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

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

### Key to symbols used

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>REF</td>
<td>List Number</td>
</tr>
<tr>
<td>IVD</td>
<td>In Vitro Diagnostic Medical Device</td>
</tr>
<tr>
<td>LOT</td>
<td>Lot Number</td>
</tr>
<tr>
<td></td>
<td>Expiration Date</td>
</tr>
<tr>
<td>2°C/4°C</td>
<td>Store at 2-8°C</td>
</tr>
<tr>
<td></td>
<td>Consult instructions for use</td>
</tr>
<tr>
<td>Manufacturer</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASSAY CD-ROM</td>
<td>Assay CD-ROM</td>
</tr>
<tr>
<td>SN</td>
<td>Serial Number</td>
</tr>
<tr>
<td>CONTROL NO.</td>
<td>Control Number</td>
</tr>
<tr>
<td>REAGENT LOT</td>
<td>Reagent Lot</td>
</tr>
<tr>
<td>REACTION VESSELS</td>
<td>Reaction Vessels</td>
</tr>
<tr>
<td>SAMPLE CUPS</td>
<td>Sample Cups</td>
</tr>
<tr>
<td>SEPTUM</td>
<td>Septum</td>
</tr>
<tr>
<td>REPLACEMENT CAPS</td>
<td>Replacement Caps</td>
</tr>
</tbody>
</table>

See REAGENTS section for a full explanation of symbols used in reagent component naming.
**SUMMARY AND EXPLANATION OF TEST**

Acquired immunodeficiency syndrome (AIDS) is caused by two types of human immunodeficiency viruses, collectively designated HIV-1 and HIV-2. HIV is the etiologic agent of AIDS. HIV is transmitted by sexual contact, exposure to blood or blood products, and perinatal infection of a fetus or perinatal infection of a newborn. Antibodies against HIV are nearly always detected in AIDS patients and HIV infected asymptomatic individuals, and HIV infection is always detected in AIDS patients and seropositive individuals by culture or amplification of viral RNA and/or proviral DNA.

Phylogenetic analysis classifies HIV-1 into groups M (major), N (non-M, non-O, and non-B), and O (outlier). Group M viruses have spread throughout the world to cause the global AIDS pandemic. In contrast, groups N and O are relatively rare and endemic to west central Africa. HIV-1 group M infections have been identified in Europe and the USA. HIV-1 group M is composed of genetic subtypes (A, B, C, D, F, G, H, J, and K) and circulating recombinant forms (CRFs).

The geographic distribution and regional predominance of HIV-1 subtypes and CRF's vary. All subtypes and many recombinant strains exist in Africa with CRF02_AG the predominant strain in west and west central Africa, subtypes A, C, and D predominant in east central Africa, and subtype C predominant in southern Africa. HIV-1 subtype B is the predominant subtype in the USA, Europe, Japan, and Australia. However, a significant percentage of new HIV-1 infections in Europe are caused by non-B subtypes.

In Asia, subtype C is found in India, and CRF01_AE (formerly called subtype E) and subtype B are in Thailand and southeast Asia. South America predominately has subtypes B and F.

Human immunodeficiency virus type 2 (HIV-2) is similar to HIV-1 in its structural morphology, genomic organization, cell tropism, in vitro cytopathogenicity, transmission routes, and ability to cause AIDS. HIV-2 is less pathogenic than HIV-1, and HIV-2 infections have a longer latency period with slower progression to disease, lower viral titers, and lower rates of vertical and horizontal transmission.

HIV-2 is endemic to west Africa but HIV-2 infections, at a low frequency compared to HIV-1, have been identified in the USA, Europe, Asia, and other regions of Africa. HIV-2 is classified into genetic subtypes A-G with most infections caused by subtypes A and B.

