ARCHITECT SYSTEM

en

Anti-HCV

IVD REF 6C37

84-5612/R5

B6C370

Read Highlighted Changes
Revised April, 2008

Anti-HCV

Customer Service
For additional product information, please contact your local customer service organization.

This package insert must be read carefully prior to product use. Package insert instructions must be followed. Reliability of assay results cannot be guaranteed if there are any deviations from the instructions in this package insert.

Key to symbols used

REF	List Number	SN	Serial Number
IVD	*In Vitro* Diagnostic Medical Device	REACTION VESSELS	Reaction Vessels
LOT	Lot Number	SAMPLE CUPS	Sample Cups
	Expiration Date	SEPTUM	Septum
2°C–8°C	Store at 2-8°C	REPLACEMENT CAPS	Replacement Caps
	Consult instructions for use	CONTROL NO.	Control Number
	Manufacturer	REAGENT LOT	Reagent Lot

See **REAGENTS** section for a full explanation of symbols used in reagent component naming.

ABBOTT
Diagnostics Division

NAME

ARCHITECT Anti-HCV

INTENDED USE

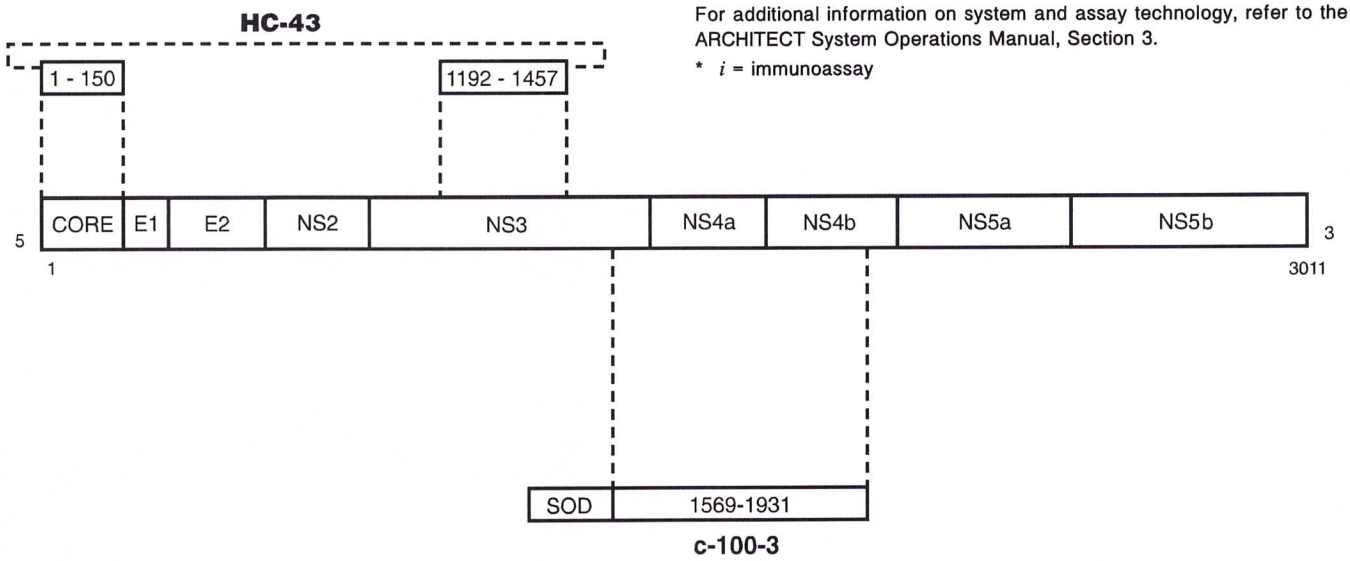
The ARCHITECT Anti-HCV assay is a chemiluminescent microparticle immunoassay (CMIA) for the qualitative detection of antibody to hepatitis C virus (anti-HCV) in human serum and plasma.

