



QC

HCV



Contents

REF	Contents
03439141	2 vials of Negative Control 2 vials of Positive Control Expected Values Card and barcode labels

Preliminary 00363160 Rev. A, 2004-06

Intended Use

For in vitro diagnostic use in monitoring the performance of the HCV assay on the ADVIA Centaur® Systems. The performance of the HCV quality control material has not been established with any other anti-HCV assays.

Control Description

Volume	Ingredients	Storage	Stability
7.0 mL/Vial	Processed human plasma negative and positive for anti-HCV with preservatives	2-8°C	Until the expiration date on the vial label or onboard-8 hours

R43 Irritant! May cause sensitization by skin contact. Avoid contact with skin. S24, S37 Wear suitable gloves. Contains: 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one



CAUTION! POTENTIAL BIOHAZARD: The controls contain human source material. No known test method can offer complete assurance that products derived from human blood will not transmit infectious agents. All products manufactured using human source material should be handled as potentially infectious. Handle this product according to established good laboratory practices and universal precautions.¹⁻³ Use eye protection and gloves when handling this product; wash hands after handling.

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

For In Vitro Diagnostic Use.

Preparing the Quality Control Material

Gently swirl and invert the vials to ensure homogeneity.

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 HCV quality control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur HCV 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 or to the online help system.

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.

- Schedule the quality control samples to the worklist.
- Label two sample cups with quality control barcode labels: one for the positive, and another for the negative.

NOTE: Each drop from the control vial is approximately 50 µL.

- Gently mix the quality control materials and dispense at least 4 to 5 drops into the appropriate sample cups.
- Load the sample cups in a rack.
- Place the rack in the sample entry queue.
- Ensure that the assay reagents are loaded.
- 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.

Reviewing, Editing, and Printing Results

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

Expected Results

Refer to the Expected Values card for the assigned values specific for the lot number of the HCV quality control material. The expected values are traceable to the standardization of the HCV assay. For additional information, refer to the reagent instructions for use.

The expected values should be used only as a guide in evaluating performance. Since performance is subject to the design and condition of each instrument or reagent system, it is recommended that each laboratory establish its own expected values and acceptable limits. The mean values established should fall within the range specified in Expected Values. Individual results may fall outside the range.

Taking Corrective Action

If the quality control results do not fall within the suggested Expected Values or within the laboratory's established values, then do the following:

- consider the sample results invalid and repeat testing if controls are out of range
- review these instructions to ensure that the assay was performed according to the procedures recommended by Bayer HealthCare
- verify that the materials are not expired
- verify that required maintenance was performed
- if necessary contact Bayer HealthCare for more assistance

Limitations

The results obtained using the HCV quality control material depend on several factors. Erroneous results can occur from improper storage, inadequate mixing, or sample handling errors associated with system or assay procedures.

- Do not return any quality control materials back into the vials after testing because evaporation and contamination can occur, which may affect results.
- Dispose of any quality control material 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.

Disposal

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 all federal, state, and local requirements.

Technical Assistance

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

References

- National Committee for Clinical Laboratory Standards. Procedures for the Handling and Processing of Blood Specimens; Approved guideline-2nd Edition. NCCLS document H18-A2. Wayne (PA):NCCLS;1999.
- 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;37:377-82, 387-8.
- National Committee for Clinical Laboratory Standards. Protection of laboratory workers from instrument biohazards and infectious disease transmitted by blood, body fluids, and tissue; approved guideline. NCCLS Document M29-A2. Wayne (PA):NCCLS;2001.

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HCV

Assay for the Detection of Immunoglobulin G (IgG) Antibodies to Hepatitis C Virus

Assay Summary

Sample Type	Serum, potassium EDTA plasma, lithium or sodium heparinized plasma
Sample Volume	10 μ L
Calibrator	HCV

Contents

REF	Contents	Number of Tests
03438099	1 ReadyPack® primary reagent pack containing ADVIA Centaur® HCV Solid Phase, Lite Reagent, and Ancillary Reagent 1 Ancillary pack containing ADVIA Centaur HCV Ancillary Reagent  ADVIA Centaur HCV Master Curve card 1 vial HCV Low Calibrator   1 vial HCV High Calibrator   ADVIA Centaur HCV Calibrator Assigned Value card	200

For a definition of symbols used in product labeling, please refer to Appendix D, *Understanding the symbols*, in the *ADVIA Centaur® Assay Manual*.

Intended Use

The ADVIA Centaur HCV assay is an *in vitro* diagnostic immunoassay for the qualitative determination of immunoglobulin G (IgG) antibodies to hepatitis C virus (HCV) in human serum and plasma (EDTA, lithium or sodium heparinized) using the ADVIA Centaur System. The assay may be used in conjunction with other serological and clinical information to aid in the diagnosis of individuals with symptoms of hepatitis and in individuals at risk for hepatitis C infection.

This product is not for use for testing or screening pooled samples containing specimens from more than one individual, or otherwise in blood or plasma screening. Purchase of this product does not convey any right or license under any relevant patents to use the product for testing or screening pooled blood samples containing specimens from more than one individual or otherwise in blood or plasma screening.

WARNING: This assay has not been FDA cleared or approved for the screening of blood or plasma donors.

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

Materials Required But Not Provided

REF	Description	Contents
03439141	ADVIA Centaur System ADVIA Centaur HCV quality control material	2 x 7 mL Negative Control  2 x 7 mL Positive Control  Expected Value card
01137199 (112351)	ADVIA Centaur Wash 1 	2 x 1500 mL/pack

Summary and Explanation of the Test

The ADVIA Centaur HCV assay is an indirect two wash sandwich immunoassay used for the detection of IgG antibody to hepatitis C virus (HCV) in human serum or plasma.

