ARCHITECT HCV Ag

REF 6L47-29

en

HCV Ag
6L47
F5-Y406-2/R11
B6L4H0

Read Highlighted Changes: Revised June 2019.

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

NAME

ARCHITECT HCV Ag

INTENDED USE

The ARCHITECT HCV Ag assay is a chemiluminescent microparticle immunoassay (CMIA) for the quantitative determination of Hepatitis C virus core antigen in human serum and plasma.

SUMMARY AND EXPLANATION OF THE TEST

ARCHITECT HCV Ag is a chemiluminescent microparticle immunoassay (CMIA) using microparticles coated with monoclonal anti-HCV for the detection of HCV Ag.

HCV Ag assays are used as an aid in the diagnosis of suspected Hepatitis C viral (HCV) infection and to monitor the status of infected individuals, i.e., whether the patient's infection has resolved or the patient has become a chronic carrier of the virus. An HCV Ag assay can detect acute HCV infection in newly infected individuals who are seronegative for antibodies to HCV due to the delayed response of HCV specific antibodies. These may include patients with an elevated risk of HCV infection for example intravenous drug users or in patients with impaired immune function such as patients undergoing hemodialysis or suffering from HIV-HCV coinfections, where HCV Ag may be the only serological marker to detect HCV infection.[1, 2] Recent studies suggest a testing algorithm using the HCV Ag test to confirm active viral replication in anti-HCV positive individuals.[19-21] Using an algorithm such as those proposed in the Mederacke, et al.[19], Ottiger, et al.[20] and Cloherty, et al.[22] publications could be helpful to accelerate access to new, improved anti-viral therapies. For the diagnosis of acute or chronic hepatitis, HCV Ag reactivity should be correlated with patient history and the presence of other Hepatitis C serological markers.[3, 4]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT HCV Ag assay is a two-step immunoassay for the quantitative determination of core antigen of Hepatitis C virus using CMIA technology with flexible assay protocols, referred to as Chemiflex.

1. Sample, Pre-Treatment Reagent 1 and Pre-Treatment Reagent 2 are combined. An aliquot of the pre-treated sample is aspirated and dispensed into a new reaction vessel. The pre-treated sample, Assay Specific Diluent and anti-HCV coated microparticles are combined. The HCV Ag present in the pre-treated sample binds to the anti-HCV coated microparticles.
2. After washing, acridinium-labeled anti-HCV conjugate is added to create a reaction mixture.
3. Following another wash cycle, Pre-Trigger and Trigger Solutions are added to the reaction mixture.
4. The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of HCV Ag in the sample and the RLUs detected by the ARCHITECT iSystem optics.

The concentration of Hepatitis C core antigen in the specimen is determined using a previously generated ARCHITECT HCV Ag calibration curve. If the concentration of the specimen is greater than or equal to 3.00 fmol/L, the specimen is considered reactive for HCV Ag.

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

REAGENTS

Kit Contents

ARCHITECT HCV Ag 6L47

REF	6L47-29
Σ	100
MICROPARTICLES	1 x 6.7 mL
CONJUGATE	1 x 6.1 mL
ASSAY SPECIFIC DILUENT	1 x 30.0 mL
PRE-TREATMENT REAGENT 1	1 x 14.5 mL
PRE-TREATMENT REAGENT 2	1 x 11.0 mL
SPECIMEN DILUENT	1 x 5.9 mL

MICROPARTICLES Murine anti-HCV antibody coated microparticles in 400 mM Bicine, 50 mM TRIS buffer with protein (bovine) stabilizer. Minimum concentration: 0.025% solids. Preservatives: sodium azide and antimicrobial agents.

CONJUGATE Murine anti-HCV antibody acridinium-labeled conjugate in 80 mM BIS-TRIS with protein (bovine) stabilizer. Minimum concentration: 0.3 µg/mL. Preservatives: sodium azide and antimicrobial agents.

ASSAY SPECIFIC DILUENT HCV Ag Assay Specific Diluent containing 1.46 N NaOH.

PRE-TREATMENT REAGENT 1 HCV Ag Pre-Treatment Reagent 1 containing 0.83 N HCl.

PRE-TREATMENT REAGENT 2 HCV Ag Pre-Treatment Reagent 2 containing 0.83 N HCl.

SPECIMEN DILUENT HCV Ag Specimen Diluent containing phosphate buffer with protein (horse serum) stabilizer. Preservatives: sodium azide and antimicrobial agents.