SUMMARY AND EXPLANATION OF TEST

The ARCHITECT Anti-HCV assay is for the detection of antibodies to hepatitis C virus (HCV). Chemiluminescent immunoassays are a variation of the enzyme immunoassay (EIA) principle. Solid phase EIAs, first described in the early 1970s, use antigens and/or antibodies coated on a surface to bind complementary analytes.[1] The bound analyte is detected by a series of antigen-antibody reactions. EIAs are available to identify antigens and antibodies related to viral hepatitis infection. In the ARCHITECT Anti-HCV final reaction, bound acridinylated conjugates are used to generate a chemiluminescent signal.

HCV is a bloodborne virus.[2,3] Serological studies employing EIAs for detection of antibodies to recombinant antigens of HCV have established HCV as the cause of most bloodborne[4-9] as well as community-acquired[10] non-A, non-B hepatitis. The presence of anti-HCV indicates that an individual may have been infected with HCV, may harbor infectious HCV, and/or may be capable of transmitting HCV infection.[11] Although the majority of infected individuals may be asymptomatic, HCV infection may develop into chronic hepatitis, cirrhosis, and/or increased risk of hepatocellular carcinoma.[12-15] The implementation of blood donation screening for anti-HCV by EIAs has led to a marked decline in the risk of transfusion-transmitted hepatitis.[16,17]

ARCHITECT Anti-HCV has been designed to detect antibodies to putative structural and nonstructural proteins of the HCV genome. The relationship between the recombinant HCV proteins in ARCHITECT Anti-HCV and the putative structural and nonstructural proteins of the HCV genome is depicted below.[18]



- HCr43: The HCr43 protein is expressed in *Escherichia coli* (*E. coli*) and is composed of two noncontiguous coding regions of the HCV genome sequence. The first region represents amino acids 1192 to 1457 (33c) of the HCV sequence. The second of the two regions represents amino acids 1 to 150 (core) of the HCV sequence. Because of the similarity of the genomic organization of the flaviviruses, it is suggested that the first sequence is from the NS3 coding region and the second sequence is from the core coding region of HCV.
- c100-3: The c100-3 antigen is a recombinant HCV protein expressed in *Saccharomyces cerevisiae* (yeast). The genomic organization of flaviviruses suggests that the cloned sequence is contained within the putative nonstructural (NS3 and NS4) regions of HCV. The c100-3 protein is a chimeric fusion protein with 154 amino acids of human superoxide dismutase (hSOD), five linker amino acids, amino acids number 1569 to 1931 of the HCV polyprotein, and the additional five amino acid linker at the carboxyl terminus.

Hepatitis C antigens HCr43 and c100-3 are prepared under US license by Chiron Corporation under a shared manufacturing agreement. The ARCHITECT Anti-HCV assay is manufactured under contract agreement from Ortho Diagnostic Systems and Chiron Corporation.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT Anti-HCV assay is a two-step immunoassay, using chemiluminescent microparticle immunoassay (CMIA) technology, for the qualitative detection of anti-HCV in human serum and plasma.

In the first step, sample, recombinant HCV antigen coated paramagnetic microparticles and Assay Diluent are combined.

Anti-HCV present in the sample binds to the HCV coated microparticles. After washing, anti-human acridinium-labeled conjugate is added in the second step. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture. The resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of anti-HCV in the sample and the RLUs detected by the ARCHITECT *i** System optics.

The presence or absence of anti-HCV in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from a previous ARCHITECT Anti-HCV calibration. If the chemiluminescent signal in the specimen is greater than or equal to the cutoff signal, the specimen is considered reactive for anti-HCV.

For additional information on system and assay technology, refer to the ARCHITECT System Operations Manual, Section 3.

* *i* = immunoassay

REAGENTS

Reagent Kit, 100 Tests/500 Tests

NOTE: Some kit sizes are not available in all countries or for use on all Architect *i* Systems. Please contact your local distributor.