HCV is endemic throughout the world and poses a serious health problem. HCV is the major etiologic agent of chronic non-A, non-B hepatitis. The presence of antibodies to HCV indicates that an individual may have been infected with HCV or may be capable of transmitting HCV infection.^{1,2}

At least 170 million individuals worldwide are chronically infected with HCV. HCV infection is often asymptomatic; however, the majority (over 55-85%) of the individuals exposed to HCV become chronically infected. In 20% of these chronically infected individuals, the disease progresses to cirrhosis, liver failure, and possibly hepatocellular carcinoma or cholangiocarcinoma.¹⁻⁴

Despite the large number of individuals chronically infected with HCV, the incidence of HCV infections per year in developed countries has declined significantly over the last few decades. This has been attributed to improved standards of living and increased public health measures in the medical community such as the screening of blood and blood products, the use of disposable syringes and needles, and the implementation of universal precautions throughout the healthcare system.²

Common modes of HCV transmission include blood transfusion, intravenous drug use, nosocomial exposure, during assisted reproductive techniques, and from mother-to-infant during pregnancy, delivery, or the postpartum period.^{2,5}

The HCV genome consists of several functional regions: the core, the envelope (including the E1 and E2 regions), and the non-structural region (including NS2, NS3, NS4, and NS5). Immunoassays for the detection of antibodies to HCV utilize a combination of synthetic or recombinant proteins as antigens.¹

The ADVIA Centaur HCV assay uses two HCV recombinant (c200 and NS5) antigens and one synthetic HCV core (c22) peptide. The c200 protein is derived from both the NS3 and NS4 sequences. At least two major epitopes are located within the NS3 and NS4 regions. These two specific epitopes have been extensively studied and shown to be critical for the detection of antibodies in individuals infected with HCV. The NS5 antigen is derived from the putative RNA polymerase portion of the HCV genome. A significant number of individuals infected with HCV develop an immunologic response to NS5. The c22 peptide is an amino acid sequence derived from the core region of the genome. This peptide contains the major HCV core epitope. An immunologic response to the core protein is often an early indicator of infection by HCV.¹

Assay Principle

The ADVIA Centaur HCV assay is an indirect two wash sandwich immunoassay. The sample is incubated with Solid Phase containing recombinant and synthetic peptide HCV antigens. Antigen-antibody complexes will form if anti-HCV antibody is present in the sample. Lite

Reagent containing monoclonal anti-human IgG labeled with acridinium ester is used to detect anti-HCV IgG in the sample.

The system automatically performs the following steps:

- dispenses 10 µL of sample into a cuvette
- dispenses 100 µl Ancillary Reagent and incubates for 5 minutes at 37°C
- dispenses 100 µL of Solid Phase reagent and 50 ul of Ancillary Reagent and incubates for 18 minutes at 37°C
- separates the Solid Phase from the mixture and aspirates the unbound reagent
- washes the cuvette with Wash 1
- dispenses 50 µL of Lite Reagent, incubates the mixture for 18 minutes at 37°C
- washes the cuvette with Wash 1
- dispenses 300 µL each of Acid Reagent and Base Reagent to initiate the chemiluminescent reaction
- reports results according to the selected option, as described in the system operating instructions or in the online help system

The relative light units (RLUs) detected by the ADVIA Centaur system are used to calculate the Index Value from the Master Curve. Assay results above the cutoff of the assay are not indicative of antibody level. Refer to *Interpretation of Results* for a description of the Cutoff Value calculation.

Specimen Collection and Handling

Serum, potassium EDTA plasma, lithium or sodium heparinized plasma are the recommended sample types for this assay.

Do not use specimens with obvious microbial contamination. The performance of the ADVIA Centaur HCV assay 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 following general recommendations for handling and storing blood samples are furnished by the National Committee for Clinical Laboratory Standards⁶, and augmented with additional sample handling studies using the ADVIA Centaur HCV assay:

- Handle all samples as if capable of transmitting disease.
- Samples 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.
- Test samples as soon as possible after collecting. Store samples at 2 to 8°C if not tested immediately.
- Store samples stoppered and upright at all times at 2 to 8°C up to 7 days.
- Freeze samples, devoid of red blood cells, at or below -20°C for longer storage. Do not store in a frost-free freezer. When 10 samples were subject to 4 freeze/thaw cycles, no clinically significant differences were observed. Thoroughly mix thawed samples and centrifuge at 10,000g for 2 min before using.
- Package and label samples for shipment in compliance with applicable federal and international regulations covering the transport of clinical samples and etiological agents. Samples refrigerated up to 7 days demonstrated no qualitative differences. Store samples stoppered and upright at 2 to 8°C upon arrival. If shipment is expected to exceed 7 days, ship specimens frozen.

Before placing samples on the system, ensure the following:

- Samples are free of fibrin or other particulate matter. Remove particulates by centrifugation. (example: 1500xg for 10 minutes; follow tube manufacturer's recommendations⁶⁾)
- Samples are free of bubbles or foam.

Reagents

 Store the reagents upright at 2–8°C. Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to Appendix C, *Handling Reagents*.

 Keep away from sunlight. Protect reagent packs from all light sources. Reagent packs loaded on the system are protected from light. Store unused reagent packs at 2–8°C away from light sources.

Reagent Pack	Reagent	Volume	Ingredients	Storage	Stability
ADVIA Centaur HCV ReadyPack primary reagent pack	Lite Reagent	10.0 mL/ reagent pack	anti-human IgG monoclonal antibody (~0.05 µg/mL) labeled with acridinium ester in buffer with bovine serum albumin, sodium azide (< 0.1%), and surfactant	2–8°C	until the expiration date on the pack label. For onboard stability, refer to <i>Onboard Stability and Calibration Interval</i> .
	Solid Phase	20.0 mL/ reagent pack	streptavidin coated paramagnetic microparticles preformed with biotinylated recombinant c200 HCV antigen and biotinylated synthetic c22p HCV antigen (~0.3 µg/mL) in buffer with surfactant, stabilizers, and preservatives	2–8°C	until the expiration date on the pack label. For onboard stability, refer to <i>Onboard Stability and Calibration Interval</i> .
	Ancillary Reagent	10.0 mL/ reagent pack	biotinylated recombinant NS5 HCV antigen (~0.5 µg/mL) in buffer with sodium azide (< 0.1%), and surfactant	2–8°C	until the expiration date on the pack label. For onboard stability, refer to <i>Onboard Stability and Calibration Interval</i> .
ADVIA Centaur HCV  Ancillary Reagent Readypack	Ancillary Reagent	20.0 mL/ Ancillary pack	bovine serum albumin, goat serum, , sodium azide (< 0.1%), and surfactant	2–8°C	until the expiration date on the pack label. For onboard stability, refer to <i>Onboard Stability and Calibration Interval</i> .
HCV calibrator vials	Calibrators	2.0 mL/ vial	processed human plasma negative and positive for anti-HCV with preservatives	2–8°C	until the expiration date on the vial or onboard–8 hours
HCV quality control material vials*	Controls	7.0 mL/ vial	processed human plasma negative and positive for anti-HCV with preservatives	2–8°C	until the expiration date on the vial or onboard–8 hours
ADVIA Centaur  Wash 1	Wash 1	1500 mL/ pack	phosphate buffered saline with sodium azide (< 0.1%) and surfactant	2–25°C	until the expiration date on the vial or onboard–14 days

* See Materials Required But Not Provided

Precautions and Warnings

For *In Vitro* Diagnostic Use.

