium ester in buffer with bovine serum albumin, mouse IgG, goat serum, surfactant, and preservatives	2–8°C	**Unopened**: Stable until the expiration date on product. **On-system**: 42 days.
ADVIA Centaur CHIV ReadyPack primary reagent pack, Ancillary Lite Reagent	5.5 mL/reagent pack recombinant HIV antigens (~0.23 µg/mL) and antibodies (~1.5 µg/mL) labeled with acridinium ester in buffer with bovine serum albumin, mouse IgG, goat serum, surfactant, and preservatives	2–8°C	**Unopened**: Stable until the expiration date on product. **On-system**: 42 days.
ADVIA Centaur CHIV Calibrator	2.0 mL/vial processed[a] human plasma negative for antibodies to HIV and spiked with antibodies to HIV-1, heat inactivated goat serum, sodium azide (< 0.1%), and preservatives	2–8°C	**Unopened**: Stable until the expiration date on product. **On-system**: 8 hours.
ADVIA Centaur CHIV Quality Controls[b]	14 mL/vial processed[a] human plasma nonreactive for HIV, reactive for HIV-1, reactive for HIV-2, reactive for HIV-1 group "O", and reactive for HIV-1 p24 antigen with sodium azide (< 0.1%) and preservatives.	2–8°C	**Unopened**: Stable until the expiration date on product. **On-system**: 8 hours.
ADVIA Centaur Probe Wash 3[b]	50.0 mL/pack sodium hypochlorite (0.5%), sodium hydroxide (< 0.5%), pH 11.0	2–8°C	**Unopened**: Stable until the expiration date on product. **On-system**: 100 days.
ADVIA Centaur Wash 1[b]	1500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C.	**Unopened**: Stable until the expiration date on product. **On-system**: 1 month.
ADVIA Centaur Wash 1[b]	2500 mL/pack phosphate-buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C.	**Unopened**: Stable until the expiration date on product. **On-system**: 1 month.

[a] Processed plasma is defibrinated and filtered plasma.

[b] See Materials Required but Not Provided.

Warnings and Precautions

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

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.[6–8]

The negative control has been assayed by FDA-approved methods and found to be nonreactive for hepatitis B virus, antibody to HCV, and antibody to HIV-1/2. The positive controls, low calibrator and high calibrator have been assayed by FDA-approved methods and found to be nonreactive for hepatitis B virus and antibody to HCV. The positive controls, low calibrator, and high calibrator contain human plasma that is reactive for antibody to HIV. The units were treated with a BPL-UV inactivation procedure,[9] however, all products manufactured using human source material should be handled as potentially infectious.

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.

H412	Harmful to aquatic life with long lasting effects.
P273, P501	Avoid release to the environment.
	Contains: Microprotect; ADVIA Centaur CHIV ReadyPack

H317	**Warning!**
P280, P272, P302+P352, P333+P313, P501	May cause an allergic skin reaction. Wear protective gloves/protective clothing/eye protection/face protection. Contaminated work clothing should not be allowed out of the workplace. IF ON SKIN: Wash with plenty of soap and water. If skin irritation or rash occurs: Get medical advice/attention. Dispose of contents and container in accordance with all local, regional, and national regulations.
	Contains: ProClin 300, ADVIA Centaur CHIV High Calibrator

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.

For *in vitro* diagnostic use.

Preparing Reagents

All reagents are liquid and ready to use.

Remove all of the reagents from the refrigerator, and mix all primary reagent packs by hand. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended before loading them onto the system. For detailed information about preparing the reagents for use, refer to the system operating instructions.

Storing and Stability

Store unused reagent packs upright at 2–8°C away from heat and light sources. Reagents are stable at 2–8°C until the expiration date on the pack label.

Store ADVIA Centaur CHIV Calibrators at 2–8°C away from heat and light sources. Calibrators are stable at 2–8°C until the expiration date on the pack label.

Do not use ADVIA Centaur materials beyond the expiration date printed on the product.

For onboard stability, refer to *On-System Stability*.

Specimen Collection and Handling

This assay has been validated for use with serum and plasma (potassium EDTA, lithium heparin, sodium heparin) samples.

Collecting the Specimen

- Specimens can be collected using recommended procedures for collection of diagnostic blood specimens by venipuncture.[10]
- Follow the instructions provided with your specimen collection device for use and processing.[11]
- Complete clot formation should take place before centrifugation.[12] Specimens are processed by centrifugation, typically followed by physical separation of the serum or plasma from the red cells. The centrifugation step may occur up to 24 hours post draw.
- Collect all blood samples observing universal precautions for venipuncture. Handle all samples as if capable of transmitting disease.
- Do not use specimens with obvious microbial contamination.
- Keep tubes stoppered at all times.
- Test samples as soon as possible after collecting. Store processed specimens at 2–8°C if not tested within 24 hours of collection.
- Do not use samples that have been stored at room temperature for longer than 24 hours.

Storing the Specimen

- Store processed specimens stoppered at all times.
- Separated specimens are stable for 24 hours at room temperature, and for 14 days at 2–8ºC.
- Specimens may be stored in primary tubes up to 14 days at 2–8°C. Primary tube specimens include serum stored on the clot, plasma stored on packed red cells, and specimens processed and stored in gel barrier blood collection tubes. When 10 specimens in these primary tubes were tested up to 14 days, no clinically significant differences were observed.
- For longer storage, specimens may be frozen for 8 months at -20ºC or colder. Freeze specimens, devoid of red blood cells, at or below -20°C for longer storage. Do not store in a frost-free freezer. When 10 specimens were subject to 5 freeze/thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed specimens and centrifuge.
- Thawed frozen specimens which are turbid must be clarified by centrifugation prior to testing.
- Specimens may be stored on the ADVIA Centaur and ADVIA Centaur XP systems for 8 hours.

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 and international regulations covering the transport of clinical samples and etiological agents.

Processed specimens maintained at room temperature up to 24 hours or 2–8°C up to 14 days demonstrated no clinically significant differences. Store specimens stoppered at 2–8°C upon arrival.

Siemens Healthcare Diagnostics recommends shipping samples at 2–8°C or frozen.

Procedure

Materials Provided

The following materials are provided:

REF	Contents	Number of Tests
10696880	1 ReadyPack primary reagent pack containing ADVIA Centaur CHIV Solid Phase, Lite Reagent, and Ancillary Lite Reagent 1 vial ADVIA Centaur CHIV Low Calibrator CAL L 1 vial ADVIA Centaur CHIV High Calibrator CAL H ADVIA Centaur systems CHIV Master Curve card ADVIA Centaur systems CHIV Calibrator Assigned Value Card	100

Materials Required but Not Provided

The following materials are required to perform this assay, but are not provided:

Item	Description	
10697214	ADVIA Centaur CHIV Quality Control Material	1 x 14 mL Negative Control CONTROL – 1 x 14 mL CHIV Positive anti-HIV-1 Control CONTROL Ab-1 + 1 x 14 mL CHIV Positive anti-HIV-2 Control CONTROL Ab-2 + 1 x 14 mL CHIV Positive anti-HIV-1 group O Control CONTROL Ab-3 + 1 x 14 mL CHIV Positive HIV-1 p24 antigen Control CONTROL Ag + Expected Value Card
03333963	ADVIA Centaur Probe Wash 3	50.0 mL PW 3
01137199 (112351)	ADVIA Centaur Wash 1 (assay wash)	2 x 1500 mL/pack WASH 1
03773025	ADVIA Centaur Wash 1[a]	2 x 2500 mL/pack WASH 1

[a] For use with systems with 2500 mL capacity.