The key immunogenic protein and antigenic target for serodetection of HIV infection is the viral (HIV) transmembrane protein (TMP). Antibodies against the TMP (anti-TMP) consistently are among the first to appear at seroconversion of HIV infected individuals. The anti-TMP response remains relatively strong throughout the course of the disease, as evidenced by the near universal presence of antibodies against the TMP in asymptomatic and symptomatic stages of HIV infection. TMPs from HIV-1 groups M and O and HIV-2 are represented in ARCHITECT System optics. The presence or absence of HIV p24 antigen or HIV-1/HIV-2 antibodies in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an ARCHITECT HIV Ag/Ab Combo calibration. Specimens with signal to cutoff (S/CO) values greater than or equal to 1.00 are considered reactive for HIV p24 antigen or HIV-1/HIV-2 antibodies. Specimens with S/CO values less than 1.00 are considered nonreactive for HIV p24 antigen or HIV-1/HIV-2 antibodies.

Specimens that are initially reactive in the ARCHITECT HIV Ag/Ab Combo assay should be retested in duplicate. Repeat reactivity is highly predictive of the presence of HIV p24 antigen and HIV-1/HIV-2 antibodies. However, as with all immunosays, the ARCHITECT HIV Ag/Ab Combo assay may yield nonspecific reactions due to other causes, particularly when testing in low prevalence populations. A repeatedly reactive specimen should be investigated further with sensitive, supplemental HIV-specific tests, such as immunoblots, antigen tests, and HIV nucleic acid tests. Supplemental testing of repeat-reactive specimens obtained from individuals at risk for HIV infection usually confirms the presence of HIV antibodies or HIV antigen, and HIV nucleic acid. A full differential diagnostic work-up for the diagnosis of AIDS and AIDS-related conditions includes an examination of the patient’s immune status and a clinical history.

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

**REAGENTS**

**NAME**

ARCHITECT HIV Ag/Ab Combo

**INTENDED USE**

The ARCHITECT HIV Ag/Ab Combo assay is a chemiluminescent microparticle immunoassay (CMIA) for the simultaneous qualitative detection of HIV p24 antigen and antibodies to HIV-1, HIV-2, and/or HIV-1/HIV-2 in human serum or plasma. The ARCHITECT HIV Ag/Ab Combo assay is intended to be used as an aid in the diagnosis of HIV-1/HIV-2 infection and as a screening test for donated blood and plasma. An ARCHITECT HIV Ag/Ab Combo result does not distinguish between the detection of HIV p24 antigen, HIV-1 antibody, or HIV-2 antibody.

**BIOLOGICAL PRINCIPLES OF THE PROCEDURE**

The ARCHITECT HIV Ag/Ab Combo assay is a two-step immunoassay to determine the presence of HIV p24 antigen and antibodies to HIV-1 (Group M and Group O) and HIV-2 in human serum and plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex. In the first step, sample, assay diluent, and paramagnetic microparticles are combined. HIV p24 antigen and HIV-1/HIV-2 antibodies present in the sample bind to the HIV-1/HIV-2 antigen and HIV p24 monoclonal antibody coated microparticles. After washing, the HIV p24 antigen and HIV-1/HIV-2 antibodies bind to the acridinium-labeled conjugates (HIV-1/HIV-2 antibodies [recombinant], synthetic peptides, and HIV p24 antibody [mouse, monoclonal]). 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 HIV antigen and antibodies in the sample and the RLUs detected by the ARCHITECT System optics. The presence or absence of HIV p24 antigen or HIV-1/HIV-2 antibodies in the specimen is determined by comparing the chemiluminescent signal in the reaction to the cutoff signal determined from an ARCHITECT HIV Ag/Ab Combo calibration. Specimens with signal to cutoff (S/CO) values greater than or equal to 1.00 are considered reactive for HIV p24 antigen or HIV-1/HIV-2 antibodies. Specimens with S/CO values less than 1.00 are considered nonreactive for HIV p24 antigen or HIV-1/HIV-2 antibodies.