CAUTION: Sodium azide can react with copper and lead plumbing to form explosive metal azides. On disposal, flush reagents with a large volume of water to prevent the buildup of azides, if disposal into a drain is in compliance with federal, state, and local requirements.



R43 **Irritant!** May cause sensitization by skin contact. Avoid contact with skin. Wear suitable gloves.
 S24 **Contains:** 5-chloro-2-methyl-2H-isothiazol-3-one and 2-methyl-2H-isothiazol-3-one; included in
 S37 Calibrators and Controls.

CAUTION! POTENTIAL BIOHAZARD: Some components of this product contain human source material. No known test method can offer complete assurance that products derived from human blood will not transmit infectious agents. All products manufactured using human source material should be handled as potentially infectious. Handle this product according to established good laboratory practices and universal precautions.⁷⁻⁹

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 control, low calibrator and high calibrator have been assayed by FDA-approved methods and found to be nonreactive for hepatitis B virus and antibody to HIV-1/2. The positive control, low calibrator, and high calibrator contain human plasma that is reactive for antibody to HCV. The units were treated with a BPL-UV inactivation procedure¹⁰, however, all products manufactured using human source material should be handled as potentially infectious.

Loading Reagents

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

CAUTION: Mix all primary reagent packs by hand before loading them onto the system. Visually inspect the bottom of the reagent pack to ensure that all particles are dispersed and resuspended. For detailed information about preparing the reagents for use, refer to Appendix C, *Handling Reagents* in the ADVIA Centaur Assay Manual.

Load the ReadyPack primary reagent packs in the primary reagent compartment using the arrows on the packs as a placement guide. The system automatically mixes the primary reagent packs to maintain homogeneous suspension of the reagents. Load the ReadyPack ancillary reagent packs in the ancillary reagent entry. For detailed information about loading reagents, refer to the system operating instructions or to the online help system.

CAUTION: 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.

CAUTION: The Ancillary Reagent provided in this kit is matched to the ReadyPack primary reagent pack. Do not mix Ancillary Reagent lots with different lots of reagent packs.

Onboard Stability and Calibration Interval

Onboard Stability	Calibration Interval
41 days	28 days

The ADVIA Centaur HCV 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

CAUTION:

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

Master Curve Calibration

The ADVIA Centaur HCV assay requires a Master Curve calibration when using a new lot number of Lite Reagent, Solid Phase, and Ancillary Reagent. For each new lot number of Lite Reagent, Solid Phase, and Ancillary 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 or to the online help system.

Calibration

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

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 HCV Calibrator barcode labels to identify the Low and High Calibrator sample cups when performing the ADVIA Centaur HCV 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 a Calibration

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 or to the online help system.

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

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

NOTE: Each drop from the calibrator bottle is approximately 50 μ L.

3. Gently mix the Low and High Calibrators and dispense at least 4 to 5 drops into the appropriate sample cups.
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.

Quality Control

For quality control of the ADVIA Centaur HCV assay, use ADVIA Centaur HCV quality control materials. Refer to the Expected Value card for the suggested expected values specific for the lot number of the positive and negative controls. Additional controls may be tested according to guidelines or requirements of local, state, and/or federal regulations or accrediting organizations.

NOTES: The quality control material furnished is intended to monitor substantial reagent failure. If additional controls are desired, it is recommended to run a negative control and positive control close to the clinically relevant point (1.0 Index). The quality control furnished is in a defibrinated plasma, e.g., serum matrix. The user should provide alternate control material for plasma when necessary.

Using 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 HCV quality control barcode labels to identify the positive and negative sample cups when performing the ADVIA Centaur HCV 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 or to the online help system.

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.

NOTE: Each drop from the control vial is approximately 50 μ L.

3. Gently mix the quality control materials and dispense at least 4 to 5 drops into the appropriate sample cups.
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 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.

Taking Corrective Action

If the quality control results do not fall within the suggested Expected Values or within the laboratory's established values, then do the following:

- consider the sample results invalid and repeat testing if controls are out of range.
- investigate and determine the cause for the unacceptable control results

- review these instructions to ensure that the assay was performed according to the procedures recommended by Bayer HealthCare.
- verify that the materials are not expired.
- verify that required maintenance was performed.
- if necessary contact Bayer HealthCare for more assistance.
- When the condition is corrected, retest the controls and confirm that results are within acceptable limits.
- It is advisable to repeat some or all patient specimens before reporting results for this run.

Sample Volume

This assay requires 10 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 *Sample Volume Requirements* in the *ADVIA Centaur Reference Manual*.

Assay Procedure

For detailed procedural information, refer to the system operating instructions or to the online help system.

CAUTION: Do not load more than one size of sample container in each rack. The rack indicator must be positioned at the correct setting for the size of sample container.

1. Prepare the sample container for each sample, and place barcode labels on the sample containers, as required.
2. Load each sample container into a rack, ensuring that the barcode labels are clearly visible.
3. Place the racks in the entry queue.
4. Ensure that the assay reagents are loaded.
5. Start the entry queue, if required.

Procedural Notes

Disposal

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 all country and local requirements.

Interpretation of Results

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

The system reports anti-HCV antibody results in Index Values and as reactive, nonreactive, or equivocal. Index values above the cutoff of the assay are not indicative of the antibody level present in the sample.

- Samples with a calculated value of less than 0.80 Index Value are considered nonreactive (negative) for IgG antibodies to HCV.

- Samples with a calculated value greater than or equal to 0.80 Index Value and less than 1.00 Index Value are considered equivocal. It is recommended that the sample be repeated in duplicate. If 2 of the 3 sample results are less than 0.80 Index Value, the sample is considered nonreactive. If 2 of the 3 sample results are greater than or equal to 1.00 Index Value, the sample is considered reactive and supplemental testing of the sample is recommended. If 2 of the 3 sample results are greater than or equal to 0.80 Index Value and less than 1.00 Index Value, supplemental testing of the sample is recommended.
- Samples with a calculated value greater than or equal to 1.00 Index Value are considered reactive for IgG antibodies to HCV. Supplemental testing of the sample is recommended.
- The Supplemental testing algorithm is described in the Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus, MMWR 2003: 52(RR03) from the Centers for Disease Control.
- Sample results are invalid and must be repeated if the controls are out of range.