ARCHITECT Anti-HCV Reagent Kit (6C37)

- **MICROPARTICLES** 1 or 4 Bottle(s) (6.6 mL per 100 test bottle/27.0 mL per 500 test bottle) HCV (*E. coli*, yeast, recombinant) antigen coated microparticles in MES buffer. Minimum concentration: 0.14% solids. Preservatives: antimicrobial agents.
- **CONJUGATE** 1 or 4 Bottle(s) (5.9 mL per 100 test bottle/ 26.3 mL per 500 test bottle) Conjugate: murine anti-IgG/anti-IgM acridinium-labeled conjugate in MES buffer. Minimum concentration: (IgG) 8 ng/mL/(IgM) 0.8 ng/mL. Preservatives: antimicrobial agents.
- **ASSAY DILUENT** 1 or 4 Bottle(s) (10.0 mL per 100 test bottle/ 50.9 mL per 500 test bottle) Anti-HCV Assay Diluent containing TRIS buffer with protein stabilizers. Preservatives: antimicrobial agents.

Other Reagents

ARCHITECT *i* Pre-Trigger Solution

- **PRE-TRIGGER SOLUTION** Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- **TRIGGER SOLUTION** Trigger Solution containing 0.35 N sodium hydroxide.

ARCHITECT *i* Wash Buffer.

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservative: antimicrobial agent.

WARNINGS AND PRECAUTIONS

- **For *In Vitro* Diagnostic Use.**

Safety Precautions

- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials be considered potentially infectious and handled with appropriate biosafety practices.

For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- **Do not pool reagents within a reagent kit or between reagent kits.**
- Prior to loading the ARCHITECT Anti-HCV Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment. For microparticle mixing instructions, refer to the **PROCEDURE, Assay Procedure** section of this package insert.
- **Septums MUST be used to prevent reagent evaporation and contamination, and to ensure reagent integrity. Reliability of assay results cannot be guaranteed if septums are not used according to the instructions in this package insert.**
- **To avoid contamination, wear clean gloves when placing a septum on an uncapped reagent bottle.**
- When handling conjugate vials, change gloves that have contacted human plasma/sera, since introduction of human IgG/IgM will result in a neutralized conjugate.
- Once a septum has been placed on an open reagent bottle, **do not invert the bottle** as this will result in reagent leakage and may compromise assay results.
- Over time, residual liquids may dry on the septum surface. These are typically dried salts and have no effect on assay efficacy.
- For a detailed discussion of handling precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 7.

Storage Instructions

- The ARCHITECT Anti-HCV Reagent Kit, Calibrator, and Controls must be stored at 2-8°C in an upright position and may be used immediately after removal from 2-8°C storage.
- When stored and handled as directed, reagents are stable until the expiration date.
- The ARCHITECT Anti-HCV Reagent Kit may be stored on board the ARCHITECT *i* System for a maximum of 30 days. After 30 days, the reagent kit must be discarded. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.
- Reagents may be stored on or off the ARCHITECT *i* System. If reagents are removed from the system, store them at 2-8°C (with septums and replacement caps) in an upright position. For reagents stored off the system, it is recommended they be stored in their original trays and boxes to ensure they remain upright. **If the microparticle bottle does not remain upright (with a septum installed) while in refrigerated storage off the system, the reagent kit must be discarded.** After reagents are removed from the system, you must initiate a scan to update the onboard stability timer.

Indications of Reagent Deterioration

When a control value is out of the specified range, it may indicate deterioration of the reagents or errors in technique. Associated test results are invalid and will require retesting. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

- The ARCHITECT Anti-HCV assay file must be installed on the ARCHITECT *i* System from the ARCHITECT *i* Assay CD-ROM prior to performing the assay. For detailed information on assay file installation and viewing and editing assay parameters, refer to the ARCHITECT System Operations Manual, Section 2.
- For information on printing assay parameters, refer to the ARCHITECT System Operations Manual, Section 5.
- For a detailed description of system procedures, refer to the ARCHITECT System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

