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 human immunodeficiency virus (HIV) p24 antigen and antibodies to HIV type 1 (HIV-1 group M and group O) and/or type 2 (HIV-2) in human serum and plasma (EDTA and heparin). The ARCHITECT HIV Ag/Ab Combo assay is intended to be used as an aid in the diagnosis of HIV-1/HIV-2 infection, including acute or primary HIV-1 infection. The assay may also be used as an aid in the diagnosis of HIV-1/HIV-2 infection in pediatric subjects (*i.e.*, children as young as two years of age) and in pregnant women.

An ARCHITECT HIV Ag/Ab Combo reactive result does not distinguish between the detection of HIV-1 p24 antigen, HIV-1 antibody, or HIV-2 antibody.

The ARCHITECT HIV Ag/Ab Combo assay is not intended for use in screening blood or plasma donors. The effectiveness of ARCHITECT HIV Ag/Ab Combo for use in screening blood or plasma donors has not been established. However, this assay can be used as a blood donor screening assay in urgent situations where traditional licensed blood donor screening tests are unavailable or their use is impractical.

SUMMARY AND EXPLANATION OF TEST

Acquired immunodeficiency syndrome (AIDS) is caused by two types of human immunodeficiency viruses, collectively designated HIV.[1-4] HIV is transmitted by sexual contact, exposure to blood or blood products, and prenatal or perinatal infection of a fetus or newborn.[5] Antibodies against HIV are nearly always detected in AIDS patients and HIV-infected asymptomatic individuals.[5,6]

Phylogenetic analysis classifies HIV type 1 (HIV-1) into groups M (major), N (non-M, non-O), O (outlier), and P.[7-10] HIV-1 group M is composed of genetic subtypes (A-D, F-H, J, and K) and circulating recombinant forms (CRFs).[8,11] Group M viruses have spread throughout the world to cause the global AIDS pandemic. However, the geographic distribution and regional predominance of HIV-1 subtypes and CRFs vary.[12] HIV-1 subtype B is the predominant subtype in North America, South America, Europe, Japan, and Australia, although other subtypes and CRFs are present in these regions as well.[12] A significant percentage of new HIV-1 infections in Europe are caused by non-B subtype strains.[13,14] All subtypes and many recombinant strains exist in Africa.[12] In Asia, subtypes B and C, and CRF01_AE (formerly called subtype E) are found.[12] HIV-1 groups N, O, and P are endemic to west central Africa and are relatively rare. [7,9,10,15,16] However, group O infections have been identified in Europe and the USA.[14,17,18]

HIV 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.[4] HIV-2 is endemic to West Africa, but HIV-2 infections have been identified in North America and Europe at a low frequency compared to HIV-1.[14,19-21]

Early after infection with HIV-1, but prior to seroconversion, HIV-1 core protein, p24 antigen, may be detected in HIV-1-infected individuals.[22] ARCHITECT HIV Ag/Ab Combo uses anti-HIV-1 p24 antibodies as reagents to detect HIV-1 p24 antigen, thereby decreasing the window period and improving early detection of HIV infection.

The key immunogenic protein for serodetection of HIV infection is the viral transmembrane protein (TMP). Antibodies against the TMP are consistently among the first to appear during

seroconversion of HIV-infected individuals and remain relatively strong throughout the asymptomatic and symptomatic stages of HIV infection.[6,23,24] ARCHITECT HIV Ag/Ab Combo detects antibodies to HIV-1 groups M and O, and HIV-2 through the use of five recombinant proteins and two synthetic peptides derived from native TMP sequences of HIV-1 groups M and O, and HIV-2.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ARCHITECT HIV Ag/Ab Combo assay for use on the ARCHITECT *i* System is a two-step immunoassay to determine the presence of HIV-1 p24 antigen, antibodies to HIV-1 (group M and group O), and antibodies to HIV-2 in human serum or plasma using CMIA technology with flexible assay protocols, referred to as Chemiflex.

In the first step, sample, ARCHITECT *i* Wash Buffer, assay diluent, and paramagnetic microparticles are combined. HIV-1 p24 antigen and HIV-1/HIV-2 antibodies present in the sample bind to the HIV-1/HIV-2 antigen and HIV-1 p24 monoclonal (mouse) antibody coated microparticles. After washing, the bound HIV-1 p24 antigen and HIV-1/HIV-2 antibodies bind to the acridinium-labeled conjugates. 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 (RLU). A relationship exists between the amount of HIV antigen and antibodies in the sample and the RLU detected by the ARCHITECT *i* System optics. The presence or absence of HIV-1 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-1 p24 antigen or HIV-1/HIV-2 antibodies. Specimens with S/CO values less than 1.00 are considered nonreactive for HIV-1 p24 antigen and 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-1 p24 antigen and/or HIV-1/HIV-2 antibodies. However, as with all immunoassays, 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 supplemental confirmatory HIV-specific tests, such as immunoblots, antigen tests, and HIV nucleic acid tests. Supplemental testing of repeatedly reactive specimens obtained from individuals with HIV infection usually confirms the presence of HIV antibodies, HIV antigen, or 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

Reagent Kit, 100/500 Tests

Note: Reagent kit configuration varies based on order. Some kit sizes are not available for use on all ARCHITECT *i* Systems. Please contact your local distributor.

ARCHITECT HIV Ag/Ab Combo Reagent Kit (2P36)

- MICROPARTICLES 1 Bottle (6.6 mL/27.0 mL) HIV-1/HIV-2 antigen and HIV p24 antibody (mouse IgG, monoclonal) coated microparticles in TRIS buffered saline. Minimum activity with PC1: 1.20 S/CO; minimum activity with PC2: 1.52 S/CO; minimum activity with PC3: 1.87; S/CO; minimum activity with PC4: 1.23 S/CO. Preservative: sodium azide.

- CONJUGATE 1 Bottle (5.9 mL/26.3 mL) Acridinium-labeled HIV-1 antigens, acridinium-labeled HIV-1/HIV-2 synthetic peptides, and acridinium-labeled HIV p24 antibody (mouse IgG, monoclonal) conjugates in phosphate buffer with protein (bovine serum albumin) additive and surfactant. Minimum concentration: 61.518 ng/mL. Preservative: sodium azide.
- ASSAY DILUENT 1 Bottle (5.9 mL/26.3 mL) HIV Ag/Ab Combo assay diluent containing TRIS buffer with protein (mouse serum and IgG) additive and surfactant. Preservative: sodium azide.

Required Common ARCHITECT *i* System Reagents

ARCHITECT *i* Pre-Trigger Solution

- PRE-TRIGGER SOLUTION containing 1.32% (w/v) hydrogen peroxide.