**NAME**

ARCHITECT HIV Ag/Ab Combo Reagent Kit (4J27)

**MICROPARTICLES**

1 or 4 Bottle(s) (6.6 mL per 100 test bottle/27.0 mL per 500 test bottle) Microparticles: HIV-1/HIV-2 antigen (recombinant) and HIV p24 antibody (mouse, monoclonal) coated microparticles in TRIS buffered saline. Minimum concentration: 0.07% solids. Preservative: Sodium Azide.

**CONJUGATE**

1 or 4 Bottle(s) (5.9 mL per 100 test bottle/26.3 mL per 500 test bottle) Conjugate: Acridinium-labeled HIV-1 antigens (recombinant), acridinium-labeled HIV-1/HIV-2 synthetic peptides, and acridinium-labeled HIV p24 antibody (mouse, monoclonal) conjugates in phosphate buffer with protein (bovine) and surfactant stabilizers. Minimum concentration: 0.05 μg/mL. Preservative: Sodium Azide.

**ASSAY DILUENT**

1 or 4 Bottle(s) (5.9 mL per 100 test bottle/26.3 mL per 500 test bottle) Assay Diluent: HIV Ag/Ab Combo assay diluent containing TRIS buffer. Preservative: Sodium Azide.

**OTHER REAGENTS**

**NAME**

ARCHITECT / Pre-Trigger Solution

**PRE TRIGGER SOLUTION**

Pre-Trigger Solution containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT / Trigger Solution

**TRIGGER SOLUTION**

Trigger Solution containing 0.35 N sodium hydroxide.

ARCHITECT / Wash Buffer

**WASH BUFFER**

WARNINGS AND PRECAUTIONS

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.
- This product contains sodium azide; for a specific listing, refer to the REAGENTS section. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- For product not classified as dangerous per European Directive 1999/45/EC as amended - Safety data sheet available for professional user on request.
- For information on the safe disposal of sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 6.

Handling Precautions

- Do not use reagent kits beyond the expiration date.
- Do not pool reagents within a kit or between reagent kits.
- Prior to loading the ARCHITECT HIV Ag/Ab Combo Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that 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.
- 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, which 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

- 2°C to 8°C: The ARCHITECT HIV Ag/Ab Combo Reagent Kit must be stored at 2-8°C and may be used immediately after removal from 2-8°C storage. The reagent kit must be stored in an upright position.
- The ARCHITECT HIV Ag/Ab Combo 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.
- When stored and handled as directed, reagents are stable until the expiration date.
- 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 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. After reagents are removed from the system, a reagent scan must be initiated 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 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 HIV Ag/Ab Combo 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 on viewing and editing assay parameters, refer to the ARCHITECT Systems 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

Verified Specimen Types

- Human serum (including serum collected in serum separator tubes)
- Plasma collected in:
  - potassium EDTA
  - sodium heparin
  - lithium heparin
  - plasma separator tubes
- The ARCHITECT i System 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 ARCHITECT HIV Ag/Ab Combo assay.

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed (> 500 mg/dL)
  - obvious microbial contamination
  - cadaver specimens or any other body fluids
- Ensure complete clot formation in serum specimens before centrifugation. Some specimens, especially those from patients receiving anticoagulant or thrombolytic therapy, may exhibit increased clotting time.
- Specimens from heparinized patients may be partially coagulated and contain fibrin. Draw the specimen prior to heparin therapy.
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells or other particulate matter.
- Use caution when handling patient specimens to prevent cross contamination. Use of disposable pipettes or pipette tips is recommended.
- For optimal results, inspect all specimens for bubbles. Remove bubbles with an applicator stick prior to analysis. Use a new applicator stick for each specimen to prevent cross contamination.
- No qualitative performance differences were observed between experimental controls and more than 20 nonreactive or more than 20 spiked reactive specimens tested with elevated levels of bilirubin (20 mg/dL), triglycerides (3000 mg/dL), protein (4 - 12 g/dL), red blood cells (0.4% v/v), or hemoglobin (500 mg/dL).