- Human serum (including serum collected in serum separator tubes) or plasma collected in potassium EDTA, lithium heparin, sodium heparin, sodium citrate, ACD, CPDA-1, CPD, CP2D, or potassium oxalate may be used in the ARCHITECT Anti-HCV assay. Other anticoagulants have not been validated for use with the ARCHITECT Anti-HCV assay. Follow the tube manufacturer's processing instructions for serum or plasma collection tubes.
- The ARCHITECT *i* System does not provide the capability to verify specimen type. It is the responsibility of the operator to verify the correct specimen types are used in the ARCHITECT Anti-HCV assay.
- Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- This assay was designed and validated for use with human serum or plasma from individual patient and donor specimens. Pooled specimens must not be used since the accuracy of their test results has not been validated.
- Do not use heat-inactivated specimens.
- Do not use grossly hemolyzed specimens.
- For optimal results, inspect all samples for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each sample to prevent cross contamination.
- **For optimal results, serum and plasma specimens should be free of fibrin, red blood cells, or other particulate matter. Such specimens may give inconsistent results and must be transferred to a centrifuge tube and centrifuged at least 10,000 RCF (Relative Centrifugal Force) for 10 minutes.**

- Ensure that complete clot formation in serum specimens has taken place prior to centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy may exhibit increased clotting time. If the specimen is centrifuged before a complete clot forms, the presence of fibrin may cause erroneous results.
- Specimens from heparinized patients may be partially coagulated and erroneous results could occur due to the presence of fibrin. To prevent this phenomenon, draw the specimen prior to heparin therapy.
- **Gravity separation is not sufficient for specimen preparation. Specimens must be separated from clots or red blood cells using centrifugation as recommended by the tube manufacturer.**
- Specimens may be stored on or off the clot or red blood cells for up to 7 days at 2-8°C.
- If testing will be delayed more than 7 days, remove serum or plasma from the clot, serum separator, or red blood cells, and store frozen (-20°C or colder).
- **Frozen specimens must be mixed THOROUGHLY after thawing by LOW speed vortexing.**
- Centrifuged specimens with a lipid layer on the top must be transferred to a sample cup or secondary tube. Care must be taken to transfer only the clarified specimen without the lipemic material.
- No qualitative differences were observed between experimental controls and the 25 nonreactive or 25 spiked reactive specimens subjected to 6 freeze/thaw cycles; however, multiple freeze/thaw cycles should be avoided.
- When shipped, specimens must be packaged and labeled in compliance with applicable state, federal, and international regulations covering the transport of specimens and infectious substances. Specimens may be shipped ambient, at 2-8°C (wet ice), or -20°C or colder (dry ice). Do not exceed the storage time limitations listed above. Prior to shipment, it is recommended that specimens be removed from the clot, serum separator, or red blood cells.
- No qualitative performance differences were observed between experimental controls and the 23 nonreactive or 23 spiked reactive specimens tested with elevated levels of bilirubin (≤ 20 mg/dL), hemoglobin (≤ 500 mg/dL), triglycerides (≤ 3,000 mg/dL), or protein (≤ 12 g/dL).
- No qualitative performance differences were observed between experimental controls and the 25 nonreactive or 25 spiked reactive specimens tested with red blood cells at ≤ 0.4% v/v.
- ARCHITECT Anti-HCV Calibrator and Controls should be mixed by gentle inversion prior to use.

PROCEDURE

Materials Provided

- 6C37 ARCHITECT Anti-HCV Reagent Kit

Materials Required but not Provided

- ARCHITECT *i* System
- 6C37-01 ARCHITECT Anti-HCV Calibrator
- 6C37-10 ARCHITECT Anti-HCV Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the volumes specified on the Patient or Control order screen.

For information on materials required for maintenance procedures, refer to the ARCHITECT System Operations Manual, Section 9.