ARCHITECT *i* Trigger Solution

- TRIGGER SOLUTION containing 0.35N sodium hydroxide.

ARCHITECT *i* Wash Buffer

- WASH BUFFER containing phosphate buffered saline solution. Preservatives: sodium azide and antimicrobial agent.

PRECAUTIONS

Safety Precautions

- **CAUTION: This product requires the handling of human specimens. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens.[25] Biosafety Level 2[26] or other appropriate biosafety practices[27,28] should be used for materials that contain or are suspected of containing infectious agents.**
- 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 information on the safe disposal of reagents containing sodium azide and a detailed discussion of safety precautions during system operation, refer to the ARCHITECT System Operations Manual, Section 8.

Handling Precautions

- Do not use reagents beyond the expiration date.
- **Do not pool reagents within a Reagent Kit or between Reagent Kits.**
- Before loading the ARCHITECT HIV Ag/Ab Combo Reagent Kit on the system for the first time, the MICROPARTICLES 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.**
  - Once a septum has been placed on the 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 HIV Ag/Ab Combo Reagent Kit 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, the reagents are stable until the expiration date.
- 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.
- 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 MICROPARTICLES 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 HIV Ag/Ab Combo assay file must be installed on the ARCHITECT *i* System from an ARCHITECT *i* System assay CD-ROM before 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

Specimen Types

- The following specimen tube types may be used with the ARCHITECT HIV Ag/Ab Combo assay:

Glass	Plastic
• Serum • Tripotassium (K_3) EDTA • Disodium (Na_2) EDTA	• Serum • Serum separator • Lithium heparin with gel separator • Sodium heparin • Dipotassium (K_2) EDTA • Dipotassium (K_2) EDTA with gel separator

- Although heparin tube types will demonstrate higher S/CO values than other tube types for specimens containing HIV antibody, there is no change to the interpretation of results.

Specimens that do not contain HIV antibody do not demonstrate higher S/CO values in heparin tube types.
- For blood screening in urgent situations, do not use samples collected directly from whole blood bags as they contain anticoagulants other than EDTA and heparin.
- Liquid anticoagulants may have a dilution effect resulting in lower S/CO values for individual patient specimens.
- 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
  - 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 accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter.** Serum specimens from patients receiving anticoagulant or thrombolytic therapy may contain fibrin due to incomplete clot formation.
- 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 before analysis. Use a new applicator stick for each specimen to prevent cross contamination.

Preparation for Analysis
- Follow the tube manufacturer's processing instructions for serum and plasma collection tubes. Gravity separation is not sufficient for specimen preparation.
- Prepare frozen specimens as follows:
  - Frozen specimens must be **completely** thawed before mixing.
  - Mix thawed specimens **thoroughly** by inverting 10 times or by low speed vortexing. Visually inspect the specimens. If layering or stratification is observed, continue mixing until specimens are visibly homogeneous. **If samples are not mixed thoroughly, inconsistent results may be obtained.**
  - Centrifuge mixed specimens as described below.
- To ensure consistency in results, specimens must be transferred to a centrifuge tube and centrifuged at > 10,000 RCF (Relative Centrifugal Force) for 10 minutes before testing if they
  - are initially reactive and require retesting in duplicate,
  - contain fibrin, red blood cells, or other particulate matter, or
  - were frozen and thawed.
- 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.
- Transfer clarified specimen to a sample cup or secondary tube for testing.
- **Specimens should not be diluted for the ARCHITECT HIV Ag/Ab Combo assay.**

Storage

- Serum or plasma specimens should be stored for no longer than 3 days at room temperature or 7 days at 2 to 8°C following specimen collection. If a storage period greater than 7 days is anticipated, the specimens should be removed from the clot, red blood cells, or separator gel, and the serum or plasma should be stored frozen at –20°C or colder.
- No more than 5 freeze-thaw cycles should be performed on any sample prior to testing.

Shipping

- Before shipping specimens, it is recommended that specimens be removed from the clot, red blood cells, or separator gel.
- When shipping specimens, package and label specimens 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 frozen (dry ice). Do not exceed the storage time limitations listed above.

PROCEDURE

Materials Provided:

- 2P36 ARCHITECT HIV Ag/Ab Combo Reagent Kit

Materials Required but not Provided:

- ARCHITECT *i* System
- 6E58 ARCHITECT *i* System Assay CD-ROM (for *i* 2000_{SR} and *i* 2000)
- 1P60 ARCHITECT *i* 1000_{SR} System Assay CD-ROM
- 2P36-01 ARCHITECT HIV Ag/Ab Combo Calibrator
- 2P36-10 ARCHITECT HIV Ag/Ab Combo Controls (or other control material)
- 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 specified volumes.

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

Assay Procedure

- Before loading the ARCHITECT HIV Ag/Ab Combo Reagent Kit on the system for the first time, the MICROPARTICLES bottle requires mixing to resuspend microparticles that may have settled during shipment. After the first time the microparticles have been loaded, no further mixing is required.
  - **Invert the MICROPARTICLES bottle 30 times.**
  - Visually inspect the bottle to ensure microparticles are resuspended. If microparticles remain 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 about placing septums on bottles, refer to the **Handling Precautions** section of this package insert.
- Load the ARCHITECT HIV Ag/Ab Combo Reagent Kit on the ARCHITECT *i* System.
  - 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 patient specimens and controls.
  - For information on ordering patient specimens and controls and for general operating procedures, refer to the ARCHITECT System Operations Manual, Section 5.
- 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 before running the test.
  - Priority: 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: 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: replace with a fresh sample (patient specimens, controls, and calibrator).**
  - If using primary or aliquot tubes, use the sample gauge to ensure sufficient patient specimen is present.
- Prepare calibrator and controls.
  - Mix ARCHITECT HIV Ag/Ab Combo Calibrator 1 and Controls by gentle inversion before use.
  - To obtain the recommended volume requirements for the ARCHITECT HIV Ag/Ab Combo Calibrator 1 (350 µL for 3 replicates) and Controls (150 µL for 1 replicate), 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 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. When a laboratory requires more frequent maintenance, follow those procedures.

Calibration

- To perform an ARCHITECT HIV Ag/Ab Combo calibration, test Calibrator 1 in replicates of three. The calibrator should be priority loaded.
- A single sample of each control level must be tested to evaluate the assay calibration.
  - Order controls as described in the **Assay Procedure** section.

  - Ensure that assay control values are within the ranges specified in the Controls package insert.
- Once an ARCHITECT HIV Ag/Ab Combo 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.

QUALITY CONTROL PROCEDURES

The recommended control requirement for the ARCHITECT HIV Ag/Ab Combo assay is that a single sample of a negative control and of four positive controls (anti-HIV-1, anti-HIV-2, HIV-1 antigen, and anti-HIV-1 group O) be tested once every 24 hours each day of use. Additional controls may be tested in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy.