Assay Procedure

The ADVIA Centaur and ADVIA Centaur XP systems automatically perform the following steps:

1. Dispense 100 µL of sample into a cuvette, and incubates for 6 minutes at 37°C.
2. Dispense 100 µL of Solid Phase and 50 µL of Ancillary Lite Reagent, and incubates for 18 minutes at 37°C.
3. Separate the Solid Phase from the mixture, and aspirates the unbound reagent.
4. Wash the cuvette with Wash 1.
5. Dispense 50 µL of Lite Reagent, and incubates for 18 minutes at 37°C.
6. Separate the Solid Phase from the mixture, and aspirates the unbound reagent.
7. Wash the cuvette with Wash 1.
8. Dispense 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction.
9. Report results according to the selected option, as described in the system operating instructions.

Note Wash 1, Acid Reagent, and Base Reagent are required for use in running the ADVIA Centaur system.

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

Preparing the System

Ensure that the system has sufficient primary reagent packs.

Load the ReadyPack primary reagent packs in the primary reagent compartment. You can use the arrows on the end label as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents.

Sampling, reagent delivery, mixing and processing are automatically performed by the ADVIA Centaur systems. For details on this processing, refer to the system operating instructions.

Preparing the Samples

This assay requires 100 µL of sample for a single determination. 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. For detailed information about determining the minimum required volume, refer to the system operating instructions.

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

- Samples are free of fibrin or other particulate matter. If not, transfer the sample to a secondary tube and centrifuge at 10,000 x g for 10 minutes. Follow the tube manufacturer's recommendations.
- Samples are free of bubbles or foam.

On-System Stability

Reagent packs loaded on the system are protected from light.

ADVIA Centaur CHIV reagents are stable onboard the system for 42 days. Discard reagent packs at the end of the onboard stability interval. Do not use products beyond the expiration date printed on the product labeling.

ADVIA Centaur CHIV Calibrators are stable on the system for 8 hours. Dispose of any calibrator remaining in the sample cups after 8 hours.

Performing Calibration

For calibration of the ADVIA Centaur CHIV assay, use ADVIA Centaur CHIV Calibrators provided with each kit. The calibrators provided in this kit are matched to the ReadyPack primary reagent pack.

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.

Note Remove the packs from the ADVIA Centaur system and gently resuspend the packs before you recalibrate the system. See the system operating instructions.

Master Curve and Calibration Values

The ADVIA Centaur CHIV assay requires a Master Curve calibration when using a new reagent lot number. For each new lot number of Lite Reagent, Solid Phase, and Ancillary Lite 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 Master Curve values, refer to the system operating instructions.

Each calibrator is packaged with a lot-specific Calibrator Assigned Value card to facilitate entering the calibration values on the system. Enter the values using the barcode scanner or the keyboard. The Calibrator Assigned Value card provided in this kit is matched to the ReadyPack primary reagent pack. Do not mix calibrator lots with different lots of reagents. For detailed information about entering calibrator values, refer to the system operating instructions.

Calibration Procedure

Note Assay quality control samples when performing a two-point calibration.

Perform the calibration procedure using the following steps:

1. Ensure that the appropriate master curve and calibration assigned values are entered on the system. Refer to *Master Curve and Calibration Values*.
2. Ensure that the required reagents are loaded for the assay.
3. Schedule the ADVIA Centaur CHIV Calibrators to the worklist.
4. Label two sample cups with ADVIA Centaur CHIV Calibrator barcode labels: one cup for the low calibrator and another cup for the high calibrator.

   Note Place the barcode label on the 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.
5. Gently mix the low and high calibrators and dispense at least 10-12 drops of each calibrator into the appropriate sample cups. Avoid bubbles.

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

   Note This procedure uses calibrator volumes sufficient to measure each calibrator in duplicate.
6. Load the sample cups in a rack. Place the low calibrator cup position before the high calibrator cup position.
7. Place the rack in the sample entry queue.
8. 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 21-day calibration interval. Additionally, this assay requires 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.

Note Assay quality control samples when performing a two-point calibration.

Performing Quality Control

Follow government regulations or accreditation requirements for quality control frequency.

Follow your laboratory internal QC procedures if the results obtained are outside acceptable limits.

Quality Control Procedure

Treat all quality control samples the same as patient samples.

Perform the quality control procedure using the following steps:

1. Ensure that the quality control definitions are defined, and that the quality control values are entered on the system using the lot-specific Expected Value card provided.
2. Ensure that the required reagents are loaded for the assay.
3. Schedule the quality control samples to the worklist.

4. Label five sample cups with ADVIA Centaur CHIV quality control barcode labels: one cup for each positive control and another cup for the negative control.

   Note Place the barcode label on the sample cup with the readable characters oriented vertically.

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

5. Gently mix the quality control materials and dispense at least 10-12 drops of each control into the appropriate sample cups. Avoid bubbles.

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

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

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

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

Quality Control Values

For quality control of the ADVIA Centaur CHIV assay, use ADVIA Centaur CHIV controls. Refer to the Expected Value card for the suggested expected values specific for the lot number of the controls. For detailed information about entering quality control values, refer to the system operating instructions.

Quality Control Frequency

To monitor system performance and chart trends, as a minimum requirement, all ADVIA Centaur CHIV controls supplied in the CHIV control kit should be assayed at least once in every 24 hours that samples are analyzed. Ensure that all control values are within the index ranges specified in the control package insert. If any of the control results are outside of the specified index range, reevaluate all test results generated since the last acceptable control results for possible adverse effects. If any test results is adversely affected, retest the sample.

Note Assay quality control samples when performing a two-point calibration.

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:

1. Determine and correct the cause of the unacceptable control results:
   a. Verify that the materials are not expired.
   b. Verify that required maintenance was performed.
   c. Verify that the assay was performed according to the instructions for use.
   d. Rerun the assay with fresh quality control samples, and confirm that quality control results are within acceptable limits before running patient samples.
   e. If the quality control results are not within acceptable limits, recalibrate the assay, and repeat step d.
   f. If necessary, contact your local technical support provider or distributor for assistance.
2. Repeat testing of patient samples before reporting results.

Perform corrective actions in accordance with your established laboratory protocol.

Results

Calculation of Results

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

Interpretation of Results

Results of this assay should always be interpreted in conjunction with the patient's medical history, clinical presentation, and other findings.

The system reports HIV antibody and/or p24 antigen results in Index Values and as reactive or nonreactive. The minimum level of antibodies to HIV-1/HIV-2 and/or p24 antigen that indicates reactivity is determined based on population studies and is assigned an Index Value of 1.0. This is the Cut-off Index Value.

The Cut-off Index Value of 1.0 is used to determine whether a specimen is reactive or nonreactive for p24 antigen and/or antibodies to HIV-1/HIV-2.