Assay Procedure

- Before loading the ARCHITECT Anti-HCV Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that may have settled during shipment:
  - **Invert the microparticle bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles still adhere to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
  - Once the microparticles have been resuspended, remove and discard the cap. Wearing clean gloves, remove a septum from the bag. Carefully snap the septum onto the top of the bottle.
  - **If the microparticles do not resuspend, DO NOT USE; contact your local Abbott representative.**
- Order calibration, if necessary.
- Order tests.
  - For information on ordering patient specimens, calibrator, and controls, and general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Load the ARCHITECT Anti-HCV Reagent Kit on the ARCHITECT *i* System. Verify that all necessary reagents are present. Ensure that septums are present on all reagent bottles.
- The minimum sample cup volume required to perform a single anti-HCV test on the ARCHITECT *i* System is 150 µL for the first anti-HCV test plus 20 µL for each additional anti-HCV test from the same sample cup. No more than 10 replicates may be sampled from the same sample cup. Verify the minimum sample volume is present in the sample cup prior to running the test. The minimum sample cup volume is calculated by the system and is displayed on the Patient, Calibrator, and Control order screens and on the Orderlist report.
  - For a sample that is priority loaded, with 3 or fewer replicates ordered, a smaller sample cup volume than is displayed on the order screen may be used. In this case, the minimum sample cup volume is 70 µL for the first anti-HCV test plus 20 µL for each additional replicate. For additional information on priority loading, refer to the ARCHITECT System Operations Manual, Section 5.
  - To minimize the effects of evaporation, all samples (patient specimens, calibrator, and controls) must be tested within 3 hours of being placed on board the ARCHITECT *i* System. If the sample is on board the system for longer than 3 hours, replace with fresh sample. For additional information on sample evaporation and volumes, refer to the ARCHITECT System Operations Manual, Section 5.
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
  - ARCHITECT Anti-HCV Calibrator and Controls should be mixed by gentle inversion prior to use. To obtain the recommended volume requirements for the ARCHITECT Anti-HCV Calibrator and Controls, hold the bottles **vertically**, and dispense 5 drops of the Calibrator or 6 drops of each Control into each respective sample cup.
- Load samples into the sample carrier and place the sample carrier in the sample load queue.
- Press RUN. The ARCHITECT *i* System performs the following functions:
  - Moves the sample carrier to the sample processing queue.
  - Loads a reaction vessel (RV) into the process path.
  - Aspirates and transfers sample into the RV.
  - Advances the RV one position and transfers microparticles and assay diluent into the RV.
  - Mixes, incubates, and washes the reaction mixture.
  - Adds conjugate to the RV.
  - Mixes, incubates, and washes the reaction mixture.
  - Adds Pre-Trigger and Trigger Solutions.
  - Measures chemiluminescent emission to detect the presence of anti-HCV in the sample.
  - Aspirates contents of RV to liquid waste and unloads RV to solid waste.
  - Calculates the result.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9. If your laboratory requires more frequent maintenance, follow those procedures.

Specimen Dilution Procedures

Specimens cannot be diluted for the ARCHITECT Anti-HCV assay.

Calibration

- To perform an ARCHITECT Anti-HCV calibration, test Calibrator 1 in replicates of three. A single sample of both anti-HCV controls must be tested to evaluate the assay calibration. Ensure that assay control values are within the ranges specified in the Controls package insert. Calibrator should be priority loaded.
- Once an ARCHITECT Anti-HCV calibration is accepted and stored, all subsequent samples may be tested without further calibration unless:
  - A reagent kit with a new lot number is used.
  - Controls are out of range.
- For detailed information on how to perform an assay calibration, refer to the ARCHITECT System Operations Manual, Section 6.

QUALITY CONTROL PROCEDURES

NOTE: It is recommended that the ARCHITECT Anti-HCV Positive Control and the Negative Control be run to verify the calibration. The recommended control requirement for the ARCHITECT Anti-HCV assay is a single sample of both ARCHITECT Anti-HCV Controls tested once every 24 hours each day of use. If the quality control procedures in your laboratory require more frequent use of controls to verify test results, follow your laboratory specific procedures. Ensure that assay Control values are within the ranges specified in the Controls package insert.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT Anti-HCV assay belongs to method group 5.

RESULTS

The ARCHITECT *i* System calculates the Anti-HCV Calibrator 1 mean chemiluminescent signal from three Calibrator 1 replicates and stores the result.

Calculation

The ARCHITECT Anti-HCV assay calculates a result based on S/CO.