Control values must be within the S/CO ranges specified in the Controls package insert. If a control result is out of its specified range, any test results generated since the last acceptable control results must be evaluated to determine if test results may have been adversely affected.[29,30] Adversely affected test results are invalid, and these samples must be retested. To troubleshoot control values that fall outside the control range, refer to the ARCHITECT System Operations Manual, Section 10.

When used as a blood donor screening test in urgent situations, controls should be run with the specimens.

RESULTS

Calculations

- The ARCHITECT *i* System calculates the cutoff RLU from the mean RLU of the three Calibrator 1 replicates and stores the result. The cutoff RLU is determined by multiplying the Calibrator 1 Mean RLU by 0.40.

  Cutoff RLU = Calibrator 1 Mean RLU x 0.40
- The ARCHITECT *i* System calculates a result based on the ratio of sample RLU to the cutoff RLU (S/CO) for each specimen and control.

  S/CO = Sample RLU/Cutoff RLU

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

ARCHITECT HIV Ag/Ab Combo Initial Result		
Initial Result (S/CO)	**Instrument Interpretation**	**Retest Procedure**
< 1.00	NONREACTIVE (NR)	No retest required.
≥ 1.00	REACTIVE (R)	Retest in duplicate.

- 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 Final Interpretation			
Initial Result (S/CO)	**Retest Results (S/CO)**	**Final Result**	**Interpretation of Final Result**
NR (< 1.00)	No retest required (NA)	NR	HIV-1 p24 Ag and HIV-1/HIV-2 Ab not detected
R (≥ 1.00)	Both tests are NR (< 1.00)	NR	HIV-1 p24 Ag and/or HIV-1/HIV-2 Ab not detected
R (≥ 1.00)	One or both tests are R (≥ 1.00)	R	Presumptive evidence of HIV-1 p24 Ag and/or HIV-1/HIV-2 Ab; perform supplemental confirmatory assay(s)

A specimen with a final result of reactive should be investigated further with supplemental confirmatory HIV-specific tests, such as immunoblots, antigen tests, and HIV nucleic acid tests.

LIMITATIONS OF THE PROCEDURE

- The interpretation of specimens with a final result of reactive by the ARCHITECT HIV Ag/Ab Combo assay and indeterminate by supplemental testing is not definitive; further clarification may be obtained by testing another specimen taken at least 1 month later.[31]
- The ARCHITECT HIV Ag/Ab Combo assay result and supplemental assay results should be interpreted in conjunction with the patient's clinical presentation, history, and other laboratory results. If the results are inconsistent with clinical evidence, additional testing is suggested to confirm the result.
- An individual who has antibodies to HIV is presumed to be infected with the virus; however, an individual who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV. Clinical correlation is indicated with appropriate counseling, medical evaluation, and possibly additional testing to determine whether a diagnosis of HIV infection is accurate.
- A test result that is nonreactive does not exclude the possibility of exposure to or infection with HIV-1 and/or HIV-2. Nonreactive results in this assay for individuals with prior exposure to HIV-1 and/or HIV-2 may be due to antigen and antibody levels that are below the limit of detection of this assay.
- The performance of this assay has not been established for individuals younger than 2 years of age. Nearly all infants born to HIV-infected mothers passively acquire maternal antibody and, in some cases, will test antibody positive until age 18 months regardless of whether they are

infected. Definitive diagnosis of HIV infection in early infancy requires other assays, including HIV nucleic acid tests or viral culture.[32]

- Specimens from patients who have received preparations of mouse monoclonal antibodies for diagnosis or therapy may contain human anti-mouse antibodies (HAMA).[33,34] Such specimens may show either falsely elevated or depressed results when tested with assay kits (such as ARCHITECT HIV Ag/Ab Combo) that employ mouse monoclonal antibodies.[33] ARCHITECT HIV Ag/Ab Combo reagents contain a component that reduces the effect of HAMA reactive specimens.
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays.[35] Patients routinely exposed to animals or to animal serum products can be prone to this interference and anomalous results may be observed. Additional information may be required for diagnosis.
- Refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert for specimen limitations.

SPECIFIC PERFORMANCE CHARACTERISTICS

Assay results obtained in individual laboratories may vary from data presented.

Precision

The ARCHITECT HIV Ag/Ab Combo assay is designed to have a Within-Laboratory (Total) CV of ≤ 10% for positive controls and for reactive samples with S/CO ≤ 4, and a Within-Laboratory (Total) CV of ≤ 15% for samples with S/CO >4.

System Reproducibility

A five-day precision study was performed for the ARCHITECT HIV Ag/Ab Combo assay based on guidance from the Clinical and Laboratory Standards Institute (CLSI) document EP15-A2.[36] Testing was conducted at three clinical sites using three lots each of ARCHITECT HIV Ag/Ab Combo Reagent Kit, Calibrator, and Controls per site. Each panel member and control was assayed in replicates of four at two separate times of day (n = 360). The system reproducibility results obtained on three ARCHITECT *i* 2000_{SR} instruments (one at each clinical site) are presented in Table 1.

Table 1: ARCHITECT HIV Ag/Ab Combo Assay System Reproducibility

Panel	Grand Mean S/CO	Within-Run		Between-Run		Between-Day		Within-Laboratory (Total) [a]		Between-Site		Between-Lot		Overall [b]	
		SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
HIV-1 Ab Group M Low Positive	2.61	0.089	3.4	0.066	2.5	0.050	1.9	0.122	4.7	0.086	3.3	0.168	6.5	0.220	8.4
HIV-1 Ab Group M High Positive	8.98	0.345	3.8	0.218	2.4	0.000	0.0	0.408	4.5	0.300	3.3	0.289	3.2	0.525	5.8
HIV-2 Ab Low Positive	2.53	0.089	3.5	0.075	3.0	0.000	0.0	0.117	4.6	0.106	4.2	0.392	15.5	0.420	16.6
HIV-2 Ab High Positive	8.34	0.267	3.2	0.209	2.5	0.000	0.0	0.339	4.1	0.269	3.2	1.317	15.8	1.366	16.4
HIV Ag Low Positive	2.73	0.101	3.7	0.041	1.5	0.000	0.0	0.109	4.0	0.084	3.1	0.121	4.4	0.175	6.4
HIV Ag High Positive	9.21	0.294	3.2	0.000	0.0	0.034	0.4	0.296	3.2	0.236	2.6	0.419	4.5	0.515	5.6
HIV-1 Ab Group O Positive	2.94	0.106	3.6	0.049	1.7	0.000	0.0	0.117	4.0	0.116	3.9	0.101	3.4	0.183	6.2
Negative Panel Member	0.08	0.020	NA	0.002	NA	0.000	NA	0.020	NA	0.016	NA	0.007	NA	0.026	NA
Negative Control	0.09	0.019	NA	0.009	NA	0.000	NA	0.021	NA	0.017	NA	0.007	NA	0.027	NA
Positive Control 1	4.28	0.151	3.5	0.081	1.9	0.000	0.0	0.171	4.0	0.165	3.9	0.101	2.4	0.241	5.6
Positive Control 2	3.63	0.115	3.2	0.087	2.4	0.026	0.7	0.146	4.0	0.169	4.7	0.530	14.6	0.571	15.7
Positive Control 3	3.07	0.111	3.6	0.069	2.3	0.037	1.2	0.136	4.4	0.048	1.6	0.100	3.3	0.171	5.6
Positive Control 4	2.24	0.068	3.0	0.043	1.9	0.007	0.3	0.081	3.6	0.095	4.2	0.244	10.9	0.270	12.1