- Specimens with an Index Value of less than 1.0 are considered nonreactive for antibodies to HIV-1 and HIV-2 and p24 antigen by the ADVIA Centaur CHIV assay.
- Specimens with an Index Value greater than or equal to 1.0 are considered initially reactive for p24 antigen and/or antibodies to HIV-1 and/or HIV-2 and should be retested in duplicate after centrifugation at 10,000 x g for 10 minutes. If one or both of the duplicates are reactive, the specimen is repeatedly reactive by the ADVIA Centaur CHIV assay.

  Note Inadequate centrifugation may result in a higher rate of repeat reactive results that must be investigated using supplemental tests for HIV-1 and/or HIV-2 and/or p24 antigen.
- Repeatedly reactive specimens must be investigated using supplemental tests for HIV-1 and/or HIV-2 and/or p24 antigen. In specimens giving indeterminate supplemental test results, testing of a subsequent sample drawn at a later date (such as 1–6 months) is recommended.
  For individuals who are confirmed positive for antibodies and/or p24 antigen, appropriate counseling and medical evaluation should be offered and is considered an important part of testing for antibody to HIV-1 and HIV-2 and/or p24 antigen.
- Specimens that are initially reactive are considered negative for HIV-1/HIV-2 antibodies and/or p24 antigen if both of the duplicates retest with an Index Value less than 1.0.
- The cut-off value for the ADVIA Centaur CHIV assay was verified based on results of Receiver-Operator characteristics (ROC) Curve.[13]

Interpretation of results was determined for this assay using the ADVIA Centaur system.

Limitations

The ADVIA Centaur CHIV assay is approved for *in vitro* diagnostic use only.

The following information pertains to limitations of the assay:

- The ADVIA Centaur CHIV assay is limited to the detection of p24 antigen and/or antibodies to HIV-1 and/or HIV-2 in human serum and plasma (potassium EDTA, lithium heparin, sodium heparin).
- Heparin tube types can show higher Index values for specimens containing antibody to HIV when compared to other tube types with no change in interpretation of results. Specimens negative for HIV Antibody do not show this elevation in Index value.
- The calculated values for anti-HIV and/or p24 antigen in a given specimen as determined by assays from different manufacturers can vary due to differences in assay methods and reagent specificity. The results reported by the laboratory to the physician must include the identity of the assay used. Values obtained with different assay methods cannot be used interchangeably. The reported antibody level and/or p24 antigen cannot be correlated to an endpoint titer.
- Heterophilic and HAMA antibodies in human samples can react with reagent antibodies, interfering with in vitro immunoassays. Patients routinely exposed to animals or to animal serum products for diagnosis or therapies can be prone to this interference and anomalous values may be observed. Specimens from patients who have received mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies and may interfere in assays that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.[14,15]
- The performance of the ADVIA Centaur CHIV assay has not been established with cord blood, neonatal specimens, cadaver specimens, heat-inactivated specimens, or body fluids other than serum and plasma, such as saliva, urine, amniotic or pleural fluids.
- The ADVIA Centaur CHIV assay has not been evaluated for testing pooled blood and plasma and products made from such pools.
- Do not use specimens with obvious microbial contamination.
- Currently available assays for the detection of p24 antigen and/or antibodies to HIV-1 and/or HIV-2 may not detect all infected individuals. A negative test result does not exclude the possibility of exposure to or infection with HIV. HIV antibodies and/or p24 antigen may be undetectable in some stages of the infection and in some clinical conditions.
- A person who has antigen or antibodies to HIV is presumed to be infected with the virus. However, a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.

Performance Characteristics

Sensitivity

A multisite clinical study was performed to compare the sensitivity of the ADVIA Centaur CHIV assay to an FDA-approved HIV 1/O/2 antibody (Ab) assay.

Sensitivity in Individuals Known to be Positive for Antibodies to HIV-1

The sensitivity of the ADVIA Centaur CHIV assay was assessed in 942 individuals (serum or plasma sample) who were known to be infected with HIV-1. Of the 942 HIV-1 known positive individuals, 355 individuals were HIV symptomatic for AIDS, 91 individuals were asymptomatic for AIDS, and 496 individuals were known positive for AIDS at study enrollment.

The 942 HIV-1 positive individuals were obtained from the following geographic regions: Florida (307 specimens, 32.59%), Minnesota (320 specimens, 33.97%), New Jersey (1 specimen, 0.11%), New York (310 specimens, 32.91%), South Dakota (2 specimens, 0.21%), and Wisconsin (2 specimens, 0.21%). The results are shown in the table below:

		ADVIA Centaur CHIV Assay			FDA-approved HIV Ab Assay		
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**
Symptomatic	355	0	355	355	0	355	355
Asymptomatic	91	0	91	91	0	91	91
Known Positive for AIDS	496	0	496	496	0	496	496
Total	**942**	**0**	**942**	**942**	**0**	**942**	**942**
Total (%)		**0.0**	**100.0**	**100.0**	**0.0**	**100.0**	**100.0**

All 942 specimens were repeatedly reactive using the ADVIA Centaur CHIV assay. The sensitivity for this population was 100.00% with an exact 95% confidence interval of 99.61–100.00%.

Sensitivity in Individuals Known to be Positive for Antibodies to HIV-1 (Plasma Samples)

The sensitivity of the ADVIA Centaur CHIV assay was assessed using the plasma specimen collected from 320 HIV-1 positive individuals. Of the 320 HIV-1 positive individuals, 115 individuals were HIV-symptomatic for AIDS, 36 individuals were asymptomatic for AIDS, 166 non-pregnant individuals were positive for AIDS at study enrollment, and 3 pregnant females were positive for HIV1 at study enrollment.

The 320 HIV-1 positive individuals were obtained from the following geographic regions: Florida (100 specimens, 31.25%), Minnesota (99 specimens, 30.94%), New York (120 specimens, 37.50%), and South Dakota (1 specimen, 0.31%).

		ADVIA Centaur CHIV Assay			FDA-approved HIV Ab Assay		
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**
Symptomatic	115	0	115	115	0	115	115
Asymptomatic	36	0	36	36	0	36	36
HIV-1 Pos Pregnant	3	0	3	3	0	3	3
Known Positive for AIDS	166	0	166	166	0	166	166
Total	**320**	**0**	**320**	**320**	**0**	**320**	**320**
Total (%)		**0.0%**	**100.0%**	**100.0%**	**0.0%**	**100.0%**	**100.0%**

All 320 plasma specimens tested were repeatedly reactive by the ADVIA Centaur CHIV assay. The sensitivity for this population was 100.00% with an exact 95% confidence interval of 98.85% to 100.00%.

Sensitivity in Individuals Known to be Positive for Antibodies to HIV-2

The sensitivity of the ADVIA Centaur CHIV assay was assessed in 201 individuals who were known to be infected with HIV-2. The results are shown in the table below:

		ADVIA Centaur CHIV Assay			FDA-approved HIV Ab Assay		
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**
Known Positive for HIV-2	201	0	201	201	0	201	201

All 201 specimens were repeatedly reactive using the ADVIA Centaur CHIV assay. The sensitivity for this population was 100.00% with an exact 95% confidence interval of 98.18% to 100.00%.