- Cutoff calculation:
  Calibrator 1 Mean RLU Value x 0.074 = Cutoff RLU
- S/CO = Sample RLU/Cutoff RLU

Interpretation of Results

- Specimens with S/CO values < 1.00 are considered nonreactive by the ARCHITECT Anti-HCV assay and need not be tested further.
- Specimens with S/CO values ≥ 1.00 are considered reactive by the ARCHITECT Anti-HCV assay.
- All initially reactive specimens should be retested in duplicate. If both retest values are nonreactive, the specimen must be considered nonreactive for anti-HCV. If either of the retest values is reactive, the specimen must be considered repeatedly reactive for anti-HCV by the criteria of ARCHITECT Anti-HCV.
- Repeatedly reactive anti-HCV specimens should be investigated further in supplemental tests such as other HCV specific immunoassays and immunoblot assays or a combination thereof and/or NAT tests.

NOTE: For details on configuring the ARCHITECT *i* System to use grayzone and high reactive interpretations, refer to the ARCHITECT System Operations Manual, Section 2. The grayzone and high reactive interpretations are editable parameters, and should be utilized per end user requirements.

Flags

- Some results may contain information in the Flags field. For a description of the flags that may appear in this field, refer to the ARCHITECT System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- False positive results can be expected with any test kit. The proportion of these falsely reactive specimens is dependent upon the specificity of the test kit, specimen integrity, and on the prevalence of HCV antibodies in the population being screened.
- If the ARCHITECT Anti-HCV results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- For diagnostic purposes, results should be used in conjunction with patient history and other hepatitis markers for diagnosis of acute or chronic infection.
- Samples containing particulate matter or red blood cells must be centrifuged prior to running the assay.
- Performance has not been established using cadaver specimens or body fluids other than human serum or plasma.
- Do not use heat-inactivated specimens.
- Specimens from heparinized patients may be partially coagulated and erroneous results could occur due to the presence of fibrin. To prevent this phenomenon, draw the specimen prior to heparin therapy

SPECIFIC PERFORMANCE CHARACTERISTICS

NOTE: Representative performance data are shown. Results obtained in individual laboratories and with different populations may vary.

Precision

The precision of ARCHITECT Anti-HCV was determined using three reagent lots. A panel composed of four unique members was tested in replicates of four with each reagent lot once daily for five days across three instruments. Each daily run also included the ARCHITECT Positive Control run in duplicate at the beginning and end of the run. The intra-assay, inter-assay, total standard deviation (SD) and percent coefficient of variation (%CV) were determined with a variance component analysis[19] for a random effects model[20] (Table I).

TABLE I
ARCHITECT Anti-HCV Precision

Panel Member	Total No. Replicates	Grand Mean (S/CO)	Intra-assay		Inter-assay[a]		Total[b]	
			SD	%CV	SD	%CV	SD	%CV
1	180	7.39	0.351	4.7	0.395	5.3	0.447	6.0
2	180	3.92	0.138	3.5	0.169	4.3	0.209	5.3
3	180	1.50	0.056	3.7	0.067	4.4	0.095	6.4
4	180	0.08	0.005	5.6	0.007	8.4	0.011	13.4
Positive Control	180	3.27	0.127	3.9	0.147	4.5	0.166	5.1

[a] Inter-assay variability contains intra-assay variability.

[b] Total assay variability contains intra-assay, inter-assay, inter-lot, and inter-instrument variability.

Specificity

A total of 8,942 serum and plasma specimens from volunteer whole blood and plasmapheresis donors were evaluated. The specimens from volunteer whole blood donors were collected from European blood centers and the plasmapheresis specimens from U.S. blood centers (Table II). There was a total of 59 repeatedly reactive specimens. Following supplemental testing with an anti-HCV immunoblot assay, 28 specimens were anti-HCV positive (reactive to two or more gene products), 15 were indeterminate (reactive to one gene product), and 16 were negative (no gene products detected).

Ninety-nine of the 1,500 specimens obtained from hospital patients were repeatedly reactive, of which 88 were anti-HCV positive, five indeterminate, and six negative by supplemental testing. In 65 specimens from individuals with medical conditions unrelated to HCV infection and specimens containing potentially interfering substances, three specimens were repeatedly reactive, and all were anti-HCV positive by supplemental testing.