Limitations

- The ADVIA Centaur HCV assay is limited to the detection of IgG antibodies to hepatitis C virus in human serum or plasma (potassium EDTA, lithium or sodium heparinized plasma).
- The results from this or any other diagnostic kit should be used and interpreted only in the context of the overall clinical picture. A negative test result does not exclude the possibility of exposure to hepatitis C virus.
- The calculated values for hepatitis C 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 cannot be correlated to an endpoint titer.
- The performance of the assay has not been established for populations of immunocompromised, immunosuppressed, infants, children, or adolescent patients.
- Assay performance characteristics have not been established when the ADVIA Centaur HCV assay is used in conjunction with other manufacturers' assays for specific HCV serologic markers.
- The performance of the ADVIA Centaur HCV assay 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.
- Do not use specimens with obvious microbial contamination.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.¹¹ 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.
- A reactive anti-HCV result does not exclude co-infection by another hepatitis virus.

Expected Results

Approximately 61.21% (1335/2181) of the study subjects in the ADVIA Centaur HCV clinical study reported no recent or current signs or symptoms of hepatitis. The asymptomatic population included patients at high risk of HCV infection due to lifestyle, behavior, occupation, disease state (eg, infection with HIV, transplant recipient, dialysis patient, and hemophilia), or due to known exposure events. In the asymptomatic population, 469 of 1335 patients (35.13%) were tested at the Florida site, 445 of 1335 patients (33.33%) were tested at the Texas site, and 421 of 1335 patients (31.54%) were tested at the New York site. The asymptomatic study population was 40.30% Caucasian, 26.30% Hispanic, 26.14% African American, 2.92% Asian, and 4.34% from unknown or other ethnicity. The majority of patients in the asymptomatic population were male (52.88% male and 47.12% female). The mean age in the asymptomatic population was 41.8 years (range of 12 to 82 years). A total of 435 of 1335 patients (32.58%) in the asymptomatic population were reactive in the ADVIA Centaur® HCV assay. (Samples were considered reactive if they were reactive in the ADVIA Centaur® HCV assay upon repeat testing). For the asymptomatic population, the following percentages of patients at each testing site had reactive ADVIA Centaur® HCV results: 32.41% at Florida, 23.15% at Texas, and 42.76% at New York.

The table below summarizes the distribution of ADVIA Centaur reactive and nonreactive results among the asymptomatic population, by age and gender.

Bayer ADVIA Centaur® HCV Assay Distribution of Asymptomatic Population by Age Group and Gender All Testing Sites								
Age (Years)	Gender	Reactive ^a		Equivocal ^b		Nonreactive ^c		Total N
		N	%	N	%	N	%	
0-9	Male	0	--	0	--	0	--	0
	Female	0	--	0	--	0	--	0
	Overall	0	--	0	--	0	--	0
10-19	Male	7	58.33	0	--	5	41.67	12
	Female	0	--	0	--	14	100.00	14
	Overall	7	26.92	0	--	19	73.08	26
20-29	Male	52	49.52	0	--	53	50.48	105
	Female	11	11.46	1	1.04	84	87.50	96
	Overall	63	31.34	1	0.50	137	68.16	201
30-39	Male	42	27.63	0	--	110	72.37	152
	Female	30	20.69	0	--	115	79.31	145
	Overall	72	24.24	0	--	225	75.76	297
40-49	Male	94	46.31	1	0.49	108	53.20	203
	Female	58	32.95	2	1.13	116	65.91	176
	Overall	152	40.11	3	0.79	224	59.10	379
50-59	Male	67	47.52	0	--	74	52.48	141
	Female	34	30.91	0	--	76	69.09	110
	Overall	101	40.24	0	--	150	59.76	251
60-69	Male	14	22.58	0	--	48	77.42	62
	Female	15	23.08	0	--	50	76.92	65
	Overall	29	22.83	0	--	98	77.17	127
≥70	Male	6	19.35	0	--	25	80.65	31
	Female	5	21.74	0	--	18	78.26	23
	Overall	11	20.37	0	--	43	79.63	54
Unknown	Male	0	--	0	--	0	--	0
	Female	0	--	0	--	0	--	0
	Overall	0	--	0	--	0	--	0
Total	Male	282	39.94	1	0.14	423	59.92	706
	Female	153	24.32	3	0.47	473	75.20	629
	Overall	435	32.58	4	0.29	896	67.12	1335

a Samples with an Index Value ≥ 1.00
 b Samples with an Index Value ≥ 0.80 and <1.00
 c Samples with an Index Value < 0.80

As with all *in vitro* diagnostic assays, each laboratory should determine its own reference range(s) for the diagnostic evaluation of patient results.¹²

Performance Characteristics

Clinical Performance

To evaluate the ability of the ADVIA Centaur HCV assay to detect anti-HCV antibody in a group of individuals that would normally be tested in a clinical situation a multi-center prospective study was conducted. A total of 2181 patients were tested. Of these 2181 patients, 1335 patients (61.21%) were from patients considered at risk for hepatitis (the high risk population) due to lifestyle, behavior, occupation, disease state (eg, infection with human immunodeficiency virus [HIV], transplant recipient, dialysis patient, and hemophilia), or due to known exposure events. A total of 846 patients (38.79%) were from individuals exhibiting signs and/or symptoms of hepatitis infection (the signs and symptoms population). The prospective study population was 44.66% Caucasian, 25.81% Hispanic, 22.24% African American, 3.12% Asian, and 4.17% from unknown or other ethnicity. The majority of patients were male (55.62% male and 44.38% female). The mean age was 45.4 years (range of 12 to 82 years). Patients in the prospective study population were from the following geographic regions: Florida (37.09%), Texas (32.10%), New York (19.58%), California (7.79%), and 3.44% were from an unknown or other geographic region.

The HCV status for each patient was determined from results of a reference assay for the detection of anti-HCV and the Chiron® RIBA® HCV 3.0 SIA.

Testing for anti-HCV using the reference method and the ADVIA Centaur® HCV assay were performed at each of 3 testing sites (Florida, Texas, and New York). Patients were enrolled at the 3 testing sites and 1 additional clinical site..

Results by Specimen Classification

Following testing with the reference anti-HCV assay and supplemental testing with the Chiron® RIBA® HCV 3.0 SIA where indicated, 2141 subjects were assigned an HCV status of HCV infected or not HCV infected based on the final results obtained with both assays as required. The HCV status of the remaining 40 subjects could not be determined due to indeterminate results with the Chiron® RIBA® HCV 3.0 SIA. Assignment of HCV status is presented in the following table.