Sensitivity in Individuals Known to be Positive for Antibodies to HIV-1 and HIV-2

The reactivity rate and clinical sensitivity of the 942 individuals who were known to be infected with HIV-1 and 201 individuals who were known to be infected with HIV-2 are summarized in the table below:

		ADVIA Centaur CHIV Assay			FDA-approved HIV Ab Assay		
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**
HIV-1 Positive	942	0	942	942	0	942	942
HIV-2 Positive	201	0	201	201	0	201	201
Total	**1143**	**0**	**1143**	**1143**	**0**	**1143**	**1143**
Total (%)		**0.0**	**100.0**	**100.0**	**0.0**	**100.0**	**100.0**

All 1143 specimens were repeatedly reactive by the ADVIA Centaur HIV Ag/Ab (CHIV) assay. The sensitivity for this population was 100.00% with an exact 95% confidence interval of 99.68% to 100.00%.

Sensitivity in Specimens Positive for Antibodies to HIV-1 Group O

The sensitivity of the ADVIA Centaur CHIV assay was assessed in 65 specimens, 15 of which were from individuals known to be positive for antibodies to HIV-1 Group O, and 50 of which were spiked/contrived Group O positive specimens. The ADVIA Centaur CHIV assay and the FDA-approved HIV Ab assay results are shown in the table below:

		ADVIA Centaur CHIV Assay			FDA-approved HIV Ab Assay		
Specimen Population	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**
Group O	15	0	15	15	0	15	15
Group O - contrived	50	0	50	50	0	50	50
Total	**65**	**0**	**65**	**65**	**0**	**65**	**65**
Total (%)		**0.0**	**100.0**	**100.0**	**0.0**	**100.0**	**100.0**

All 50 spiked/contrived Group O specimens were repeatedly reactive using the ADVIA Centaur CHIV assay. The sensitivity for this population was 100.00% with an exact 95% confidence interval of 92.89% to 100.00%.

All 15 Group O specimens known to be positive were repeatedly reactive using the ADVIA Centaur CHIV assay. The sensitivity for this population was 100.00% with an exact 95% confidence interval of 78.20% to 100.00%.

Reactivity in Specimens Presumably Positive for HIV-1 p24 Antigen, Antibody Negative and Western Blot Negative

The sensitivity of the ADVIA Centaur CHIV assay was assessed in a total of 94 presumably antigen positive, antibody negative, and Western Blot negative specimens. Of these, 44 were authentic p24 Ag positive, HIV Ab negative specimens that consisted of 24 samples from seroconversion panels, 10 samples from p24 antigen Mixed Titer Panels, and 10 aliquots from individual donor units. Fifty (50) of the 94 specimens were contrived by spiking individual HIV negative specimens with aliquots of authentic p24 Ag positive, HIV Ab negative specimens. These specimens were tested with the ADVIA Centaur CHIV and the results are shown in the table below.

		ADVIA Centaur CHIV Assay		
Specimen Population	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**
Authentic p24 Ag+/Ab- Specimens[a]	44	1	43	43
Contrived/Spiked Samples[b]	50	1	49	49
Total	94	2	92	92
Total (%)		**2.13**	**97.87**	**97.87**

[a] One mixed titer panel sample that was nonreactive for the ADVIA Centaur CHIV, was found to be reactive in two p24 Ag assays but was nonreactive in a third p24 Ag assay and in an RNA test.

[b] One contrived sample was found to be nonreactive when tested using the ADVIA Centaur CHIV assay. This contrived sample was targeted to be close to the clinical cut-off (1.00 Index) but due to sample imprecision around the cut-off, the recovered value, 0.95 Index, was close to but slightly less than the cut-off Index.

A total of 43 of the 44 authentic p24 Ag positive/Ab negative specimens were reactive using the ADVIA Centaur CHIV assay. The sensitivity for this population was 97.73% with an exact 95% confidence interval of 87.98% to 99.94%.

A total of 49 of the 50 contrived specimens were repeatedly reactive using the ADVIA Centaur CHIV assay. The sensitivity for this population was 98.00% with an exact 95% confidence interval of 89.35% to 99.95%.

HIV-1 p24 Antigen Analytical Sensitivity

Analytical sensitivity of the ADVIA Centaur CHIV assay to HIV-1 p24 antigen was determined using 1st International Reference Reagent, NIBSC code 90/636 and a Zeptometrix standard. The antigen sensitivity was tested using a standard from the Zeptometrix EIA kit with 5 lots of reagents and showed mean sensitivity to HIV-1 p24 Ag of 9.04 pg/mL (range 6.1–11.4 pg/mL). The analytical sensitivity was also verified with the HIV-1 p24 1st International Reference Reagent, NIBSC code 90/636. The standard was used to prepare a dilution series that was assayed using 5 lots of reagents. Linear regression was used to determine the concentration of the International Reference Reagent that corresponds to the ADVIA Centaur CHIV cut-off value (Index value = 1.00). The HIV-1 p24 Antigen, 1st International Reference Reagent concentration at the assay cut-off value ranged from 0.74–1.39 IU/mL. The mean sensitivity to the HIV-1 p24 Ag was 1.05 IU/mL.

Detection of HIV-1 and HIV-2 Antigen Subtypes

Forty seven HIV-1 viral isolates and 1 HIV-2 viral lysate were tested using the ADVIA Centaur CHIV assay on the ADVIA Centaur system, and were reactive. The results are shown in the table below:

Viral Lysate Subtype	Number Tested	Number Reactive
HIV-1 A	2	2
HIV-1 B	10	10
HIV-1 C	7	7
HIV-1 D	3	3
HIV-1 F	4	4
HIV-1 G	2	2
HIV-1 AE	10	10
HIV-1 AG	3	3
HIV-1 O	2	2
HIV-1 IIIB	2	2
HIV-1 strain MN & BA-L	2	2
HIV-2 NIHZ	1	1
Total	**48**	**48**

Genotype study

A group of 45 worldwide specimens known to be infected with subtypes (clades) descended from HIV-1 group M genotype and HIV-1 group O, were sourced from Seracare, and were tested with the ADVIA Centaur CHIV assay and the FDA-approved HIV Ab assay. All samples were reactive using the ADVIA Centaur CHIV and FDA-approved HIV Ab assays. The results are shown in the table below:

HIV-1 Subtype	Number Tested	Number Reactive
A	2	2
B	3	3
C	2	2
D	3	3
E	4	4
F	4	4
G	4	4
H	1	1
J	1	1
A1	2	2
F2	2	2
O	5	5
CRF01-AE	4	4
CRF02-AG	4	4
CRF06	2	2
CRF11	1	1
CRF13	1	1
Total	**45**	**45**

Seroconversion Panels

Fifteen commercially available seroconversion panels were evenly divided among the three testing sites, and were tested with the ADVIA Centaur CHIV assay and the FDA-approved HIV Ab assay for comparison. The results are shown in the table below:

Panel ID	Number Tested	Number of Reactive Panel Members		Days to First Reactive Result		Difference in Days to First Reactive Result (Based on Bleed Date)[a]
		ADVIA Centaur CHIV Assay	FDA-approved HIV Ab Assay	ADVIA Centaur CHIV Assay	FDA-approved HIV Ab Assay	
PRB926	6	4	2	7	27	20
PRB940	8	7	7	7	7	0
PRB942	4	1	0	14	--[b]	--[b]
PRB943	7	4	2	12	19	7
PRB946	4	2	0	7	--[b]	--[b]
PRB948	4	1	0	23	--[b]	--[b]
PRB954	7	2	1	17	21	4
PRB955	5	3	1	7	14	7
PRB956	5	2	1	47	50	3
PRB960	9	2	0	28	--[b]	--[b]
PRB961	9	2	0	27	--[b]	--[b]
PRB962	6	2	0	14	--[b]	--[b]
PRB963	7	2	0	17	--[b]	--[b]
PRB964	6	1	0	22	--[b]	--[b]
PRB966	10	3	2	44	48	4
Total	**97**	**38**	**16**	**NA[c]**	**NA**	**NA**

[a] The dates of the first reactive test results were compared for the FDA-approved HIV Ab assay and the ADVIA Centaur CHIV assay. If the first reactive test result occurred on the same day, then the difference is 0; if ADVIA Centaur CHIV assay had an earlier date, then the difference is positive; if ADVIA Centaur CHIV assay had a later date, then the difference is negative.