Other Reagents

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

TRIGGER SOLUTION ARCHITECT Trigger Solution containing 0.35 N sodium hydroxide.

WASH BUFFER ARCHITECT Wash Buffer containing phosphate buffered saline solution. Preservatives: antimicrobial agents.

Warnings and Precautions

- IVD
- 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 in accordance with the OSHA Standard on Bloodborne Pathogens. Biosafety Level 2 or other appropriate biosafety practices should be used for materials that contain or are suspected of containing infectious agents.[5-8]

The following warnings and precautions apply to: **MICROPARTICLES**	
WARNING:	Contains sodium azide, polyethylene glycol octylphenyl ether and sodium 4-(methoxycarbonyl)phenolate.
H402*	Harmful to aquatic life.
H412	Harmful to aquatic life with long lasting effects.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P273	Avoid release to the environment.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

* Not applicable where regulation EC 1272/2008 (CLP) has been implemented.

The following warnings and precautions apply to: **SPECIMEN DILUENT**	
Contains sodium azide.	
EUH032	Contact with acids liberates very toxic gas.
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to: **CONJUGATE**	
	
WARNING:	Contains cetyltrimethylammonium bromide, polyethylene glycol octylphenyl ether, benzethonium chloride, sodium fluoride and sodium azide.
H400	Very toxic to aquatic life.
H411	Toxic to aquatic life with long lasting effects.
EUH032	Contact with acids liberates very toxic gas.
Prevention	
P273	Avoid release to the environment.
Response	
P391	Collect spillage.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to: **ASSAY SPECIFIC DILUENT**	
	
DANGER:	Contains sodium hydroxide.
H314	Causes severe skin burns and eye damage.
H290	May be corrosive to metals.
Prevention	
P234	Keep only in original container.
P260	Do not breathe mist / vapors / spray.
P264	Wash hands thoroughly after handling.
P280	Wear protective gloves / protective clothing / eye protection.
Response	
P301+P330+P331	IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P303+P361+P353	IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water / shower.
P310	Immediately call a POISON CENTER or doctor / physician.
P390	Absorb spillage to prevent material damage.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

The following warnings and precautions apply to: **PRE-TREATMENT REAGENT 1** / **PRE-TREATMENT REAGENT 2**	
	
DANGER:	Contains hydrochloric acid, dodecyltrimethylammonium bromide, citric acid monohydrate, Hexadecyldimethyl(3-sulphonatopropyl)ammonium, n-Octadecyldimethyl(3-sulfopropyl) ammonium hydroxide and polyethylene glycol octylphenyl ether.
H314	Causes severe skin burns and eye damage.
H332	Harmful if inhaled.
H400	Very toxic to aquatic life.
H410	Very toxic to aquatic life with long lasting effects.
H290	May be corrosive to metals.
Prevention	
P234	Keep only in original container.
P260	Do not breathe mist / vapors / spray.
P264	Wash hands thoroughly after handling.
P280	Wear protective gloves / protective clothing / eye protection.
P273	Avoid release to the environment.
Response	
P301+P330+P331	IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P303+P361+P353	IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water / shower.
P304+P340	IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P310	Immediately call a POISON CENTER or doctor / physician.
P390	Absorb spillage to prevent material damage.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.

For a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Reagent Handling

- Do not use reagent kits beyond the expiration date.
- **Do not open the ASSAY SPECIFIC DILUENT plastic bag until ready to use.**
- **If leaking is observed with the Assay Specific Diluent bottle, the reagent kit cannot be used due to a lack of homogeneity which may impact results. The Assay Specific Diluent contains sodium hydroxide, and can cause severe skin and eye burns. Leaking bottles should be handled with appropriate safety precautions.**
- **Do not pool reagents within a kit or between kits.**
- Before loading the reagent kit on the system for the first time, **the reagents shipped on dry ice must be completely thawed and mixed thoroughly.** For 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.
  - 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.

Reagent Storage

When stored and handled as directed, reagents are stable until the expiration date.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened/ Opened*	2-8°C	Until expiration date	Shipped on dry ice, must be stored at 2-8°C after receipt Store in upright position.
On board	System temperature	30 days	Discard after 30 days. For information on tracking onboard time, refer to the ARCHITECT System Operations Manual, Section 5.

* Reagents may be stored on or off the ARCHITECT iSystem. 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 that 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.** For information on unloading reagents, refer to the ARCHITECT System Operations Manual, Section 5.

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 samples must be retested. Assay recalibration may be necessary. For troubleshooting information, refer to the ARCHITECT System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The ARCHITECT HCV Ag assay file must be installed on the ARCHITECT iSystem from an ARCHITECT iSystem 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.