Reference Anti-HCV Assay Result	Chiron® RIBA® HCV 3.0 SIA Result	HCV Status
Nonreactive	Not Applicable	Not Infected^a
Repeatedly Reactive	Positive	Infected State or Associated Disease Not Determined
Repeatedly Reactive	Negative	Not Infected^a
Repeatedly Reactive	Indeterminate	Not Determined HCV Status Cannot be Determined

a. A negative test result does not exclude the possibility of exposure to hepatitis C virus.

Comparison of Results

The following table compares Centaur HCV results with HCV status according to a ranking of the risk of HCV infection in study subjects (N=2181). The ranking was based on a clinical evaluation of the chances of acquiring the disease through the following modes of transmission, with the most common given higher rankings. Each patient was assigned only one risk (the highest). Assignment of HCV status was according to the algorithm presented in the previous table.

Bayer ADVIA Centaur® HCV HCV Status and ADVIA Centaur® HCV Assay Results for the Prospective Population by Presumptive Diagnosis and Risk Groups for Hepatitis ADVIA Centaur® HCV Assay vs. HCV Status All Testing Sites										
Presumptive Diagnosis and Risk Groups	HCV Status ^a									Total ^f
	Infected			Not Determined			Not Infected			
	ADVIA Centaur® HCV Assay ^b			ADVIA Centaur® HCV Assay			ADVIA Centaur® HCV Assay			
	Reactive	Equivocal	Non-reactive	Reactive	Equivocal	Non-reactive	Reactive	Equivocal	Non-reactive	
	N	N	N	N	N	N	N	N	N	
Signs and Symptoms	632	0	0	23	0	1	5	0	185	846
Hemophiliac	77	0	0	1	0	0	0	0	3	81
Intravenous drug user, current or past	192	0	0	4	0	0	3	0	55	254
Dialysis	30	0	0	5	0	0	2	0	163	200
Transfusion/Trans-plant	66	0	0	1	0	0	0	2	172	241
High Risk Sex ^d	21	0	0	4	0	0	1	1	197	224
Healthcare Worker	8	0	0	0	0	0	0	0	201	209
HIV infected	1	0	0	0	0	0	0	0	10	11
Other ^e	17	0	0	1	0	0	1	1	95	115
None Specified	0	0	0	0	0	0	0	0	0	0
Overall	1044	0	0	39	0	1	12 ^f	4 ^g	1081	2181

- a Final HCV status was based on the reference test results and Chiron® RIBA® HCV 3.0 SIA supplemental testing of samples that were repeatedly reactive by reference anti-HCV assay testing.
- b Final ADVIA Centaur® HCV status was based on the initial test result and retest of initially reactive samples.
- c Total number of test results by risk population.
- d The high risk sex group includes patients with a diagnosis of a sexually transmitted disease, a sexual partner with a history of hepatitis, same sex sexual preference, multiple sex partners, HIV infected partner, or prostitutes.
- e The Other risk group includes patients with the following risk factors: sharing straw cocaine, tattoo, history of incarceration, body piercing, family history of hepatitis, immunocompromised patient, tattoo artist, mortician, or other known hepatitis exposure event.
- f These 12 patients had nonreactive results in the reference anti-HCV assay and/or had negative results in the Chiron® RIBA® HCV 3.0 SIA assay and were considered to be HCV not infected. Eleven of these 12 patients had reactive results in the ADVIA Centaur® HCV assay, 4 patients had reactive results in both the ADVIA Centaur® HCV and the reference anti-HCV assays, and 1 patient had nonreactive results in the ADVIA Centaur® HCV assay. (Although this patient was initially nonreactive in the ADVIA Centaur® HCV assay, retest Index Values were reactive [> 1.0] and the patient was considered to have a reactive result in the Centaur® method).
- g These 4 patients had nonreactive results in the reference anti-HCV assay and/or had negative results in the Chiron® RIBA® HCV 3.0 SIA assay and were considered to be HCV not infected. All of these 4 patients had equivocal results in the ADVIA Centaur® HCV assay.

Note The data described in footnotes f and g did not result in any modifications to the calculations of percent agreement described below.

The HCV status of 40 patients in the prospective population was considered to be not determined. Samples from these patients were repeatedly reactive in the reference anti-HCV assay and were indeterminate in the Chiron® RIBA® HCV 3.0 SIA assay. Additional testing for these patient samples was performed by using the COBAS AMPLICOR® HCV test, version 2.0 (COBAS AMPLICOR HCV-NAT). Results of the ADVIA Centaur® anti-HCV testing, COBAS AMPLICOR HCV-NAT supplemental testing, and HCV status as determined by HCV-NAT testing are shown in the following table.

Bayer ADVIA Centaur® HCV NAT Supplemental Testing of HCV Status Not Determined Specimens ADVIA Centaur® HCV Assay vs. HCV Status All Testing Sites				
Centaur® HCV Assay Results	COBAS – Amplicor® HCV-NAT^a	HCV Status Following HCV-NAT Test	Number of Samples	Presumptive Diagnosis and Risk Groups
Reactive ^b	Detected (P)	Infected	19	Signs and Symptoms
			1	Hemophiliac
			2	IVDU, current or past
			1	Dialysis
			1	Transfusion/Transplant
			3	High Risk Sex
Reactive ^c	Not Detected (N)	Not determined	4	Signs and Symptoms
			2	IVDU, current or past
			4	Dialysis
			1	High Risk Sex
			1	Other
Negative ^d	Not Detected (N)	Not Determined	1	Signs and Symptoms
Total			40	

- a Subjects found to have indeterminate HCV status by Chiron® RIBA® 3.0 SIA.
- b On the basis of detection of HCV by COBAS AMPLICOR® HCV-NAT testing, an accurate laboratory diagnosis of HCV infected was made for these 27 patients who were classified as HCV not determined due to positive results of reference anti-HCV testing and indeterminate results of Chiron® RIBA® HCV 3.0 SIA testing. The reactive Centaur® HCV result was presumed to be correct (true positive).
- c Because HCV was not detected by COBAS AMPLICOR® HCV-NAT testing, an accurate laboratory diagnosis of HCV status was not possible for these 12 patients who were classified as HCV not determined due to positive results of reference anti-HCV testing indeterminate results of Chiron® RIBA® HCV 3.0 SIA testing. The reactive Centaur® HCV result was presumed to be incorrect.
- d Because HCV was not detected by COBAS AMPLICOR® HCV-NAT testing, an accurate laboratory diagnosis of HCV status was not possible for this patient who was classified as HCV not determined due to positive results of reference anti-HCV testing and indeterminate results of Chiron® RIBA® HCV 3.0 SIA testing. The nonreactive Centaur® HCV result was presumed to be incorrect.