Preparation for Analysis

- Specimens must be separated from clots or red blood cells using centrifugation as recommended by the tube manufacturer. Gravity separation is not sufficient for specimen preparation.
- To ensure consistency in results, specimens containing particulate matter or red blood cells, specimens that have been thawed, and specimens that require retesting must be transferred to a centrifuge tube and centrifuged at ≥ 10,000 RCF (Relative Centrifugal Force) for 10 minutes prior to testing.
- Mix thawed specimens by inverting 10 times. Visually inspect the specimens for the absence of stratification. If layering or stratification is observed repeat inversion cycles until specimens are visibly homogeneous. Centrifuge prior to testing.
- 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.
Storage
- Specimens may be stored on or off the clot or red blood cells for up to 14 days refrigerated at 2-8°C. If testing will be delayed more than 14 days, remove serum or plasma from the clot, separator, or red blood cells and store frozen at -20°C or colder.
- No qualitative performance differences were observed between experimental controls and 25 nonreactive or 25 spiked reactive specimens subjected to 6 freeze/thaw cycles; however, multiple freeze/thaw cycles should be avoided.

Shipping
- Before shipping specimens, it is recommended that specimens be removed from the clot, separator, or red blood cells.
- When shipped, specimens must be packaged and labeled in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.
- Specimens may be shipped at 2-8°C (wet ice), or at -20°C or colder (dry ice). Do not exceed the 14-day storage time for specimens shipped at 2-8°C (wet ice).
- Specimens may be stored on or off the clot or red blood cells for up to 14 days refrigerated at 2-8°C.
- If testing will be delayed more than 14 days, remove serum or plasma from the clot, separator, or red blood cells and store frozen at -20°C or colder.
- No qualitative performance differences were observed between experimental controls and 25 nonreactive or 25 spiked reactive specimens subjected to 6 freeze/thaw cycles; however, multiple freeze/thaw cycles should be avoided.

PROCEDURE
Materials Provided:
- 4J27 ARCHITECT HIV Ag/Ab Combo Reagent Kit

Materials Required but not Provided:
- ARCHITECT / System
- ARCHITECT / ASSAY CD-ROM
- 4J27-01 ARCHITECT HIV Ag/Ab Combo Calibrator
- 4J27-10 ARCHITECT HIV Ag/Ab Combo 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 5.

Assay Procedure
- Before loading the ARCHITECT HIV Ag/Ab Combo Reagent Kit on the system for the first time, the microparticle bottle requires mixing to resuspend microparticles that have settled during shipment:
  - Invert the microparticle bottle 30 times.
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain adhered to the bottle, continue inverting the bottle until the microparticles have been completely resuspended.
  - **If the microparticles do not resuspend, DO NOT USE.**
- 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.
- 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 general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
  - **Load the ARCHITECT HIV Ag/Ab Combo Reagent Kit on the ARCHITECT System.**
  - Verify that all necessary reagents are present. Ensure that septums are present on all reagent bottles.
  - **The minimum sample cup volume is calculated by the system and is printed on the Orderlist report. No more than 10 replicates may be sampled from the same sample cup. To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.**
  - Priority: 150 μL for the first ARCHITECT HIV Ag/Ab Combo test plus 100 μL for each additional HIV Ag/Ab Combo test from the same sample cup.
  - ≤ 3 hours on board: 150 μL for the first ARCHITECT HIV Ag/Ab Combo test plus 100 μL for each additional ARCHITECT HIV Ag/Ab Combo test from the same sample cup.
  - > 3 hours on board: additional sample volume is required. 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 sample volume is present.
  - Prepare calibrator and controls.
    - ARCHITECT HIV Ag/Ab Combo Calibrator 1 and Controls should be mixed by gentle inversion prior to use.
    - To obtain the recommended volume requirements for the ARCHITECT HIV Ag/Ab Combo Calibrator 1 and Controls, hold the bottles vertically and dispense 20 drops of calibrator or 10 drops of each control into each respective sample cup.
  - Load samples.
    - For information on loading samples, refer to the ARCHITECT System Operations Manual, Section 5.
    - Press RUN.
  - For optimal performance, it is important to follow the routine maintenance procedures defined in the ARCHITECT System Operations Manual, Section 9.