[b] All bleeds in these panels were nonreactive with the FDA-approved HIV Ab assay.

[c] NA = Not applicable

Dilutional Sensitivity

Dilutional sensitivity was evaluated by testing known anti-HIV-1 and anti-HIV-2 reactive samples that had undergone serial 2-fold dilutions with a negative sample. Results were comparable between the ADVIA Centaur CHIV assay and an FDA-approved HIV Ab assay.

For the HIV-1 samples, the ADVIA Centaur CHIV assay dilutional sensitivity ranged from 1/16–1/64 and the FDA-approved HIV Ab assay ranged from 1/8–1/64. For the HIV-2 samples, the CHIV assay dilutional sensitivity ranged from 1/32–1/64 and the FDA-approved HIV Ab assay ranged from 1/16–1/64.

High-Dose Hook Effect

Anti-HIV-1 and anti-HIV-2 positive samples with an index above 1000 were tested in the ADVIA Centaur CHIV assay and the samples reported an index >12. At index >1000, no hook effect was observed.

Recombinant p24 antigen spiked into a negative sample was tested in the ADVIA Centaur CHIV assay and the sample reported an index >12. At 1 µg/mL of p24 antigen, no hook effect was observed.

Specificity

A multisite clinical study was performed to compare the specificity of the ADVIA Centaur CHIV assay to the FDA-approved HIV Ab assay. HIV confirmatory testing was performed using FDA-approved HIV-1 Western Blot, HIV-2 EIA and HIV-1 RNA PCR tests and using research-use-only HIV-2 Western Blot and HIV-1 p24 Antigen assays.

Reactivity in Low Risk/Apparently Healthy Populations for HIV-1

The specificity of the ADVIA Centaur CHIV Assay was determined in patients who were at low risk for HIV infection (i.e., low prevalence setting, apparently healthy individuals and pregnant females). The low-risk population (6140 specimens) included 5746 specimens from apparently healthy subjects (of which 2006 were from blood donors) and 254 specimens from pregnant females. Of the 254 specimens from pregnant females, 157 were prospectively collected and 97 were retrospectively collected. The remaining 140 specimens in the low risk population included 110 low-risk pediatric subjects and 30 hospitalized patients, all of which were prospectively collected.

The reactivity of specimens from the low risk/apparently healthy population is shown in the table below:

		ADVIA Centaur CHIV assay			**FDA-approved HIV Ab Assay**			**Repeatedly Reactive Specimens (Number Reactive/Positive by Method)**			
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**HIV-1 Western Blot**	**HIV-2 EIA**	**HIV-1 p24 Antigen**	**HIV-1 RNA PCR**
Apparently Healthy	5746	5727	28	19	5739	11	7	2	0	0	0
Apparently Healthy - Pregnant (Prospective)	157	157	0	0	157	0	0	NA[a]	NA	NA	NA
Apparently Healthy - Pregnant (Retrospective)	97	97	0	0	97	0	0	NA	NA	NA	NA
Pediatric HIV Low-risk	110	110	0	0	110	0	0	NA	NA	NA	NA
Hospitalized	30	30	1	0	30	0	0	NA	NA	NA	NA
Total	**6140**	**6121**	**29**	**19**	**6133**	**11**	**7**	**2**	**0**	**0**	**0**
Total (%)		**99.69**	**0.47**	**0.31**	**99.89**	**0.18**	**0.11**	**0.03**	**0**	**0**	**0**

[a] NA = Not applicable

Of the 19 repeatedly reactive specimens,* 2 specimens from the apparently healthy population were confirmed positive for HIV-1 by Western Blot. The results from these 2 specimens were excluded from the specificity calculation. No additional testing was done on the other 17 repeatedly reactive samples and no follow-up was done on the 17 subjects. The specificity of the ADVIA Centaur CHIV assay in the low risk population was 99.72% (i.e., (6140 subjects – 19 CHIV repeatedly reactive subjects) / (6140 subjects – 2 confirmed positives) = 6121/6138) with exact 95% confidence interval of 99.56% to 99.84%.

* HIV confirmatory testing was done on all 19 repeatedly reactive specimens.

Reactivity in Low Risk/Apparently Healthy Populations for HIV-1 (Plasma Samples)

The specificity of the ADVIA Centaur CHIV Assay was determined using plasma collected from 1052 patients who were at low risk for HIV infection. The plasma specimens from this apparently healthy population were prospectively collected from blood donors.

		ADVIA Centaur CHIV assay			FDA-approved HIV Ab Assay			
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Confirmatory Assay**
Apparently Healthy	1052	1051	1	1	1051	2	1	0
Total (%)		**99.90%**	**0.10%**	**0.10%**	**99.90%**	**0.19%**	**0.10%**	**0.00%**

One plasma specimen was found to be repeatedly reactive with the ADVIA Centaur CHIV assay only and a second plasma specimen was found to be repeatedly reactive with the FDA-approved HIV Ab assay only, both of which were confirmed negative for HIV-1 and HIV-2 by the FDA-approved HIV-1/HIV-2 Ag/Ab test. The specificity of the ADVIA Centaur CHIV assay in the low risk population was 99.90% (i.e., ((1052 subjects - 1 CHIV repeatedly reactive subject) / 1052 subjects) = 1051/1052) with exact 95% confidence interval of 99.47% to 100.00%.

Blood Donor Population and Low Risk Eligible Donors

Of the 6140 individuals in the Low Risk/Apparent Healthy Populations for HIV-1 tested above, a total of 2179 were eligible to donate blood. This group included 1916 specimens collected prospectively from a blood donor population, 157 apparently healthy pregnant females and nine 18-21 year old low risk pediatric subjects who were eligible to donate blood, and retrospectively from 97 apparently healthy pregnant females. The reactivity of specimens from this blood donor/eligible donor is shown in the table below:

		ADVIA Centaur CHIV assay			FDA-approved HIV Ab Assay			Repeatedly Reactive Specimens (Number Reactive/Positive by Method)			
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**HIV-1 Western Blot**	**HIV-2 EIA**	**HIV-1 p24 Antigen**	**HIV-1 RNA PCR**
Blood Donors	1916	1907	11	9	1910	6	6	2	0	0	0
Low Risk Eligible Blood Donors	263	263	0	0	263	0	0	0	0	0	0
Total	**2179**	**2170**	**11**	**9**	**2173**	**6**	**6**	**2**	**0**	**0**	**0**
Total %		**99.59%**	**0.50%**	**0.41%**	**99.72%**	**0.28%**	**0.28%**	**0.09%**	**0.00%**	**0.00%**	**0.00%**

Of the 9 CHIV repeatedly reactive specimens, 2 specimens from the blood donor population were confirmed positive for HIV-1 by Western blot; these 2 specimens were excluded from the specificity calculation. The specificity of the ADVIA Centaur CHIV assay in the blood donor population was 99.68% (= (2179 subjects - 9 CHIV repeatedly reactive subjects) / (2179 subjects - 2 confirmed positives) = 2170/2177) with exact 95% confidence interval of 99.34% to 99.87%.