NA = not applicable

[a] Within-Laboratory (Total) variability contains the within-run, between-run, and between-day variance components.

[b] Overall contains the within-run, between-run, between-day, between-lot, between-site and lot-site interaction variance components.

Within-Laboratory Precision

A 20-day precision study was performed for the ARCHITECT HIV Ag/Ab Combo assay based on guidance from the CLSI document EP5-A2.[37] Testing was conducted at Abbott Laboratories using three ARCHITECT HIV Ag/Ab Combo assay Reagent Kit lots, three Calibrator lots, one Controls lot, and three instruments (ARCHITECT *i* 2000_{SR}, ARCHITECT *i* 2000, and ARCHITECT *i* 1000_{SR}). Controls and panels were assayed in replicates of three (to obtain a minimum of two replicates) at two separate times of day for 20 different days. The within-laboratory precision is presented in Table 2.

Table 2: ARCHITECT HIV Ag/Ab Combo Assay Within-Laboratory Precision

	ARCHITECT *i* 2000_{SR}						ARCHITECT *i* 2000						ARCHITECT *i* 1000_{SR}					
			Within-Run		Within-Laboratory (Total) [a]				Within-Run		Within-Laboratory (Total) [a]				Within-Run		Within-Laboratory (Total) [a]	
Panel	n	Grand Mean S/CO	SD	% CV	SD	% CV	n	Grand Mean S/CO	SD	% CV	SD	% CV	n	Grand Mean S/CO	SD	% CV	SD	% CV
HIV-1 Ab Group M Low Positive	360	2.62	0.057	2.2	0.072	2.7	360	2.64	0.075	2.8	0.084	3.2	360	2.58	0.082	3.2	0.095	3.7
HIV-1 Ab Group M High Positive	359	8.99	0.196	2.2	0.289	3.2	360	8.97	0.249	2.8	0.264	2.9	360	9.21	0.273	3.0	0.363	3.9
HIV-2 Ab Low Positive	360	2.53	0.054	2.1	0.073	2.9	360	2.56	0.068	2.7	0.074	2.9	360	2.80	0.086	3.1	0.106	3.8
HIV-2 Ab High Positive	360	8.42	0.169	2.0	0.220	2.6	360	8.42	0.215	2.6	0.234	2.8	360	9.53	0.282	3.0	0.346	3.6
HIV Ag Low Positive	359	2.74	0.052	1.9	0.055	2.0	359	2.75	0.061	2.2	0.063	2.3	360	2.74	0.076	2.8	0.092	3.4
HIV Ag High Positive	360	9.28	0.159	1.7	0.176	1.9	360	9.26	0.175	1.9	0.187	2.0	360	9.28	0.244	2.6	0.310	3.3
HIV-1 Ab Group O Positive	360	2.95	0.072	2.4	0.097	3.3	360	2.95	0.078	2.7	0.087	2.9	360	2.96	0.102	3.4	0.115	3.9
Negative Panel Member	360	0.08	0.014	NA	0.015	NA	360	0.10	0.017	NA	0.019	NA	358	0.07	0.009	NA	0.009	NA
Negative Control [b]	360	0.09	0.019	NA	0.020	NA	359	0.10	0.019	NA	0.020	NA	358	0.08	0.010	NA	0.011	NA
Positive Control 1	360	4.21	0.090	2.1	0.130	3.1	360	4.16	0.139	3.3	0.149	3.6	359	4.34	0.149	3.4	0.171	3.9
Positive Control 2	360	3.56	0.073	2.1	0.106	3.0	360	3.55	0.116	3.3	0.121	3.4	360	4.14	0.120	2.9	0.155	3.7
Positive Control 3	360	3.11	0.104	3.3	0.110	3.5	359	3.10	0.149	4.8	0.155	5.0	359	3.10	0.106	3.4	0.109	3.5
Positive Control 4	360	2.23	0.046	2.0	0.058	2.6	360	2.20	0.075	3.4	0.082	3.7	360	2.60	0.085	3.3	0.097	3.7

NA = not applicable

[a] Within-laboratory (Total) variability contains the within-run, between-run, and between-day variance components.

[b] On the ARCHITECT *i* 2000, one replicate that had an S/CO value of 4.54 was excluded from the above analysis. When this replicate was included in the analysis, the mean S/CO was 0.11. The within-run SD was 0.235, and the within-laboratory (Total) SD was 0.235.

Clinical Performance

A multicenter study was conducted to establish the performance of the ARCHITECT HIV Ag/Ab Combo assay in the following populations: individuals at low risk for HIV, known HIV-1 antigen positive samples, known HIV-1 and HIV-2 antibody positive specimens, individuals at increased risk for HIV, pregnant females, and pediatric subjects. For specimens from the low and increased risk populations that were repeatedly reactive by ARCHITECT HIV Ag/Ab Combo and/or an FDA-licensed HIV-1/2/O Antibody assay, supplemental testing was performed using FDA-licensed HIV-1 Western blot, HIV-2 EIA, and HIV-1 RNA PCR tests and using research-use-only HIV-2 Western blot and HIV-1 p24 Antigen assays.

Specificity

A total of 6,164 prospectively collected specimens from a low risk for HIV population in the US (age range: 16 to 89 years) were tested by the ARCHITECT HIV Ag/Ab Combo and an FDA-licensed HIV-1/2/O Antibody assay. The low risk for HIV population includes individuals in a low prevalence setting,[38] apparently healthy individuals, and pregnant females in the first trimester of pregnancy.

The results for the 6,164 specimens from ARCHITECT HIV Ag/Ab Combo and the FDA-licensed HIV-1/2/O Antibody assays are presented in Table 3.