Specimen Dilution Procedures
Specimens cannot be diluted for the ARCHITECT HIV Ag/Ab Combo assay.

Calibration
- **To perform an ARCHITECT HIV Ag/Ab Combo calibration, test Calibrator 1 in replicates of three. Calibrator 1 should be priority loaded. A single sample of each ARCHITECT HIV Ag/Ab Combo Control must be tested to evaluate the assay calibration. Ensure that assay control values are within the S/CO ranges specified in the control package insert.**
- Once an ARCHITECT HIV Ag/Ab Combo calibration is accepted and stored, all subsequent samples may be tested without further calibration unless one or both of the following occur:
  - 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
The recommended control requirement for the ARCHITECT HIV Ag/Ab Combo assay is that a single sample of each control 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 HIV Ag/Ab Combo 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 must be retested. Recalibration may be indicated.

It is recommended that each laboratory establish a control range for the ARCHITECT HIV Ag/Ab Combo Positive Control 1 when a new lot of ARCHITECT HIV Ag/Ab Combo reagents is used.

Verification of Assay Claims
For protocols to verify package insert claims, refer to the ARCHITECT System Operations Manual, Appendix B. The ARCHITECT HIV Ag/Ab Combo assay belongs to method group 5.
RESULTS

The ARCHITECT System calculates the cutoff (CO) using the mean chemiluminescent signal (RLU) from three replicates of the Calibrator 1 and stores the result.

Calculation

The ARCHITECT System calculates for the ARCHITECT HIV Ag/Ab Combo assay a result based on the ratio of the sample RLU(s) to the cutoff RLU for each specimen and control:

- Cutoff (CO) = Calibrator 1 mean RLU Value x 0.40
- S/CO = Sample RLU/Cutoff RLU
- The cutoff RLU is stored for each reagent lot calibration.

Interpretation of Results

- Specimens with S/CO values < 1.00 are considered nonreactive (NR).
- Specimens with S/CO values ≥ 1.00 are considered reactive (R).

NOTE: All specimens that are initially reactive must be centrifuged and retested in duplicate. Refer to the SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS section in this package insert.

ARCHITECT HIV Ag/Ab Combo Results

<table>
<thead>
<tr>
<th>Initial Results (S/CO)</th>
<th>Retest Results</th>
<th>Final Result</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>Both tests are NR</td>
<td>NR</td>
<td>HIV p24 Ag and/or HIV-1/HIV-2 Ab not detected</td>
</tr>
<tr>
<td>R</td>
<td>One or both tests are reactive</td>
<td>R</td>
<td>Presumptive evidence of HIV p24 Ag and/or HIV-1/HIV-2 Ab; perform a supplemental assay</td>
</tr>
<tr>
<td>NR</td>
<td>No retest required</td>
<td>NR</td>
<td>HIV p24 Ag and/or HIV-1/HIV-2 Ab not detected</td>
</tr>
</tbody>
</table>

- The Interpretation of Results for specimens with a final result of reactive by the ARCHITECT HIV Ag/Ab Combo assay and indeterminate by supplemental testing is unclear; further clarification may be obtained by testing another specimen taken three to six weeks later.
- ARCHITECT HIV Ag/Ab Combo and supplemental assay results should be interpreted in conjunction with the patient’s clinical presentation, history, and other laboratory results.

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

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 PROEDURE

- If the assay results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- 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 that employ mouse monoclonal antibodies.\(^\text{**}\) ARCHITECT HIV Ag/Ab Combo reagents contain a component that reduces the effect of HAMA reactive specimens. Additional clinical or diagnostic information may be required to determine patient status.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with in vitro immunoassays.\(^\text{***}\) 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.