TABLE II
Reactivity of the ARCHITECT Anti-HCV Assay in Specimens from Whole Blood Donors, Plasmapheresis Donors, Hospital Patients, Individuals with Medical Conditions Unrelated to HCV Infection, and in Specimens Containing Potentially Interfering Substances

Category	Number Tested	IR (% of Total)	RR (% of Total)	Number of Positive by Supplemental Testing[a] (% of Repeatedly Reactive)
Volunteer Whole Blood Donors				
Serum[b]	3,000	14 (0.47)	12 (0.40)	0
Plasma	2,508	11 (0.44)	11 (0.44)	0
Plasmapheresis Donors	3,434	37 (1.08)	36 (1.05)	28 (77.78)
Total Donors	8,942	62 (0.69)	59 (0.66)	28 (47.46)
Hospital Patients	1,500	100 (6.67)	99 (6.60)	88 (88.89)
Medical Conditions Unrelated to HCV Infection and Potentially Interfering Substances[c]	65	3 (4.62)	3 (4.62)	3 (100.00)

IR = Initially Reactive; RR = Repeatedly Reactive

[a] A positive result was defined as reactive to two or more gene products by an immunoblot assay.

[b] Includes a subset of 500 matched serum/plasma pairs; only the serum results were included in the specificity calculation.

[c] Category included the following: anti-CMV positive (5), anti-EBV positive (5), anti-HAV positive (5), HBsAg positive (5), anti-HIV-1 positive (5), syphilis (5), rheumatoid factor (5), alcoholic liver disease (5), anti-HBc positive (5), anti-HTLV-I positive (5), human anti-mouse antibody positive (10), and influenza vaccine recipients (5).

Sensitivity

A total of 117 specimens from 50 individuals with chronic HCV infection, 42 individuals that were anti-HCV and HCV RNA positive, and 25 individuals at increased risk for HCV infection were tested. Of the 117 specimens, 100 were repeatedly reactive, and were anti-HCV positive by supplemental testing (Table III).

TABLE III
Reactivity of the ARCHITECT Anti-HCV Assay in Selected Populations with Chronic HCV Infection, Anti-HCV/HCV RNA Positive, and at Increased Risk for HCV Infection

Category	Number Tested	Number Repeatedly Reactive (% of Total)	Number of Positive by Supplemental Testing[a] (% of Repeatedly Reactive)
Chronic HCV Infection	50	50 (100.00)	50 (100.00)
Anti-HCV/HCV RNA Positive	42	42 (100.00)	42 (100.00)
Increased Risk for HCV Infection[b]	25	8 (32.00)	8 (100.00)
TOTAL	117	100 (85.47)	100 (100.00)

[a] A positive result was defined as reactive to two or more gene products by an immunoblot assay.

[b] Category included the following: intravenous drug users (5), hemophilia patients (10), men sex men (5), and female prostitutes (5).

Overall Specificity and Sensitivity

Overall specificity and sensitivity were estimated from the results of 10,624 serum and plasma specimens summarized in Tables II and III.

The overall specificity was 99.60% (10,361/10,403) with a 95% confidence interval of 99.45% to 99.71%. Specificity observed from different sites ranged between 99.20% (496/500) to 99.70% (1994/2000). The sensitivity was 99.10% with a 95% confidence interval of 96.77% to 99.89%.

Seroconversion

The ability of the ARCHITECT Anti-HCV assay to detect anti-HCV was evaluated by testing 20 HCV seroconversion panels from blood and plasmapheresis donors who seroconverted over the course of their donation history. The panels were also tested by an approved assay. The ARCHITECT Anti-HCV assay detected anti-HCV three days (one bleed) earlier than the comparator assay in 1 of the 20 panels. The comparator assay detected anti-HCV five to six days (one bleed) earlier than ARCHITECT Anti-HCV in 3 of the 20 panels. Both assays exhibited equivalent detection of anti-HCV in 16 of the 20 panels.

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The following US Patents are relevant to the ARCHITECT *i* System or its components. There are other such patents and patent applications in the United States and worldwide.

5,468,646	5,543,524	5,545,739
5,565,570	5,669,819	5,783,699

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April 2008