Percent Agreement

Percent positive and percent negative agreement between the Centaur HCV assay and HCV status were calculated for subjects with various risks for viral hepatitis or HCV infection, and for the overall study population (N=2181). The table below summarizes these calculations and provides the upper and lower 95% exact confidence intervals. For the purposes of calculating percent agreement, Centaur HCV assay reactive samples whose HCV status remained 'Not Determined' following supplemental NAT testing were considered 'Not HCV Infected', and Centaur HCV assay nonreactive samples whose HCV status remained 'Not Determined' following supplemental NAT testing were considered 'HCV Infected'.

Bayer ADVIA Centaur® HCV Percent Agreement and Confidence Intervals for Infected and Not Infected HCV Status and ADVIA Centaur® anti-HCV Assay: Positive and Negative Results by Presumptive Diagnosis and Risk Groups for Hepatitis ADVIA Centaur® HCV Assay vs. HCV Status All Testing Sites				
Presumptive Diagnosis and Risk Groups	Positive Percent Agreement % (x/n) ^a	95% Exact Confidence Interval	Negative Percent Agreement % (x/n) ^a	95% Exact Confidence Interval
Signs and Symptoms	99.85 (651/652)	99.15 to 100.00	95.36 (185/194)	91.38 to 97.86
Hemophiliac	100.00 (78/78)	95.38 to 100.00	100.00 (3/3)	29.24 to 100.00
IVDU, current or past	100.00 (194/194)	98.12 to 100.00	91.67 (55/60)	81.61 to 97.24
Dialysis	100.00 (31/31)	88.78 to 100.00	96.45 (163/169)	92.43 to 98.69
Transfusion/ Transplant	100.00 (67/67)	94.64 to 100.00	98.85 (172/174)	95.91 to 99.86
High Risk Sex ^b	100.00 (24/24)	85.75 to 100.00	98.50 (197/200)	95.68 to 99.69
Healthcare Worker	100.00 (8/8)	63.06 to 100.00	100.00 (201/201)	98.18 to 100.00
HIV infected	100.00 (1/1)	2.50 to 100.00	100.00 (10/10)	69.15 to 100.00
Other ^c	100.00 (17/17)	80.49 to 100.00	96.94 (95/98)	91.31 to 99.36
None Specified	--	--	--	--
Overall	99.91 (1071/1072)	99.48 to 100.00	97.48 (1081/1109)	96.37 to 98.32

a x = the number of ADVIA Centaur® HCV results that were reactive (or were nonreactive) in agreement with the final HCV status as determined by supplemental testing where necessary; n = the total number of final HCV infected status (or final HCV not infected status) results as determined by supplemental testing, where necessary.

Positive/negative % agreement = $\{[\text{Number of ADVIA Centaur® HCV reactive (confirmed) or non-reactive in agreement with the HCV infected status or HCV not infected HCV status} / (\text{Total number of HCV infected status or HCV noninfected HCV status})] \times 100$.

b The high risk sex group included patients with a diagnosis of a sexually transmitted disease, a sexual partner with a history of hepatitis, same sex sexual preference, multiple sex partners, HIV infected partner, or prostitutes.

c The other risk group includes patients with the following risk factors: sharing straw cocaine, tattoo, history of incarceration, body piercing, family history of hepatitis, immunocompromised patient, tattoo artist, mortician or other known hepatitis exposure event.

The overall positive percent agreement between the ADVIA Centaur® HCV assay results and HCV infected status for the prospective population was 99.91% (1071 of 1072 patients). The overall negative percent agreement between the ADVIA Centaur® HCV assay results and HCV not infected status for the prospective population was 97.48% (1081 of 1109 patients). There were no differences among the presumptive diagnosis and risk groups for HCV infection in the percent positive or percent negative agreements.

Seroconversion Panels

Commercially available HCV patient seroconversion panels were tested using the ADVIA Centaur HCV assay to determine the seroconversion sensitivity of the assay. The performance of the ADVIA Centaur HCV assay on the seroconversion panels closely matched the performance of the reference assay. The following results were obtained:

**Bayer ADVIA Centaur® HCV
Days to Evidence of HCV Infection
Seroconversion Panels**

Panel ID	Reference anti-HCV assay ^a		Centaur® HCV Assay ^b			Difference in Days to Anti-HCV Reactive Results ^c Reference – Centaur®
	N ^d	R ^e	N ^d	E ^f	R ^e	
SC0400	11	14	11		14	0
SC0406	0	9	0		9	0
PHV905	11	14	7		11	3
6211	171	182	171		182	0
6213	37	43	35		37	6
6215	10	20	10		20	0
6222	36	40	36		40	0
6216	17	23	17		23	0
6226	37	39	32		37	2
6229	10	17	10		17	0
9058	7	10	7		10	0
6228	24	28	28		31	-3
9041	31	62	31		62	0
6227	46	74	46		74	0
9054	77	82	77		82	0
9047	21	28	21		28	0
SC0403	0	6	0		6	0
PHV908	13	19	5	11	13	6
6212	12	14	0		12	2
6214	25	30	25		30	0

- a Reference HCV assay interpreted results: Reactive (R), or Nonreactive (N)
 - b ADVIA Centaur® HCV interpreted results: Reactive (R), Equivocal (E), or Nonreactive (N)
 - c The dates of the first reactive test results were compared in the reference assay and ADVIA Centaur® assay: if the first reactive test result occurred on the same day then difference = 0, if Centaur® had an earlier date then the difference was positive, otherwise negative.
 - d Post bleed day of last nonreactive result, usually denoted previous bleed from first reactive result.
 - e Post bleed day of first reactive result.
 - f Post bleed day of first equivocal result.
- Note: Bleed day is calculated as the blood draw date for the appropriate result minus the date of first blood draw for the panel. The first draw date was bleed day 0.

Compared to the reference assay results, the first reactive time point for the ADVIA Centaur® HCV assay occurred earlier in 5 panels, at the same time in 14 panels, and later in 1 panel. Overall, compared to the reference anti-HCV assay, the ADVIA Centaur® HCV assay demonstrated efficacy for the detection of the appearance of anti-HCV following HCV infection.