SPECIFIC PERFORMANCE CHARACTERISTICS

Precision

The ARCHITECT HIV Ag/Ab Combo demonstrated an imprecision of ≤ 14% for samples that were three times the cutoff value in a study where three calibrator lots, three control lots, and a panel consisting of four reactive samples were tested. The study was performed at four external sites (France, Italy, Switzerland, Germany) each using one instrument and one internal site using two instruments. Panel members were tested in replicates of three across two reagent lots at the external site and across three reagent lots at the internal site. Each combination of instruments, panel members, and reagent lots was tested in four runs, with the exception of one reagent lot at the internal site that was tested in six runs on one instrument. The intra-run and inter-run standard deviation (SD) and percent coefficient of variation (%CV) were analyzed with a variance components analysis\(^\text{**}\) using a mixed analysis of variance model.\(^\text{**}\) The data from the study are summarized in Table 1.*

<table>
<thead>
<tr>
<th>Panel</th>
<th>Intra-assay</th>
<th>Inter-assay</th>
</tr>
</thead>
<tbody>
<tr>
<td>Member (units)</td>
<td>n</td>
<td>Mean</td>
</tr>
<tr>
<td>Calibrator 1 (RLUs)</td>
<td>432</td>
<td>5629</td>
</tr>
<tr>
<td>NC(^\text{**}) (S/CO)</td>
<td>1224</td>
<td>0.09</td>
</tr>
<tr>
<td>PC(^\text{**}) 1 (S/CO)</td>
<td>1224</td>
<td>3.96</td>
</tr>
<tr>
<td>PC(^\text{**}) 2 (S/CO)</td>
<td>1224</td>
<td>3.57</td>
</tr>
<tr>
<td>PC(^\text{**}) 3 (S/CO)</td>
<td>1224</td>
<td>3.19</td>
</tr>
<tr>
<td>PM(^\text{**}) 1 (S/CO)</td>
<td>432</td>
<td>2.57</td>
</tr>
<tr>
<td>PM(^\text{**}) 2 (S/CO)</td>
<td>432</td>
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</tr>
<tr>
<td>PM(^\text{**}) 3 (S/CO)</td>
<td>432</td>
<td>2.36</td>
</tr>
<tr>
<td>PM(^\text{**}) 4 (S/CO)</td>
<td>432</td>
<td>1.44</td>
</tr>
</tbody>
</table>

- Inter-assay variability contains intra-assay variability.
- Negative Control
- Positive Control
- Panel Member
- Representative performance data are shown. Results obtained at individual laboratories may vary.

Specificity

The ARCHITECT HIV Ag/Ab Combo assay demonstrated a specificity of ≥ 99.5% in a study where specimens from a blood donor population with an assumed HIV infection prevalence of zero were tested. The testing was performed at two external sites and one internal site on a total of 6365 serum and plasma specimens collected from four blood-donation centers. Data from this study are summarized in Table 2.*

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Initially Reactive</th>
<th>Repeat Reactive</th>
<th>Specificity (%)</th>
<th>Specificity 95% CI</th>
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<tbody>
<tr>
<td>Plasma</td>
<td>2747</td>
<td>3</td>
<td>3</td>
<td>99.89</td>
</tr>
<tr>
<td>Serum</td>
<td>3618</td>
<td>6</td>
<td>4</td>
<td>99.89</td>
</tr>
<tr>
<td>Total</td>
<td>6365</td>
<td>9</td>
<td>7</td>
<td>99.89</td>
</tr>
</tbody>
</table>

- Specificity \(95\% \text{ CI}\)
- Representative performance data are shown. Results obtained at individual laboratories may vary.