Reactivity in High Risk Populations for HIV-1

Individuals at high risk of HIV-1 infection included a total of 1100 specimens (1077 prospective and 23 retrospective specimens) with the following risk factors: illicit injection drug use, MSM (men who have sex with men), multiple transfusion recipient, renal dialysis patient, known history of sexually transmitted diseases (STD), hemophiliac, and others. Of the 1100 specimens at high risk for HIV-1 infection, there were 401 specimens from pregnant females, 204 pediatric specimens, and 495 specimens from other individuals at high risk for HIV-1. The specimens were collected from individuals ranging in age from 4 months to 79 years.

The reactivity of specimens from an HIV-1 high risk population is shown in the table below:

		ADVIA Centaur CHIV assay			FDA-approved HIV Ab Assay			Repeatedly Reactive Specimens (Number Reactive/Positive by Method)			
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**HIV-1 Western Blot**	**HIV-2 EIA**	**HIV-1 p24 Antigen**	**HIV-1 RNA PCR**
Illicit Injection Drug Use	47	47	0	0	47	0	0	NA[a]	NA	NA	NA
MSM	32	31	1	1	32	0	0	0	0	0	0
Multiple Transfusions	40	40	0	0	40	0	0	NA	NA	NA	NA
Renal Dialysis	27	27	1	0	27	0	0	NA	NA	NA	NA
STD	108	108	0	0	108	0	0	NA	NA	NA	NA
Other	216	209	7	7	212	4	4	1	0	0	1
Hemophiliac - Prospective	2	2	0	0	2	0	0	NA	NA	NA	NA
Hemophiliac - Retrospective	23	23	0	0	23	0	0	NA	NA	NA	NA
Pregnant	401	379	23	22	379	22	22	18	2[b]	0	0
Pediatric	204	202	2	2	202	2	2	2	NA	NA	NA
Total	**1100**	**1068**	**34**	**32**	**1072**	**28**	**28**	**21**	**2**	**0**	**1**
Total %		**97.09**	**3.09**	**2.91**	**97.50**	**2.55**	**2.55**	**1.91**	**0.18**	**0.00**	**0.09**

[a] NA = Not applicable

[b] Confirmed by HIV-2 Western Blot

The 24 specimens confirmed positive by Western Blot, HIV-2 EIA or HIV-1 RNA testing were repeatedly reactive using the ADVIA Centaur CHIV assay (24/24 or 100% detection). Of the 1100 prospectively collected specimens tested with the ADVIA Centaur CHIV assay, 2.91% (32/1100) were repeatedly reactive of which 75.00% (24/32) were confirmed positive by HIV-1 Western Blot, HIV-2 EIA, or HIV-1 RNA testing. Of the 1100 specimens tested with the FDA-approved HIV Ab assay, 2.55% (28/1100) were repeatedly reactive and 24 of these 28 specimens, or 85.71% (24/28) were confirmed positive by HIV-1 Western Blot, HIV-2 EIA, or HIV-1 RNA testing.

A comparison of the ADVIA Centaur CHIV assay results versus the FDA-approved HIV Ab assay results are summarized in the table below. None of the specimens that were repeatedly reactive only on the ADVIA Centaur CHIV assay were confirmed positive.

	FDA-approved HIV Ab Assay		
ADVIA Centaur CHIV Assay	**Repeatedly Reactive**	**Nonreactive**	**Total**
Repeatedly Reactive	28	4[a]	32
Nonreactive	0	1068	1068
Total	28	1072	1100

[a] Four specimens were nonreactive by HIV-1 WB, HIV-2 EIA, HIV-1 P24 Ag, and HIV-1 RNA PCR.

For the ADVIA Centaur CHIV assay, 24 of the 32 repeatedly reactive specimens from the high risk prospective population were positive for HIV-1 by Western blot, HIV-2 EIA, or RNA testing. The results from these 24 specimens were excluded from the specificity calculation. The specificity of the ADVIA Centaur CHIV assay in the high risk prospective population for HIV-1 was 99.26% (1068/ (1100-24)) with exact 95% confidence interval of 98.54–99.68%.

Reactivity in High Risk Populations for HIV-2 in Endemic Area

Individuals at high risk of HIV-2 infection included 501 prospectively enrolled from Guinea-Bissau, an HIV-2 endemic area. The specimens were collected from individuals ranging in age from 18 to 85 years. The specimens were tested by the ADVIA Centaur CHIV assay and the FDA-approved HIV Ab assay and the results are shown in the table below:

		ADVIA Centaur CHIV assay			FDA-approved HIV Ab Assay			Repeatedly Reactive Specimens (Number Reactive/Positive by Method)			
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**HIV-1 Western Blot**	**HIV-2 EIA**	**HIV-1 p24 Antigen**	**HIV-1 RNA PCR**
Individuals at increased Risk from an HIV-2 Endemic Area	501	473	29	28	474	27	27	23	2[a]	0	0
Total (%)		**94.41**	**5.79**	**5.59**	**94.60**	**5.39**	**5.39**	**4.59**	**0.40**	**0.00**	**0.00**

[a] Confirmed by HIV-2 Western Blot

All 23 specimens confirmed positive by Western Blot were repeatedly reactive using the ADVIA Centaur CHIV assay (23/23, 100% detection). The 2 specimens confirmed positive by HIV-2 ABS (EIA) were repeatedly reactive using the ADVIA Centaur CHIV assay (2/2, 100% detection). A total of 29 samples (26 of which were repeatedly reactive for both assays, 1 of which was repeatedly reactive for the FDA-approved HIV Ab assay only, and 2 of which were repeatedly reactive for the ADVIA Centaur CHIV assay) were tested by means of one or more confirmatory tests. Of these 29 samples, 25 samples were confirmed positive. All 25 confirmed positive samples were found to be repeatedly reactive by the ADVIA Centaur CHIV and the FDA-approved HIV Ab assays. Of the 26 samples that were found to be repeatedly reactive for both assays, 25 samples (25/26, 96.15% detection, with exact 95% confidence interval of 80.36% to 99.90%) were confirmed positive using one or more confirmatory tests.

For the ADVIA Centaur CHIV assay, since 25 of the 501 repeatedly reactive specimens from the high risk prospective population were positive for HIV-1 or HIV-2 by Western Blot, the results from these 25 specimens were excluded from the specificity calculation. The specificity of the ADVIA Centaur CHIV assay in the high risk prospective population for HIV-2 was 99.37% (473/476) with exact 95% confidence interval of 98.17% to 99.87%.

A comparison of the ADVIA Centaur CHIV assay results versus the FDA-approved HIV Ab assay results are summarized in the table below:

	FDA-approved HIV Ab Assay		
ADVIA Centaur CHIV Assay	**Repeatedly Reactive**	**Nonreactive**	**Total**
Repeatedly Reactive	26	2[a]	28
Nonreactive	1[b]	472	473
Total	27	474	501

[a] Two specimens were nonreactive by HIV-1 Western Blot, HIV-2 EIA, HIV-1 p24 Ag, and HIV-1 RNA PCR.