If the ARCHITECT Anti-HCV assay and the ARCHITECT HCV Ag assay are run on the same ARCHITECT iSystem, the Anti-HCV assay file must be installed from ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com, prior to the installation of the HCV Ag assay file.

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.

Alternate Result Units

Edit assay parameter "Result concentration units" to select an alternate unit.

(Concentration in fmol/L) x (0.02) = (Concentration in pg/mL)

Default result unit	Conversion factor	Alternate result unit
fmol/L	0.02	pg/mL

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

Verified specimen types to be used with this assay:

Specimen Types	Collection Tubes
Human serum	Serum
	Serum separator tubes
Human plasma	Sodium EDTA
	Potassium EDTA
	Lithium Heparin
	Sodium Heparin
	Sodium Citrate
	CPD

- Other specimen collection tube types have not been tested with this assay.
- Liquid anticoagulants may have a dilution effect resulting in lower concentrations for individual patient specimens.
- The instrument does not provide the capability to verify specimen type. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed
  - obvious microbial contamination
- Performance has not been established for the use of cadaveric specimens or the use of body fluids other than human serum and plasma.
- 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 3000 x g for 10 minutes. Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- When using plasma primary tubes, samples must be priority loaded immediately after centrifugation to minimize disturbance of the red blood cells.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- Mix thawed specimens thoroughly by low speed vortexing or by inverting 10 times. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and **centrifuged at 3000 x g for 10 minutes** before testing if
  - they contain fibrin, red blood cells, or other particulate matter,
  - they require repeat testing, or
  - they were frozen and thawed.
- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.
- Inspect all specimens for bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Specimen Storage

Specimen Type	Storage Temperature	Maximum Storage Time
Serum or plasma	2-8°C	≤ 5 days
	- 20°C or colder	--

Specimen may be stored on or off the clot, red blood cells, or separator gel for up to 5 days refrigerated at 2-8°C.

If testing will be delayed more than 5 days, remove serum or plasma from the clot, red blood cells, or separator gel and store frozen at -20°C or colder.

Avoid more than two freeze/thaw cycles.

Specimen Shipping

- Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Do not exceed the storage limitations listed above.

PROCEDURE

Materials Provided

6L47 ARCHITECT HCV Ag Reagent Kit

Materials Required but not Provided

- ARCHITECT HCV Ag Assay file obtained from the ARCHITECT iSystem e-Assay CD-ROM found on www.abbottdiagnostics.com.
- 6L47-02 ARCHITECT HCV Ag Calibrators
- 6L47-11 ARCHITECT HCV Ag Controls
- ARCHITECT Pre-Trigger Solution
- ARCHITECT Trigger Solution
- ARCHITECT Wash Buffer
- ARCHITECT Reaction Vessels
- ARCHITECT Sample Cups
- ARCHITECT Septum
- ARCHITECT 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 reagent kit on the system for the first time, **the reagents shipped on dry ice must be completely thawed and mixed thoroughly**. After the first time the reagents have been loaded, no further mixing is required.
  - Tear open the ASSAY SPECIFIC DILUENT plastic bag.
  - Invert **all the reagent bottles** 30 times.
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles are still adhered to the bottle, continue to invert the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE. Contact your local Abbott representative.**
  - Once the microparticles have been resuspended, place a septum on the bottle. For instructions on placing septums on bottles, refer to the **Reagent Handling** section of this package insert.
- Load the reagent kit on the ARCHITECT iSystem.
  - Verify that all necessary reagents are present.
  - Ensure that septums are present on all reagent bottles.
- Order calibration, if necessary.
  - For information on ordering calibrations, refer to the ARCHITECT System Operations Manual, Section 6.
- Order tests.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- Minimum sample cup volume is calculated by the system and printed on the Orderlist report. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.

  Maximum number of replicates sampled from the same sample cup: 10
  - Priority:

    Sample volume for first test: 158 µL

    Sample volume for each additional test from same sample cup: 108 µL
  - ≤ 3 hours on board:

    Sample volume for first test: 158 µL

    Sample volume for each additional test from same sample cup: 108 µL
  - > 3 hours on board: replace with a fresh sample (patient specimens, controls, and calibrators).
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare ARCHITECT HCV Ag Calibrators and Controls.
  - Mix calibrator(s) and controls by gentle inversion before use.
  - Hold bottles **vertically** and dispense recommended volumes into each respective sample cup.
  - Recommended volumes:

    for each calibrator: 12 drops

    for each control: 7 drops
- Load samples.
  - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
- Press RUN.
- For additional information on principles of operation, refer to the ARCHITECT System Operations Manual, Section 3.
- For optimal performance, it is important to perform routine maintenance as described in the ARCHITECT System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Specimen Dilution Procedures

Specimens with an HCV Ag concentration of > 20,000 fmol/L will be flagged as ">20,000" and may be diluted with either the Automated Dilution Protocol or the Manual Dilution Procedure.