Specimens from randomly selected hospitalized patients and specimens containing potentially interfering substances, which includes those from individuals with medical conditions unrelated to HIV infection, were tested at four different sites with the ARCHITECT HIV Ag/Ab Combo assay. Of the 2870 hospitalized patient specimens (HP) and the 322 specimens containing potentially interfering substances (IS), 29 HP and 12 IS specimens were confirmed as having HIV infection by confirmation testing. These specimens were excluded from the study. The data from the remaining 2841 HP specimens and the 310 IS specimens are summarized in Table 3.*
and precharacterized for HIV antigen and antibodies. Table 5 shows data from 31 seroconversion panels. These panels are commercially available.

<table>
<thead>
<tr>
<th>Panel</th>
<th>BBI</th>
<th>PRB959</th>
<th>7</th>
</tr>
</thead>
<tbody>
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<td>10</td>
<td>192.13</td>
<td>11</td>
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<td></td>
<td>16</td>
<td>75.41</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>26</td>
<td>66.46</td>
<td>21</td>
</tr>
</tbody>
</table>

These panels were used to test the sensitivity and specificity of the ARCHITECT HIV Ag/Ab Combo assay. Results obtained at individual laboratories may vary.

Sensitivity

The ARCHITECT HIV Ag/Ab Combo assay demonstrated the sensitivity values provided in Table 4. These values were determined in a study where specimens from individuals clinically diagnosed with HIV infection and classified disease status were tested.

Table 4

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Total n</th>
<th>Reactive</th>
<th>Sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HIV-1</td>
<td>520</td>
<td>520</td>
<td>100.0</td>
</tr>
<tr>
<td>Anti-HIV-2</td>
<td>111</td>
<td>111</td>
<td>100.0</td>
</tr>
<tr>
<td>Anti-HIV-3</td>
<td>6</td>
<td>6</td>
<td>100.0</td>
</tr>
</tbody>
</table>

* An additional 29 diluted anti-HIV gO specimens were found to be reactive by the ARCHITECT HIV Ag/Ab Combo assay.

* Representative performance data are shown. Results obtained at individual laboratories may vary.

Sensitivity

One hundred specimens from patients at increased risk for HIV infection were tested by ARCHITECT HIV Ag/Ab Combo. Of these 100 specimens, 70 were repeat reactive by ARCHITECT HIV Ag/Ab Combo. Sixty-nine of these 70 repeat reactive specimens were positive by confirmation testing.

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Days Since 1st Bleed</th>
<th>Western Blot</th>
<th>HIV Ag A (S/CO)</th>
<th>PCR A (Copies/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-HIV-1</td>
<td>0</td>
<td>Neg b</td>
<td>2.3</td>
<td>80,000</td>
</tr>
<tr>
<td>Anti-HIV-2</td>
<td>7</td>
<td>Neg</td>
<td>4.05</td>
<td>500,000</td>
</tr>
<tr>
<td>Anti-HIV-3</td>
<td>14</td>
<td>Neg</td>
<td>4.05</td>
<td>500,000</td>
</tr>
</tbody>
</table>

a The IS specimens belonged to the following categories: Viral infection (HBV, HSV, CMV, Rubella, HAV, HCV, EBV, HTLV-I, HTLV-II); fungal/yeast/protozoal/bacterial infection (C. albicans, T. pallidum, T. gondii, E. coli, C. trachomatis, N. gonorrhea); autoimmune (rheumatoid factor [RF], antinuclear antibodies [ANA]); other conditions (pregnant females all trimesters, multiparous females, elevated IgG, elevated IgM, monoclonal gammopathy, flu vaccine recipients, HAMA, hemodialysis patients, hemophiliacs, multiple transfusion recipients).

* Representative performance data are shown. Results obtained at individual laboratories may vary.

**BIBLIOGRAPHY**


46. Major glycoprotein antigens that induce antibodies in AIDS patients are encoded by HTLV-III. Science 1985;228:1094-6.


The following US Patents are relevant to the ARCHITECT i System or its components. There are other such patents and patent application 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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