[b] One specimen was nonreactive by HIV-1 Western Blot, HIV-2 EIA, HIV-1 p24 Ag, and HIV-1 RNA PCR.

One specimen that was found to be nonreactive for the ADVIA Centaur CHIV assay and repeatedly reactive for the FDA-approved HIV Ab assay was found to be nonreactive for the HIV-2 EIA confirmatory assay. Two specimens that were found to be repeatedly reactive for the ADVIA Centaur CHIV assay and nonreactive for the FDA-approved HIV Ab assay were found to be nonreactive for the HIV-2 EIA confirmatory assay.

Pregnancy Population Studies

A multisite clinical study was performed to compare the performance of the ADVIA Centaur CHIV assay to the FDA-approved HIV Ab assay using specimens from pregnant females. Prospectively and retrospectively collected samples from 718 pregnant women across all three trimesters were tested at three testing sites. Initially reactive specimens were repeat-tested and repeatedly reactive apparently healthy and high risk samples were tested by HIV confirmatory testing. The reactivity of the ADVIA Centaur CHIV assay in pregnant females is given in the table below:

		ADVIA Centaur CHIV assay			FDA-approved HIV Ab Assay			Repeatedly Reactive Specimens (Number Reactive/Positive by Method)			
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**HIV-1 Western Blot**	**HIV-2 EIA**	**HIV-1 p24 Antigen**	**HIV-1 RNA PCR**
HIV-Positive Pregnant Females	63	0	63	63	0	63	63	NA[a]	NA	NA	NA
High-Risk Pregnant Females	401	379	23	22	379	22	22	18	2[b]	0	0
Apparently Healthy - Pregnant (Prospective)	157	157	0	0	157	0	0	NA	NA	NA	NA
Apparently Healthy - Pregnant (Retrospective)	97	97	0	0	97	0	0	NA	NA	NA	NA
Total	**718**	**633**	**86**	**85**	**633**	**85**	**85**	**18**	**2**	**0**	**0**
Total (%)		**88.16**	**11.98**	**11.84**	**88.16**	**11.84**	**11.84**	**2.51**	**0.28**	**0.00**	**0.00**

[a] NA = Not applicable

[b] Confirmed by HIV-2 Western Blot

All 63 HIV positive pregnant female specimens were repeatedly reactive by the ADVIA Centaur CHIV assay and the FDA-approved HIV Ab assay. The sensitivity for this population was 100.00% (63/63) with an exact 95% confidence interval of 94.31% to 100.00%.

Of the 401 high risk pregnant female specimens tested, 22 were found to be repeatedly reactive for both the ADVIA Centaur CHIV and the FDA-approved HIV Ab assays. From the 22 samples, 20 were confirmed positive by HIV confirmatory testing. The ADVIA Centaur CHIV assay identified 20 newly infected pregnant female specimens from this population.

A total of 633 low and high risk pregnant female specimens were nonreactive by the ADVIA Centaur CHIV assay. Since 20 high risk pregnant female specimens were confirmed positive by either HIV-1 Western Blot or HIV-2 EIA, they were excluded from the specificity calculation. The specificity by the ADVIA Centaur CHIV assay for the low and high risk pregnant female prospective population was 99.63% with an exact 95% confidence interval of 98.66% to 99.95%. The specificity by the ADVIA Centaur CHIV assay for the low risk pregnant female retrospective population was 100.00% (97/97) with an exact 95% confidence interval of 96.27% to 100.00%. The table below shows the reactivity of the pregnant females at high risk for infection with HIV.

		ADVIA Centaur CHIV assay			FDA-approved HIV Ab Assay		
Population	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**
First Trimester	57	51	6	6	51	6	6
Second Trimester	98	96	2	2	96	2	2
Third Trimester	246	232	15	14	232	14	14
Total	**401**	**379**	**23**	**22**	**379**	**22**	**22**
Total (%)		**94.51**	**5.74**	**5.49**	**94.51**	**5.49**	**5.49**

Pediatric Population Study

A multisite clinical study was performed to compare the performance of the ADVIA Centaur CHIV assay to the FDA-approved HIV Ab assay using pediatric specimens. A total of 364 pediatric specimens that were tested across three sites included both prospective as well as vendor supplied retrospective samples. The pediatric samples included 110 low risk, 204 high risk and 50 HIV reactive samples. The prospective and retrospective samples were collected from children in the age range from 2–21 years of age.

Repeatedly reactive low risk and high risk samples were tested by HIV confirmatory testing. The reactivity of the ADVIA Centaur CHIV assay with pediatric samples is summarized in the table below:

		ADVIA Centaur CHIV assay			FDA-approved HIV Ab Assay			Repeatedly Reactive Specimens (Number Reactive/Positive by Method)
Specimen Category	**Number Tested**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**Non-reactive**	**Initially Reactive**	**Repeatedly Reactive**	**HIV-1 Western Blot**
Pediatric HIV Low Risk	110	110	0	0	110	0	0	NA[a]
Pediatric HIV High Risk	204	202	2	2	202	2	2	2
Pediatric HIV Positive - Prospective	15	0	15	15	0	15	15	NA
Pediatric HIV Positive - Retospective	35	0	35	35	0	35	35	NA
Total	**364**	**312**	**52**	**52**	**312**	**52**	**52**	**2**
Total (%)		**85.71**	**14.29**	**14.29**	**85.71**	**14.29**	**14.29**	**0.55**

[a] NA = Not applicable

All 50 HIV presumed positive specimens were repeatedly reactive by the ADVIA Centaur CHIV assay and were confirmed positive by the HIV-1 Western Blot confirmatory test. The sensitivity for both the prospective and retrospective populations was 100.00% (equal to 15/15 for the prospective population and equal to 35/35 for the retrospective population), with an exact 95% confidence interval of 78.20% to 100.00% for the prospective population and an exact 95% confidence interval of 90.00% to 100.00% for the retrospective population.

A total of 312 of the 314 low and high risk pediatric specimens were nonreactive by the ADVIA Centaur CHIV assay. Two high risk specimens that were repeatedly reactive by the ADVIA Centaur CHIV assay and the FDA-approved HIV Ab assay were confirmed to be reactive by HIV-1 Western Blot. The ADVIA Centaur CHIV assay identified two newly infected pediatric specimens from the high risk population. These results were excluded from the specificity calculation. The specificity by the ADVIA Centaur CHIV assay for the low and high risk pediatric population was 100% (312/312) with an exact 95% confidence interval of 98.82% to 100.00%.

The distribution of the results by age range and gender for the pediatric specimens categorized as high risk for HIV is presented in the table below.