Automated Dilution Protocol

The system performs a 1:9 dilution of the specimen and automatically calculates the concentration of the specimen before dilution and reports the result.

Manual Dilution Procedure

Suggested dilution: 1:20

1. Add 20 µL of the patient specimen to 380 µL of ARCHITECT HCV Ag Negative Control.
2. The operator must enter the dilution factor in the Patient or Control order screen. The system will use this dilution factor to automatically calculate the concentration of the sample before dilution and report the result. The result (before the dilution factor is applied) should be greater than 3.00 fmol/L.

For detailed information on ordering dilutions, refer to the ARCHITECT System Operations Manual, Section 5.

Calibration

- Test Calibrators A-F in duplicate and a single sample of each control level as below,
  1. Order the calibration. **DO NOT START THE RUN.**
  2. Order 1 rep of CONTROL+2, 1 rep of CONTROL+1 and 1 rep of CONTROL- in this order.
  3. Then, start the run.

  The calibrators should be priority loaded. Ensure that assay control values are within the concentration ranges specified in the control package insert.
- Calibration Range: 0 – 20,000 fmol/L.
- Once an ARCHITECT HCV Ag 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 or
  - 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

- The recommended control requirement for the ARCHITECT HCV Ag assay is that a single sample of each control level be 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.
- The ARCHITECT HCV Ag Control values must be within the acceptable ranges specified in the control package insert. If a control is out of its specified range, the associated test results are invalid and samples must be retested. Recalibration may be indicated.

Verification of Assay Claims

For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B.

The ARCHITECT HCV Ag assay belongs to method group 5.

RESULTS

The ARCHITECT HCV Ag assay utilizes a 4 Parameter Logistic Curve fit data reduction method (4PLC, Y-weighted) to generate a calibration curve.

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.

Interpretation of Results

Concentration Value	Interpretation
< 3.00 fmol/L	Nonreactive for HCV Ag
≥ 3.00 fmol/L	Reactive for HCV Ag

Specimens with concentration values ≥ 3.00 fmol/L to < 10.00 fmol/L should be retested in duplicate.

Duplicate Retest Results

Instrument Interpretation	Specimen Classification
Both retest values nonreactive	Specimen considered nonreactive for HCV Ag.
One or both of the duplicates is (are) ≥ 3.00 fmol/L	Specimen considered repeatedly reactive for HCV Ag, and the initial value is used as the final reported value.

For details on configuring the ARCHITECT iSystem to use grayzone interpretations, refer to the ARCHITECT System Operations Manual, Section 2.