Table 3: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Individuals at Low Risk for Infection with HIV

Specimen Category	ARCHITECT HIV Ag/Ab Combo				Repeatedly Reactive Specimens (Number Positive by Method)		
	Number of Specimens Tested	Number of Nonreactive Specimens (%)	Number of Initially Reactive Specimens (%)	Number of Repeatedly Reactive Specimens (%)	HIV-1 Western Blot (%)	HIV-1 p24 Antigen (%)	HIV-1 RNA PCR (%)
Individuals in Low Prevalence Setting - Serum	2663	2652 (99.59)	13 (0.49)	11 (0.41)	9 (0.34)	0 (0.00)	0 (0.00)
Individuals in Low Prevalence Setting - Plasma	2671	2631 (98.50)	41 (1.54)	40 (1.50)	27 (1.01)	1 (0.04)	1 (0.04)
Individuals in Low Prevalence Setting - Fresh Plasma [a]	580	580 (100.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Low Risk Pregnant Females - Plasma	250	250 (100.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Total	**6164**	**6113 (99.17)**	**54 (0.88)**	**51 (0.83)**	**36 [b]**	**1 [b]**	**1 [b]**

[a] Not frozen prior to testing

[b] 36 specimens confirmed positive by HIV-1 Western blot, 1 specimen negative by HIV-1 Western blot was positive by both HIV-1 p24 Antigen test and HIV-1 RNA PCR.

As shown in Table 3 above, 99.17% (6113/6164) of the low risk population was nonreactive, 0.88% (54/6164) was initially reactive, and 0.83% (51/6164) was repeatedly reactive with ARCHITECT HIV Ag/Ab Combo assay. Of the 6164 specimens, 37 were confirmed positive (36 by HIV-1 Western blot and 1 by both HIV-1 p24 antigen and HIV-1 RNA PCR). The specificity of the ARCHITECT HIV Ag/Ab Combo assay in the low risk population in this study was 99.77% (6113/6127) with an exact 95% confidence interval of 99.62% to 99.88%.

Sensitivity

HIV-1 p24 Antigen Analytical Sensitivity

The ARCHITECT HIV Ag/Ab Combo assay was designed to have an analytical sensitivity of < 50 pg/mL for HIV-1 p24 antigen. In an internal study, the ARCHITECT HIV Ag/Ab Combo antigen sensitivity was verified with an antigen panel derived from the Agence française de sécurité sanitaire des produits de santé (AFSSAPS) HIV1 p24 antigen standard across three lots of reagents and three instruments (ARCHITECT *i* 2000_{SR}, ARCHITECT *i* 2000, and ARCHITECT *i* 1000_{SR}). The results demonstrated a mean sensitivity to HIV-1 p24 antigen of 18.39 pg/mL (range 17.80 to 19.68 pg/mL).

Detection of HIV-1 Antigen

HIV-1 antigen positive samples (n=63) were tested with the ARCHITECT HIV Ag/Ab Combo assay.

The 63 HIV-1 antigen positive samples included 5 antibody-negative HIV-1 antigen group M specimens (subtypes C, B and CRF02), 20 commercially available HIV-1 antibody-negative antigen panel members, and 38 unique viral isolates that were propagated in cell culture and classified as HIV-1 group M (subtypes A-D, F, G, CRF01, CRF02, and URFs) and HIV-1 group O. The sensitivity of the ARCHITECT HIV Ag/Ab Combo assay in this study was 100.00% (63/63) with an exact 95% confidence interval of 94.31% to 100.00%. The reactivity for HIV-1 antigen positive antibody-negative samples is presented in Table 4.

Table 4: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay for HIV-1 Antigen-Positive Antibody-Negative Samples

Specimen Category	Number of Specimens Tested	ARCHITECT HIV Ag/Ab Combo	Repeatedly Reactive Specimens (Number Positive by Method)		
		Number of Repeatedly Reactive Specimens (%)	Direct HIV-1 p24 Antigen (%)	Neutralization HIV-1 p24 Antigen/ Number Tested	HIV-1 RNA PCR (%)
HIV-1 Antigen Specimens [a]	5	5 (100.00)	5 (100.00)	5/5	ND
HIV-1 Antigen Panel 1 [a]	4	4 (100.00)	3 (75.00)	3/3	4 (100.00)
HIV-1 Antigen Panel 2 [a]	16	16 (100.00)	14 (87.50)	14/14	16 (100.00)
HIV-1 Viral Isolate Panel	38	38 (100.00)	36 (94.74)[b]	21/22[c]	ND
Total	**63**	**63 (100.00)**	**58 (92.06)**	**43/44**	**20 (100.00)**

ND = not done (specimens of known subtype)

[a] Of the 25 HIV-1 antigen specimens and panel members, 17 specimens were nonreactive by the FDA-Licensed HIV-1/2/O Antibody Assay, and all 25 were negative by HIV-1 Western blot.

[b] Two group O samples were non-reactive by the Direct HIV-1 p24 Antigen Assay.

[c] 14 of the 36 repeatedly reactive specimens by the Direct HIV-1 p24 Antigen Assay were not tested by neutralization due to limited volume, and one sample (group M subtype CRF01_AE) that was repeatedly reactive by the Direct HIV-1 p24 Antigen Assay did not confirm by neutralization.

Detection of HIV-1 Antigen Subtypes

Nine HIV-1 antigen group M subtype specimens and the 38 HIV-1 viral isolates were tested with the ARCHITECT HIV Ag/Ab Combo assay. The reactivity by HIV-1 antigen subtype and country of origin is presented in Table 5.

Table 5: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay for HIV-1 Antigen Group M Specimens and HIV-1 Viral Isolates (by Subtype and Country of Origin)

			ARCHITECT HIV Ag/Ab Combo	HIV-1 p24 Tests	
Source (# of Specimens)	**Subtype**	**Number of Specimens Tested**	**Number of Repeatedly Reactive Specimens (%)**	**Direct Antigen Repeatedly Reactive [a] (%)**	**Neutralization Antigen Positive/ Number Tested [a]**
Group M Specimens [b] (9)					
S. Africa	B	2	2 (100.00)	2 (100.00)	2/2
S. Africa	C	6	6 (100.00)	6 (100.00)	6/6
Cameroon	CRF02_AG	1	1 (100.00)	1 (100.00)	1/1
Viral Isolates [a] (38)					
Uganda	A	2	2 (100.00)	2 (100.00)	1/1
United States (4), Thailand (2), Brazil (1)	B	7	7 (100.00)	7 (100.00)	4/4
Uganda (2), Zambia (1), Ethiopia (1), Senegal (1), Somalia (1)	C	6	6 (100.00)	6 (100.00)	3/3
Senegal (1), Uganda (3)	D	4	4 (100.00)	4 (100.00)	3/3
Brazil	F	4	4 (100.00)	4 (100.00)	2/2
Kenya	G	1	1 (100.00)	1 (100.00)	1/1
Côte d'Ivoire (1), Thailand (1)	URF[c]	2	2 (100.00)	2 (100.00)	1/1
Thailand (6), Indonesia (2)	CRF01_AE	8	8 (100.00)	8 (100.00)	6/7
Djibouti	CRF02_AG	2	2 (100.00)	2 (100.00)	ND
United States (1), Spain (1)	Group O	2	2 (100.00)	0 (0.00) [d]	NA
	Total	**47**	**47 (100.00)**	**45 (95.74)**	**30/31 (96.77%)**