Distribution of Pediatric Specimens Categorized as High Risk for HIV

			ADVIA Centaur CHIV assay			FDA-approved HIV Ab Assay			HIV-1 Western Blot
Age	**Gender**	**Number Tested**	**Nonreactive**	**Initially Reactive**	**Repeatedly Reactive**	**Nonreactive**	**Initially Reactive**	**Repeatedly Reactive**	
2 to 5 Years	Female	7	7	0	0	7	0	0	NA[a]
	Male	10	10	0	0	10	0	0	NA
6 to 10 Years	Female	34	34	0	0	34	0	0	NA
	Male	27	27	0	0	27	0	0	NA
11 to 15 Years	Female	44	43	1	1	43	1	1	1
	Male	27	27	0	0	27	0	0	NA
16 to 21 Years	Female	27	26	1	1	26	1	1	1
	Male	28	28	0	0	28	0	0	NA
Total		**204**	**202**	**2**	**2**	**202**	**2**	**2**	**2**
Total (%)			**99.02**	**0.98**	**0.98**	**99.02**	**0.98**	**0.98**	**0.98**

[a] NA = Not applicable

Reproducibility Study

The precision of the ADVIA Centaur Combo HIV assay was evaluated utilizing a total of three reagents lots. Each site utilized two reagent lots. Each lot was run at two sites and each site used two lots, as balanced, incomplete blocks. Subsequently, on different days, they performed their second reagent lot's study. An 8-member panel was assayed in replicates of 4 with 2 runs per day over 5 days for each lot (n = 240 for each sample). The panel members consisted of HIV-1 antibody low and high positive samples, HIV-2 antibody low and high positive samples, p24 antigen low and high positive samples, one HIV-1 Group O antibody positive sample and one HIV negative sample. Calibrators (tested as unknown samples) and controls were run in parallel in replicates of 4. The results are shown in the table below:

Specimen Type	Mean (Index)	Within-Run Repeatability		Between-Run		Between-Day		Within Site and Lot		Between-Site		Between-Lot		Total Precision (Within-Lab)	
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)
Negative Pool	0.77	0.02	N/A	0.04	N/A	0.01	N/A	0.05	N/A	0.02	N/A	0.06	N/A	0.08	N/A
Low HIV-1 Pool	1.27	0.03	2.7	0.06	4.7	0.00	0.0	0.07	5.5	0.03	2.5	0.07	5.8	0.11	8.3
High HIV-1 Pool	3.80	0.08	2.1	0.20	5.3	0.09	2.5	0.24	6.2	0.10	2.5	0.11	2.9	0.28	7.3
Low HIV-2 Pool	1.34	0.04	3.2	0.06	4.4	0.00	0.0	0.07	5.4	0.06	4.4	0.08	5.8	0.12	9.0
High HIV-2 Pool	3.60	0.11	3.0	0.14	4.0	0.00	0.0	0.18	5.0	0.11	3.0	0.17	4.8	0.27	7.5
Type O Pool	3.07	0.13	4.4	0.16	5.1	0.00	0.0	0.21	6.7	0.13	4.2	0.25	8.2	0.35	11.4
Low p24 Pool	2.91	0.08	2.8	0.14	4.9	0.02	0.6	0.16	5.7	0.11	3.8	0.39	13.3	0.43	14.9
High p24 Pool	5.64	0.16	2.8	0.26	4.6	0.11	2.0	0.33	5.8	0.15	2.6	1.04	18.4	1.10	19.4

Interferences

The ADVIA Centaur CHIV assay was evaluated on the ADVIA Centaur system for potential cross-reactivity with other viral infections and disease state specimens. The reactive HIV status of each specimen was verified using an FDA-approved HIV Ab assay. The results are shown in the table below:

		Number of Reactive CHIV Results	
Clinical Category	**Number Tested**	**ADVIA Centaur Assay**	**FDA-approved HIV Ab Assay**
Alcoholic Hepatitis	5	1[a]	1[a]
Anti-Nuclear Antibody (ANA)	9	0	0
Crohn's Disease	10	0	0
Cytomegalovirus (CMV) IgG	5	0	0
Cytomegalovirus (CMV) IgM	10	0	0
Diabetes	10	0	0
Escherichia coli Ag	1	0	0
Epstein-Barr Virus (EBV) IgG	5	0	0
Epstein-Barr Virus (EBV) IgM	10	0	0
Fibromyalgia condition	10	0	0
Flu Vaccine recipient	22	0	0
Grave's Disease	8	0	0
HAMA	18	0	0
Hepatitis A Infection (HAV) IgM	5	0	0
Hepatitis B Infection (HBsAg)	10	0	0
Hepatitis C Infection (HCV) Ag	5	0	0
Hepatitis C Infection (HCV) Ab	10	0	0
Herpes Simplex Virus (HSV1/2) IgG	5	0	0
Herpes Simplex Virus (HSV1/2) IgM	10	0	0
High Human Immunoglobulin A	11	0	0
High Human Immunoglobulin G	13	0	0
High Human Immunoglobulin M	9	0	0
Human T-cell Lymphotropic virus (HTLV I/II)	10	0	0
Mixed Connective Tissue Disease (MCTD)	9	0	0
Rheumatoid Factor positive	10	0	0
Rubella IgG	10	0	0
Rubella IgM	10	0	0
Scleroderma	10	0	0
Staphylococcus aureus Ag	1	0	0
Syphilis IgG	9	0	0
Syphilis IgM	10	0	0
Systemic Lupus Erythematosus (SLE)	9	0	0
Toxoplasma IgG	10	0	0

		Number of Reactive CHIV Results	
Clinical Category	**Number Tested**	**ADVIA Centaur Assay**	**FDA-approved HIV Ab Assay**
Toxoplasma IgM	12	0	0
Ulcerative colitis	9	0	0
Varicella Zoster Virus (VZV) IgG	10	0	0
MPO and PR3 for Vasculitis	10	0	0
Candidiasis (yeast infection)	5	0	0

[a] One sample from an alcoholic hepatitis patient was reactive using both the ADVIA Centaur CHIV assay and the FDA-approved HIV Ab assay. This sample was confirmed HIV-1 reactive with an FDA-approved differentiation assay.

Interfering substances at the levels indicated in the table below were tested as described in CLSI Document EP7-A2[16] using the ADVIA Centaur CHIV assay on the ADVIA Centaur system. For each endogenous substance level the following samples were assayed; a negative sample (neat), an HIV-1 antibody sample, an HIV-2 antibody sample, an HIV-1 Type O antibody sample and an HIV antigen sample. All positive samples tested were generated by spiking the analyte into a confirmed negative (neat) donor sample to a target lndex ranging between 2-4. These specimens were spiked with the interferents and assayed with ADVIA Centaur CHIV assay. None of the interferents at the levels tested produced a change in clinical interpretation of the assay. ln addition, a potentially interfering effect of biotin was evaluated and no interference was observed.

Serum Specimens That Are	**Demonstrate ≤ 10% Change in Results Up To**
hemolyzed	500 mg/dL of hemoglobin
lipemic	1000 mg/dL of triglycerides
icteric	40 mg/dL of conjugated bilirubin
icteric	40 mg/dL of unconjugated bilirubin
proteinemic	3.5 g/dL of protein[a]
hyper-IgG	60 mg/mL of immunoglobulin G
hyperproteinemic	12 g/dL of protein

[a] Demonstrates ≤ 10% change in results with protein as low as 3.5 g/dL.

Specimens That Contain	**Demonstrate ≤ 10% Change in Results Up To**
cholesterol	400 mg/dL
biotin	500 ng/mL

Technical Assistance

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

www.siemens.com/diagnostics

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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	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
0°C	Do not freeze (> 0°C)			Temperature limitation
	Lower limit of temperature			Upper limit of temperature
	Keep away from sunlight and heat	UP		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

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