LIMITATIONS OF THE PROCEDURE

- For diagnostic purposes, results should be used in conjunction with other data; e.g., symptoms, results of other tests, clinical impressions, etc.
- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA). Such specimens may show either falsely elevated or depressed values when tested with assay kits such as ARCHITECT HCV Ag that employ mouse monoclonal antibodies. Additional information may be required for diagnosis.[9, 10] The ARCHITECT HCV Ag reagents contain a component that reduces the effect of HAMA reactive specimens. Additional clinical or diagnostic information may be required to determine patient status.
- If the ARCHITECT HCV Ag results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- Samples containing particulate matter or red blood cells must be centrifuged prior to running the assay. Insufficiently separated plasma specimens from clots or red blood cells must not be used.
- Specimens from patients with high levels of IgM, e.g., specimens from patients with multiple myeloma, may generate “3350 Unable to process test, aspiration error for (Sample Pipettor) at (RV 24)”.
- **The ARCHITECT Anti-HCV assay (LN 6C37) may cause falsely elevated HCV Ag results in the ARCHITECT HCV Ag assay when both assays are run on the same module. As a preventive measure to protect the integrity of test results, it is important that one of the following actions be taken:**
  - **a. Multiple iSystem module customers should run the ARCHITECT HCV Ag and ARCHITECT Anti-HCV assays on separate modules or,**
  - **b. If you are unable to run these assays on separate modules:**
    - **i. Segregate the ARCHITECT HCV Ag samples and run them immediately following the ARCHITECT 6041 Daily Maintenance procedure.**
    - **ii. After running the ARCHITECT HCV Ag samples, it is recommended to immediately perform the ARCHITECT 6041 Daily Maintenance procedure again, as an extra precaution.**
    - **iii. It is recommended that duplicate retest be performed on samples between the range of 3 - 15 fmol/L instead of the range of 3 - 10 fmol/L in the RESULTS section.**
- Due to the naturally occurring diversity of hepatitis C viruses, including amino acid variations within the core gene, rare specimens from HCV infected patients may produce unexpectedly low or negative results in the ARCHITECT HCV Ag assay.[12-14] Two studies noted reduced assay sensitivity among a subpopulation of individuals infected with HCV genotype 3a.[13, 14] Additional studies have reported varying detection rates for genotype 3 samples on the ARCHITECT HCV Ag test when compared to HCV RNA testing.[13-18]
  - In patients that are anti-HCV positive but HCV Ag negative, it is advisable to perform additional clinical or diagnostic testing (e.g. molecular testing) to determine patient status.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT HCV Ag assay precision is < 10% total CV. A study was performed as described in the National Committee for Clinical Laboratory Standards (NCCLS) Protocol EP5-A2.[11] Five samples consisting of two buffer protein based HCV Ag positive controls and three serum based panels were assayed in replicates of two at two separate times per day for twenty days (n=80 for each sample), using three lots of reagents. Data from this study are summarized in the following table.*

Table I: ARCHITECT HCV Ag Precision

		Reagent		Mean Value	Within Run		Total	
Sample	Instrument	Lot	n	(fmol/L)	SD	%CV	SD	%CV
Level 1	1	1	80	52.41	4.82	9.2	4.96	9.5
	1	2	80	50.08	3.76	7.5	4.07	8.1
	1	3	80	52.92	3.80	7.2	4.10	7.8
	2	1	80	53.57	4.40	8.2	4.73	8.8
	2	2	80	52.31	3.81	7.3	3.81	7.3
	2	3	80	51.98	3.21	6.2	3.28	6.3
Level 2	1	1	80	303.18	20.60	6.8	23.01	7.6
	1	2	80	288.91	17.27	6.0	18.91	6.5
	1	3	80	303.95	22.83	7.5	24.03	7.9
	2	1	80	320.62	20.53	6.4	20.53	6.4
	2	2	80	311.64	14.79	4.7	15.64	5.0
	2	3	80	306.22	11.98	3.9	13.32	4.3
Panel 1	1	1	80	67.54	4.74	7.0	4.90	7.3
	1	2	80	65.09	4.35	6.7	5.13	7.9
	1	3	80	67.14	3.54	5.3	4.64	6.9
	2	1	80	65.57	4.61	7.0	5.00	7.6
	2	2	80	63.70	4.12	6.5	4.47	7.0
	2	3	80	63.09	4.64	7.4	4.64	7.4
Panel 2	1	1	80	327.17	22.40	6.8	24.81	7.6
	1	2	80	310.52	16.11	5.2	26.28	8.5
	1	3	80	324.36	15.22	4.7	17.29	5.3
	2	1	80	337.09	21.37	6.3	22.06	6.5
	2	2	80	322.28	19.84	6.2	21.83	6.8
	2	3	80	310.09	14.46	4.7	17.65	5.7
Panel 3	1	1	80	7629.26	406.99	5.3	549.08	7.2
	1	2	80	7765.96	545.13	7.0	599.72	7.7
	1	3	80	7360.23	318.91	4.3	363.50	4.9
	2	1	80	8231.22	475.04	5.8	508.93	6.2
	2	2	80	7553.65	361.03	4.8	420.65	5.6
	2	3	80	7516.93	254.33	3.4	359.53	4.8

* Representative data; results in individual laboratories may vary from these data.

Specificity

The ARCHITECT HCV Ag assay demonstrated a specificity of ≥ 99.5% in a study where specimens from a blood donor population, hospitalized patients and specimens containing potentially interfering substances were tested. This study includes the specimens from individuals with medical conditions unrelated to HCV infection (Table II). A total of 5027 serum and plasma specimens from blood donors were evaluated. The initial and repeat reactive rates were 0.24% (12/5027) and 0.02% (1/5027), respectively. Four of 250 specimens obtained from hospital patients were repeatedly reactive and confirmed positive for HCV infection. In 126 specimens from individuals with medical conditions unrelated to HCV infection and specimens containing potentially interfering substances, five specimens were repeatedly reactive and confirmed positive for HCV infection.