CRF = circulating recombinant form, URF = unique recombinant form, NA = not applicable, ND = not done

[a] Of the 38 viral isolates, 36 were repeatedly reactive by the Direct HIV-1 p24 Antigen Assay. Of the 36, 21 were confirmed by neutralization, 1 did not confirm (group M subtype CRF01_AE), and 14 were not tested by neutralization due to limited specimen volume.

[b] Of the 9 HIV-1 antigen group M specimens, 2 (subtype C) were nonreactive by the FDA-Licensed HIV-1/2/O Antibody Assay and 5 were negative by HIV-1 Western blot.

[c] One viral isolate subtype was B/A/B, and one viral isolate subtype was A/G/G.

[d] Two group O samples were nonreactive by the Direct HIV-1 p24 Antigen Assay.

Seroconversion Panels

In an internal study, a total of 31 HIV seroconversion panel sets were obtained from commercial vendors and tested using three ARCHITECT HIV Ag/Ab Combo reagent lots across the three instrument systems (ARCHITECT *i* 2000_{SR}, ARCHITECT *i* 2000, and ARCHITECT *i* 1000_{SR}) and an FDA-licensed HIV-1/2/O Antibody assay.

Each ARCHITECT HIV Ag/Ab Combo reagent lot detected a greater overall number of reactive bleeds (n = 137) compared to the FDA-licensed HIV-1/2/O Antibody assay (n = 87). The first reactive bleed (i.e., panel member) for the ARCHITECT HIV Ag/Ab Combo assay occurred at the same bleed in 3 panels and earlier in 28 panels than for the FDA-licensed HIV-1/2/O Antibody assay. These 28 panels contained bleeds that were labeled by the commercial vendors as HIV-1 p24 antigen and/or HIV RNA positive and not confirmed by Western blot; the bleeds so labeled were nonreactive for HIV antibody by the FDA-licensed HIV-1/2/O Antibody assay and repeatedly reactive by ARCHITECT HIV Ag/Ab Combo. For the 28 panels, the ARCHITECT HIV Ag/Ab Combo reduced the time to detection of HIV (i.e., window period) by a median of 7 days (overall range: 0 to 20 days) compared to the FDA-licensed HIV-1/2/O Antibody assay. This demonstrates the capability of ARCHITECT HIV Ag/Ab Combo assay to detect acute and primary HIV infection. The seroconversion sensitivity is presented in Table 6.

Table 6: Performance of the ARCHITECT HIV Ag/Ab Combo Assay on Seroconversion Panel Specimens Compared to an FDA-licensed HIV-1/2/O Assay

Panel ID	Number of Panel Members Tested	Number of Reactive Panel Members		Days to First Reactive Result		Difference in Days to First Reactive Result (Based on Bleed Date) [a]
		ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay	ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay	
HIV6240	11	6	4	23	30	7
HIV6246	18	7	7	56	56	0
HIV6247	10	4	0	21	--[b]	--[b]
HIV9011	11	2	2	36	36	0
HIV9012	8	3	2	16	21	5
HIV9013	7	1	0	25	--[b]	--[b]
HIV9016	10	2	0	30	--[b]	--[b]
HIV9018	11	3	2	28	32	4
HIV9021	17	4	1	47	57	10
HIV9023	22	3	1	78	85	7
HIV9026	7	1	0	44	--[b]	--[b]
HIV9028	7	2	0	53	--[b]	--[b]
HIV9030	16	3	1	47	54	7
HIV9032	14	7	5	24	36	12
HIV9034	13	3	1	46	53	7
HIV9076	10	3	2	66	69	3
HIV9077	29	18	16	45	52	7
HIV9079	25	17	14	40	49	9
PRB927	5	4	4	28	28	0
PRB924	8	4	3	26	33	7
PRB926	6	4	2	7	27	20
PRB944	6	4	2	7	14	7
PRB951	6	4	1	8	19	11
PRB952	6	4	3	10	14	4
PRB953	4	2	1	7	10	3
PRB954	7	2	1	17	21	4
PRB955	5	4	2	3	12	9
PRB957	7	2	1	23	28	5
PRB958	6	4	2	7	15	8

PRB959	7	7	5	0 [c]	9 [c]	9 [c]
PRB941	6	3	2	18	21	3
	Total	**137**	**87**			

[a] The dates of the first reactive test results were compared for the FDA-licensed HIV-1/2/O Antibody Assay and ARCHITECT HIV Ag/Ab Combo assay. If the first reactive test result occurred on the same day, then the difference is 0; if ARCHITECT HIV Ag/Ab Combo assay had an earlier date, then the difference is positive; if ARCHITECT HIV Ag/Ab Combo assay had a later date, then the difference is negative.
[b] All bleeds in these panels were nonreactive with the FDA-licensed HIV-1/2/O Antibody Assay.
[c] The ARCHITECT HIV Ag/Ab Combo result was reactive with the initial bleed, which was collected 9 days earlier than the bleed detected by the FDA-licensed HIV-1/2/O Antibody Assay.

Detection of HIV Antibodies

A total of 1003 serum and plasma specimens were collected from HIV-infected individuals in a US population and confirmed positive for HIV-1 antibodies by Western blot and tested using the ARCHITECT HIV Ag/Ab Combo and FDA-Licensed HIV-1/2/O Antibody assays. All 1003 specimens were repeatedly reactive using the ARCHITECT HIV Ag/Ab Combo assay. The sensitivity of the ARCHITECT HIV Ag/Ab Combo assay in this study was 100.00% (1003/1003) with an exact 95% confidence interval of 99.63 to 100.00%. The results from specimens positive for antibodies to HIV-1 are presented in Table 7.