Genotype Detection

Genotype detection was assessed using the Teragenix Corporation Genotype Panel. The Panel consisted of 25 human plasma samples that were predetermined by the supplier to include the most common recognized genotypes of HCV and their subtypes (1a, 1b, 1a/b, 2a/c, 3a, 4a, 4c/d, 4h). All of the anti-HCV positive panel members were observed to be reactive in the ADVIA Centaur® HCV assay. The ability of the ADVIA Centaur® HCV assay to detect antibodies to various HCV genotypes were also assessed by testing 100 individual genotype samples. These genotype samples included 20 type 1, 20 type 2, 20 type 3, 20 type 4, 10 type 4 non-A, and 10 type 5 samples. All of the confirmed HCV positive samples were found to be reactive in the ADVIA Centaur® HCV assay.

Potentially Cross –Reacting Subgroups

Samples from patients in the prospective population who were determined to be HBV infected or HAV infected were tested in the ADVIA Centaur® HCV assay and reference anti-HCV assay. Hepatitis B infection was determined to be acute, chronic, early recovery, recovery, or recovered stages of infection by HBsAg, HBeAg, anti-HBc Total, anti-HBc IgM, anti-HBeAg, and anti-HBs assays. Hepatitis A infection was determined from the medical history of the patient. Results of the anti-HCV assays were presented for patients with HCV infected status, HCV not determined status, and HCV not infected status by presumptive diagnosis and risk groups for HCV infection in the following table.

Bayer ADVIA Centaur® HCV HCV Status and ADVIA Centaur® HCV Assay Results Among HBV Infected Patients as Determined by Marker Testing ^a ADVIA Centaur® HCV Assay vs. HCV Status All Testing Sites										
Presumptive Diagnosis and Risk Groups	HCV Status ^b									Total ^f
	Infected			Not Determined			Not Infected			
	ADVIA Centaur® HCV Assay ^c			ADVIA Centaur® HCV Assay			ADVIA Centaur® HCV Assay			
	Reactive	Equivocal	Non-reactive	Reactive	Equivocal	Non-reactive	Reactive	Equivocal	Non-reactive	
	N	N	N	N	N	N	N	N	N	
Signs and Symptoms	161	0	0	3	0	0	1	0	99	264
Hemophiliac	1	0	0	0	0	0	0	0	0	1
Intravenous drug user, current or past	65	0	0	0	0	0	1	0	2	68
Dialysis	5	0	0	1	0	0	0	0	20	26
Transfusion/Transplant	6	0	0	0	0	0	0	2	19	27
High Risk Sex ^e	7	0	0	3	0	0	0	0	35	45
Healthcare Worker	1	0	0	0	0	0	0	0	10	11
HIV infected	0	0	0	0	0	0	0	0	4	4
Other ^d	1	0	0	0	0	0	0	0	19	20
None Specified	0	0	0	0	0	0	0	0	0	0
Overall	247	0	0	7	0	0	2	2	208	466

- a Hepatitis B infected patients included acute, chronic, early recovery, recovery, and recovered stages of infection.
- b Final HCV status was based on the reference test results and Chiron® RIBA® HCV 3.0 SIA supplemental testing of samples that were repeatedly reactive by reference anti-HCV assay testing.
- c Final ADVIA Centaur® HCV was based on the initial test result and retest of initially reactive samples.
- d Total number of test results by risk population.
- e The high risk sex group includes patients with a diagnosis of a sexually transmitted disease, a sexual partner with a history of hepatitis, same sex sexual preference, multiple sex partners, HIV infected partner, or prostitutes.
- f The Other risk group includes patients with the following risk factors: sharing straw cocaine, tattoo, history of incarceration, body piercing, family history of hepatitis, immunocompromised patient, tattoo artist, mortician or other known hepatitis exposure event.

Among patients in the prospective population who had ongoing or previous HBV infection (466 patients), the overall positive percent agreement between the ADVIA Centaur® HCV method and HCV infected status was 100.00% (247 of 247 HCV infected patients). The overall negative percent agreement between the ADVIA Centaur® HCV assay and HCV not infected status was 98.11% (208 of 212 HCV not infected patients) among patients in the prospective population who had ongoing or previous HBV infection.

Bayer ADVIA Centaur® HCV HCV Status and ADVIA Centaur® HCV Assay Results Among HAV Infected Patients* ADVIA Centaur® HCV Assay vs. HCV Status All Testing Sites										
Presumptive Diagnosis and Risk Groups	HCV Status ^b									Total ^f
	Infected			Not Determined			Not Infected			
	ADVIA Centaur® HCV Assay ^c			ADVIA Centaur® HCV Assay			ADVIA Centaur® HCV Assay			
	Reactive	Equivocal	Non-reactive	Reactive	Equivocal	Non-reactive	Reactive	Equivocal	Non-reactive	
	N	N	N	N	N	N	N	N	N	
Signs and Symptoms	26	0	0	1	0	0	0	0	19	46
Hemophiliac	0	0	0	0	0	0	0	0	0	0
Intravenous drug user, current or past	2	0	0	0	0	0	0	0	2	4
Dialysis	0	0	0	0	0	0	0	0	2	2
Transfusion/Transplant	0	0	0	0	0	0	0	0	4	4
High Risk Sex ^e	2	0	0	0	0	0	0	0	7	9
Healthcare Worker	0	0	0	0	0	0	0	0	9	9
HIV infected	0	0	0	0	0	0	0	0	0	0
Other ^f	0	0	0	0	0	0	0	0	0	0
None Specified	0	0	0	0	0	0	0	0	0	0
Overall	30	0	0	1	0	0	0	0	43	74

- a Patients with hepatitis type A.
- b Final HCV status was based on the reference test results and Chiron® RIBA® HCV 3.0 SIA supplemental testing of samples that were repeatedly reactive by reference anti-HCV assay testing.
- c Final ADVIA Centaur® HCV was based on the initial test result and retest of initially reactive samples.
- d Total number of test results by risk population.
- e The high risk sex group includes patients with a diagnosis of a sexually transmitted disease, a sexual partner with a history of hepatitis, same sex sexual preference, multiple sex partners, HIV infected partner, or prostitutes.
- f The Other risk group includes patients with the following risk factors: sharing straw cocaine, tattoo, history of incarceration, body piercing, family history of hepatitis, immunocompromised patient, tattoo artist, mortician or other known hepatitis exposure event.

Among patients in the prospective population who had ongoing or previous HAV infection (74 patients), the overall positive percent agreement between the ADVIA Centaur® HCV method and HCV infected status was 100.00% (30 of 30 HCV infected patients), and the overall negative percent agreement with HCV not infected status was 100.00% (43 of 43 HCV not infected patients).