Table II: Reactivity of the ARCHITECT HCV Ag Assay in Specimens from Blood 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 RR)
Blood Donors				
Serum	2256	7 (0.31)	1 (0.04)	0 (0.00)
EDTA Plasma	411	0 (0.00)	0 (0.00)	0 (0.00)
Na Citrate Plasma	1180	2 (0.17)	0 (0.00)	0 (0.00)
Heparin Plasma	1180	3 (0.25)	0 (0.00)	0 (0.00)
Total Donors	5027	12 (0.24)	1 (0.02)	0 (0.00)
Hospital Patients	250	4 (1.60)	4 (1.60)	4 (100.0)
Individuals with Medical Conditions Unrelated to HCV Infection and Specimens Containing Potentially Interfering Substances[b]	126	5 (3.97)	5 (3.97)	5 (100.0)

IR = Initially Reactive; RR = Repeatedly Reactive

[a] A positive result was defined as reactive to Abbott AxSYM Anti-HCV (1D30), Roche Amplicor HCV, and/or Abbott RealTime HCV (4J86).

[b] Category includes the following: anti-CMV positive (5), anti-EBV positive (5), anti-HAV positive (5), HBsAg positive (5), anti-HIV-1 positive (9), anti-HIV-2 positive (1), HIV Ag positive (5), anti-HTLV-1 positive (5), anti-HBc positive (5), Syphilis positive (5), rheumatoid factor (5), alcoholic liver disease (5), human anti-mouse antibody positive (5), *E. coli* (5), anti-HSV-1 positive (5), multiparous female (5), hemodialysis patients (5), anti-nuclear antibody positive (5), elevated IgG (5), elevated IgM (5), multiple myeloma (3), pregnant female (5), influenza vaccine recipients (5), Toxoplasma positive (3), West Nile virus positive (5), multiple transfusion recipients (5).

Sensitivity

The ARCHITECT HCV Ag assay has a sensitivity of ≤ 3.00 fmol/L.

A total of 452 serum and plasma specimens known to be positive for HCV RNA including genotypes 1a, 1b, 2a, 2b, 3a, 3k, 4a, 5a, 6a, and 6i, were tested. Of the 452 specimens, 97.8% (442/452) were reactive.

Seroconversion

Sensitivity of the ARCHITECT HCV Ag assay was evaluated utilizing 10 commercially available panels of sequential specimens from patients who seroconverted for the detection of anti-HCV antibodies. In each panel, a positive result in the ARCHITECT HCV Ag assay was obtained prior to detection of anti-HCV antibody, resulting in an average reduction between the times of infection and detection of 35.8 days.

Interference

The ARCHITECT HCV Ag assay is designed to have a mean interference of ≤ 10% difference in concentration for patient samples with triglycerides (3000 mg/dL), bilirubin (20 mg/dL), hemoglobin (500 mg/dL), and protein (9.2 g/dL).

In a representative study, the interference from hemoglobin, bilirubin, triglycerides, and protein was evaluated in the ARCHITECT HCV Ag assay. The following interferences were obtained:

- Hemoglobin < 10% at 500 mg/dL
- Bilirubin < 10% at 20 mg/dL
- Triglycerides < 10% at 3000 mg/dL
- Protein < 10% at 9.2 g/dL

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Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
ASSAY SPECIFIC DILUENT	Assay Specific Diluent
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
CONTROL NO.	Control Number
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRE-TREATMENT REAGENT 1	Pre-Treatment Reagent 1
PRE-TREATMENT REAGENT 2	Pre-Treatment Reagent 2
PRE-TRIGGER SOLUTION	Pre-Trigger Solution
PRODUCED FOR ABBOTT BY	Produced for Abbott by
PRODUCT OF JAPAN	Product of Japan
REACTION VESSELS	Reaction Vessels
REAGENT LOT	Reagent Lot
REF	List Number
REPLACEMENT CAPS	Replacement Caps
SAMPLE CUPS	Sample Cups
SEPTUM	Septum
SN	Serial number
SPECIMEN DILUENT	Specimen Diluent
TRIGGER SOLUTION	Trigger Solution
WASH BUFFER	Wash Buffer

Anti-HCV monoclonal antibodies are prepared under US license by Chiron Corporation under a shared manufacturing agreement.

The ARCHITECT HCV Ag assay is manufactured under contract agreement from Ortho Diagnostic Systems and Chiron Corporation.

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