Table 7: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Specimens Positive for Antibodies to HIV-1

Specimen Category	Number of Specimens Tested	ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay	HIV-1 Western Blot (%)
		Number Repeatedly Reactive Specimens (%)	Number Repeatedly Reactive Specimens (%)	
Asymptomatic	416	416 (100.00)	416 (100.00)	416 (100.00)
Symptomatic	183	183 (100.00)	182 (99.45)	183 (100.00)
Diagnosed with AIDS	404	404 (100.00)	404 (100.00)	404 (100.00)
Total	**1003**	**1003 (100.00)**	**1002 (99.90) [a]**	**1003 (100.00)**

[a] A second aliquot for the one specimen that was nonreactive by the FDA-licensed HIV-1/2/O Antibody assay was tested and was repeatedly reactive.

A total of 201 plasma specimens confirmed positive by HIV-2 Western blot from Côte d'Ivoire were tested using the ARCHITECT HIV Ag/Ab Combo and FDA-licensed HIV-1/2/O Antibody assays (Table 8). All 201 specimens were repeatedly reactive with the ARCHITECT HIV Ag/Ab Combo assay. The sensitivity of the ARCHITECT HIV Ag/Ab Combo assay in this study was 100.00% (201/201) with an exact 95% confidence interval of 98.18 to 100.00%.

Table 8: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Specimens Positive for Antibodies to HIV-2

Specimen Category	Number of Specimens Tested	ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay	HIV-2 Western Blot (%)
		Number of Repeatedly Reactive Specimens (%)	Number of Repeatedly Reactive Specimens (%)	
Anti-HIV-2 Positive	201	201 (100.00)	201 (100.00)	201 (100.00)

Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay for Specimens with Antibodies to HIV-1 Groups M, O, and N and Antibodies to HIV-2

In an internal study, a total of 693 specimens identified as anti-HIV-1 group M, group O, and group N and anti-HIV-2 were tested. Of the 693 specimens, 500 anti-HIV-1 group M subtypes and 8 anti-HIV-1 group N specimens from Argentina, Brazil, Cameroon, Ghana, Saudi Arabia, South Africa, Thailand, Uganda, and United Kingdom were reactive by the ARCHITECT HIV Ag/Ab Combo assay. In addition, a total of 65 anti-HIV-1 group O specimens from Cameroon, Equatorial Guinea, Spain, and United States and 120 anti-HIV-2 specimens from Côte d'Ivoire were reactive by the ARCHITECT HIV Ag/Ab Combo assay. The HIV-1/HIV-2 antibody sensitivity is summarized in Table 9.

Table 9: HIV-1/HIV-2 Antibody Sensitivity

HIV Antibody Type	Subtype	ARCHITECT HIV Ag/Ab Combo Number of Repeatedly Reactive/Number Tested
HIV-1 Group M Antibody	A	54/54
	B	44/44
	C	44/44
	D	40/40
	F	24/24
	G	20/20
	CRF 01	92/92
	CRF 02	51/51
	CRF 09	2/2
	CRF 11	12/12
	CRF 13	4/4
	URF	113/113
HIV-2 Antibody	NA	120/120
HIV-1 Group O Antibody	NA	65/65
HIV-1 Group N Antibody	NA	8/8
	Total	**693/693**

CRF = circulating recombinant form; URF = unique recombinant form; NA = not applicable

Reactivity in Individuals at Increased Risk for HIV Infection

A total of 693 specimens from individuals in a US population at increased risk for infection with HIV were tested using the ARCHITECT HIV Ag/Ab Combo and an FDA-licensed HIV-1/2/O Antibody assay. The specimens were collected from individuals (age range: 18 to 66 years) with one or more of the following risk factors: injecting drug users, unprotected sex with someone who is infected with HIV, diagnosed or treated for a sexually transmitted disease (STD), hepatitis or tuberculosis, multiple sex partners, men who have sex with men, unprotected sex with someone who has been diagnosed or treated for an STD, and risk factor not identified but requested an HIV test.

Table 10: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Individuals at Increased Risk for Infection with HIV

Specimen Category	Number of Specimens Tested	Number of Repeatedly Reactive Specimens (%)		Repeatedly Reactive Specimens (Number Reactive/Positive by Method)				
		ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay	HIV-1 Western Blot (%)	HIV-2 EIA (%)	HIV-2 Western Blot (%)	HIV-1 p24 Antigen (%)	HIV-1 RNA PCR (%)
Individuals at Increased Risk for HIV - US Population	693	71 (10.25)	77 (11.11)	65 (9.38)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

Of the 693 specimens from individuals at increased risk in the US, 71 (10.25%) were repeatedly reactive by ARCHITECT HIV Ag/Ab Combo assay. Of these 71 specimens, 65 were confirmed positive by HIV-1 Western blot, and all 65 were also repeatedly reactive by the FDA licensed assay.

A comparison of the ARCHITECT HIV Ag/Ab Combo results versus the FDA-Licensed HIV-1/2/O Antibody assay results is summarized in Table 11. None of the specimens that were repeatedly reactive only on ARCHITECT HIV Ag/Ab Combo or only on the FDA-licensed Antibody assay were confirmed positive.

Table 11: ARCHITECT HIV Ag/Ab Combo and FDA-Licensed HIV-1/2/O Antibody Assay Results in Individuals at Increased Risk for Infection with HIV

ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay		
	RR	NR	Total
RR	69	2 [a]	71
NR	8 [b]	614	622
Total	77	616	693

[a] Both specimens were negative by HIV-1 Western blot, HIV-2 EIA, HIV-1 p24 Antigen Assay, and HIV-1 RNA PCR.

[b] Seven specimens were negative by HIV-1 Western blot, and 1 specimen was HIV-1 Western blot indeterminate. All 8 specimens were negative by HIV-2 EIA, HIV-1 p24 Antigen Assay and HIV-1 RNA PCR.

Reactivity in Individuals at Increased Risk for Infection with HIV-2

A total of 513 specimens from individuals at increased risk for infection with HIV from an HIV-2 endemic area (Côte d'Ivoire) were tested by the ARCHITECT HIV Ag/Ab Combo and an FDA-licensed HIV-1/2/O Antibody assay. The specimens were collected from individuals (age range: 17 to 60 years) with one or more of the following risk factors: unprotected sex with someone who is infected with HIV, multiple sex partners, men who have sex with men, and injecting drug users.

Table 12: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Individuals at Increased Risk for Infection with HIV-2

Specimen Category	Number of Specimens Tested	Number of Repeatedly Reactive Specimens (%)		Repeatedly Reactive Specimens (Number Reactive/Positive by Method)				
		ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay	HIV-1 Western Blot (%)	HIV-2 EIA (%)	HIV-2 Western Blot (%)	HIV-1 p24 Antigen (%)	HIV-1 RNA PCR (%)
Individuals at Increased Risk from an HIV-2 Endemic Area	513	89 (17.35)	87 (16.96)	79 (15.40) [a]	82 (15.98)	24 (4.68) [b]	1 (0.19) [c]	1 (0.19) [c]

[a] Specimens were repeatedly reactive by ARCHITECT HIV Ag/Ab Combo and an FDA-licensed HIV-1/2/O Antibody assay.