System Reproducibility

The ADVIA Centaur® HCV precision and reproducibility study was performed at 3 external sites utilizing 2 reagent lots per site. Three reagent lots were used for the study. A 5-member panel and controls were assayed in replicates of 5 on a single run per day over 6 days for each lot. The study was completed with a single calibration of the assay (one calibration interval). Standard deviation and percent CV were calculated for within run, between run, and total. The data from all 3 sites and from all 3 reagent lots were combined to achieve SD and percent CV for within run, between run, between testing site, between lot, and total. The precision estimates were derived from variance component analysis. The reproducibility results are presented in the following table.

Bayer ADVIA Centaur® HCV Assay Reproducibility Between Testing Sites and Between Reagent Lots Estimates (Across All Reagent Lots and All Testing Sites)												
Panel Member	Mean ADVIA Centaur® HCV Index Value	Within Run ^a		Between Run ^b		Between Testing Site ^c		Between Lot ^d		Total ^e		Number of Observations
		SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	SD	CV (%)	
1	0.03	0.004	NA	0.005	NA	0.041	NA	0.011	NA	0.043	NA	180
2	1.22	0.066	5.43	0.076	6.23	0.000	0.00	0.076	6.21	0.126	10.34	180
3	3.95	0.177	4.48	0.288	7.29	0.070	1.77	0.363	9.19	0.501	12.68	180
4	6.32	0.267	4.22	0.376	5.95	0.221	3.49	0.718	11.36	0.881	13.94	180
5	9.56	0.716	7.49	0.553	5.78	0.494	5.16	0.855	8.94	1.339	14.00	180
Negative Control	0.08	0.014	NA	0.012	NA	0.032	NA	0.057	NA	0.068	NA	180
Positive Control	5.72	0.404	7.06	0.328	5.73	0.387	6.76	0.406	7.09	0.765	13.36	180

- a Variability of the assay performance within day (all testing sites and reagent lots).
 b Variability of the assay performance between days (all testing sites and reagent lots).
 c Variability of the assay performance between testing sites (from testing site to testing site).
 d Variability of the assay performance between reagent lots (from reagent lot to reagent lot, across all testing sites).
 e Variability of the assay performance incorporating all testing sites, all reagent lots, and all days.

NA = Not applicable

Note: 5 replicates per panel in 1 run per day for 6 days

Cross-Reactivity

The ADVIA Centaur HCV assay was evaluated for potential cross-reactivity with other viral infections and disease state specimens. The reactive HCV status of each specimen was verified using an anti-HCV reference assay. The following results were obtained using the ADVIA Centaur HCV assay:

<i>Clinical Category</i>	<i>Number Tested</i>	<i>Number of Reactive Anti-HCV Results</i>	
		<i>ADVIA Centaur Assay</i>	<i>Reference Assay</i>
Hepatitis A Infection (HAV)	5	0	0
Non-viral Liver Disease	10	1	1
Epstein-Barr Virus (EBV) IgG	10	0	0
Epstein-Barr Virus (EBV) IgM	10	0	0
Herpes Simplex Virus (HSV) IgG	10	0	0
Herpes Simplex Virus (HSV) IgM	10	0	0
Syphilis IgG	14	0	0
Human Immunodeficiency Virus (HIV1/2)	10	1	1
Varicella Zoster (VZV) IgG	10	0	0
Cytomegalovirus (CMV) IgG	10	0	0
Cytomegalovirus (CMV) IgM	3	0	0
Rubella IgG	10	0	0
Toxoplasma IgG	10	0	0
Multiparity	10	0	0
Flu Vaccine Recipient	10	2	2
Rheumatoid Arthritis (RF)	9	1	1
Anti-Nuclear Antibody (ANA) & Systemic Lupus Erythematosus (SLE)	7	0	0
Total Samples Tested	1158	5	5

Endogenous Interferents

The ADVIA Centaur HCV assay was evaluated for interference according to NCCLS Document EP7-P¹³. None of the interferents at the levels tested produced a change in clinical interpretation of the assay.

<i>Serum specimens that are . . .</i>	<i>Demonstrate ≤10% change in results up to . . .</i>
hemolyzed	500 mg/dL of hemoglobin
lipemic	1000 mg/dL of triglycerides
icteric	60 mg/dL of conjugated bilirubin
icteric	40 mg/dL of unconjugated bilirubin
proteinemic	12 g/dL of protein
proteinemic	3.5 g/dL of protein

Technical Assistance

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

References

1. Urdea MS, Wuestchube LJ, et al. Hepatitis C: diagnosis and monitoring. *Clinical Chemistry* 1997, 43:1507-1511.
2. Zanetti AR, Romano L, Bianchi S. Primary prevention of hepatitis C virus infection. *Vaccine* 2003 Jan, 21(7-8): 692-695.
3. El-Serag HB. Hepatocellular carcinoma: an epidemiologic view. *J Clin Gastroenterol* 2002 Nov-Dec, 35(5-2):S72-8.
4. Kunio O, Nakanuma Y, Miyazaki M. Cholangiocarcinoma: recent progress. Part I: epidemiology and etiology. *Journal of Gastroenterol and Hepatology* 2002, 17:1409-1055.
5. Alter MJ. Prevention of hepatitis C. *Hepatology* 2002 Nov, 36(5-1):S93-8.
6. National Committee for Clinical Laboratory Standards. Procedures for handling and processing of blood specimens; approved guideline. NCCLS Document H18-A2. Wayne (PA):NCCLS;1999.
7. 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;37:377-82, 387-8.
8. National Committee for Clinical Laboratory Standards. Protection of laboratory workers from instrument biohazards and infectious disease transmitted by blood, body fluids, and tissue; approved guideline. NCCLS Document M29-A2. Wayne (PA):NCCLS;2001.
9. Federal Occupational Safety and Health Administration, Bloodborne Pathogens Standard, 29 CFR 1910.1030.
10. Yoshizawa H, Itoh, et al. Beta-propranolol for the inactivation of non-A/non-B type 1 hepatitis virus capable of inducing cytoplasmic tubular ultrastructures in chimpanzees. *Vox Sang.* 1984, 46: 86-91.
11. Boscatto LM, Stuart MC. Heterophilic antibodies: a problem for all immunoassays. *Clin Chem* 1988;34:27-33.
12. National Committee for Clinical Laboratory Standards. How to define, determine, and utilize reference intervals in the clinical laboratory; approved guideline. NCCLS Document C28-A. Wayne (PA):NCCLS;1995.
13. National Committee for Clinical Laboratory Standards. Interference Testing in Clinical Chemistry; proposed guideline. NCCLS document EP7-P. Wayne (PA):NCCLS;1986

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