[b] 24 specimens were repeatedly reactive by both methods, of which 3 were positive by HIV-2 Western blot and 21 were positive by both HIV-1 and HIV-2 Western blot. These 21 specimens were further differentiated by an FDA-approved HIV-1/HIV-2 immunoassay; of these, 14 were HIV-1, 3 were HIV-2, and 4 were undifferentiated.

[c] One specimen was repeatedly reactive by both methods and was negative by HIV-1 Western blot and was confirmed positive by the HIV-1 p24 Antigen Assay and HIV-1 RNA PCR.

Of the 513 specimens from the HIV-2 endemic area, 89 (17.35%) were repeatedly reactive by ARCHITECT HIV Ag/Ab Combo assay. Of the repeatedly reactive specimens, 83 were confirmed positive by HIV-1 Western blot, HIV-2 Western blot, HIV-1 p24 antigen assay, or HIV-1 RNA PCR. Of these, 1 was negative by HIV-1 and HIV-2 Western blot and positive by HIV-1 p24 antigen assay and HIV-1 RNA PCR.

A comparison of the ARCHITECT HIV Ag/Ab Combo results versus the FDA-Licensed HIV-1/2/O Antibody assay results is summarized in Table 13. None of the specimens that were repeatedly reactive only on ARCHITECT HIV Ag/Ab Combo or only on the FDA-licensed Antibody assay were confirmed positive.

Table 13: ARCHITECT HIV Ag/Ab Combo and FDA-Licensed HIV-1/2/O Antibody Assay Results in Individuals at Increased Risk for Infection with HIV-2

ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay		
	RR	NR	Total
RR	86	3 [a]	89
NR	1 [b]	423	424
Total	87	426	513

[a] One specimen was repeatedly reactive by HIV-2 EIA and indeterminate by HIV-2 Western blot, and two specimens were nonreactive by HIV-2 EIA. All 3 specimens were negative by HIV-1 Western blot, HIV-1 p24 Antigen Assay, and HIV-1 RNA PCR.

[b] This specimen was negative by HIV-1 Western blot, HIV-2 EIA, HIV-1 p24 Antigen Assay, and HIV-1 RNA PCR.

Pregnant Females

Four hundred fifty-three (453) specimens from a pregnant female US population were tested using the ARCHITECT HIV Ag/Ab Combo assay and an FDA-licensed HIV-1/2/O Antibody assay. The specimens included individuals at low risk for HIV infection (n=250, Table 3) and individuals at increased risk for HIV infection (n=203). In addition, 60 specimens from known HIV-1 antibody positive pregnant females (n=60) were tested using the ARCHITECT HIV Ag/Ab Combo assay.

Reactivity in Pregnant Females at Increased Risk for Infection with HIV

For the 203 specimens from pregnant females at increased risk for infection with HIV, the risk factors, if known, were documented and included: multiple sex partners during pregnancy, unprotected sex with an HIV-infected individual, unprotected sex with an HIV high-risk individual, unprotected sex with an individual diagnosed or treated for an STD, and history of sexually transmitted disease. The reactivity in this population is presented in Table 14. There were no specimens that were repeatedly reactive on the FDA-licensed Antibody assay and confirmed positive that were non-reactive on the ARCHITECT HIV Ag/Ab Combo.

Table 14: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Pregnant Females at Increased Risk for Infection with HIV

Specimen Category	Number of Specimens Tested	ARCHITECT HIV Ag/Ab Combo		FDA-Licensed HIV-1/2/O Antibody Assay	Number Confirmed Positive Specimens (%)
		Number of Nonreactive Specimens (%)	Number of Repeatedly Reactive Specimens (%)	Number of Repeatedly Reactive Specimens (%)	
First Trimester	30	27 (90.00)	3 (10.00)	3 (10.00)	3 (10.00)
Second Trimester	36	34 (94.44)	2 (5.56)	3 (8.33)	2 (5.56)
Third Trimester	137	137 (100.00)	0 (0.00)	3 (2.19)	0 (0.00)
Total	**203**	**198 (97.54)**	**5 (2.46)**	**9 (4.43)**	**5 (2.46)** [a]

[a] Confirmed positive by HIV-1 Western blot.

Specificity

Specificity was determined using presumed negative specimens from 448 pregnant females (age range: 16 to 44 years) based on the FDA-licensed HIV-1/2/O antibody assay and supplemental testing. The pregnant females specimens were prospectively collected plasma specimens from pregnant females across all trimesters. Specificity of ARCHITECT HIV Ag/Ab Combo in a pregnant female population in this study was 100.00% (448/448) with an exact 95% confidence interval of 99.18% to 100.00%.

Sensitivity

Sensitivity was estimated using a total of 65 specimens, which included 60 serum and plasma specimens from pregnant females known to be HIV-positive by HIV-1 Western blot (refer to Table 15) and 5 specimens from the increased risk for HIV population that were confirmed positive by HIV-1 Western blot (refer to Table 14). The sensitivity of the ARCHITECT HIV Ag/Ab Combo assay in a pregnant female population in this study was 100.00% (65/65) with an exact 95% confidence interval of 94.48% to 100.00%

The reactivity for the 60 known HIV positive pregnant females is presented in Table 15.

Table 15: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Pregnant Females Known To Be Infected with HIV

Specimen Category	ARCHITECT HIV Ag/Ab Combo		Number of HIV-1 Western Blot Confirmed Specimens (%)
	Number of Specimens Tested	Number of Repeatedly Reactive Specimens (%)	
First Trimester	22	22 (100.00)	22 (100.00)
Second Trimester	18	18 (100.00)	18 (100.00)
Third Trimester	20	20 (100.00)	20 (100.00)
Total	**60**	**60 (100.00)**	**60 (100.00)**

Pediatric Subjects

A total of 591 prospectively-collected specimens obtained from pediatric subjects were tested by the ARCHITECT HIV Ag/Ab Combo and the FDA-licensed HIV-1/2/O Antibody assay. Of the 591 pediatric subjects, 542 (age range 2 to 21 years) were from the United States and 49 (age range: 17 to 21 years) were from an HIV-2 endemic area (Côte d'Ivoire). The distribution of the results by age range and gender for the 591 pediatric subjects is presented in Table 16.

Table 16: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Pediatric Subjects at Low and Increased Risk for Infection with HIV

Age Range	Gender	ARCHITECT HIV Ag/Ab Combo		FDA-Licensed HIV-1/2/O Antibody Assay		Number of Confirmed Positive Specimens (%)
		Number of Nonreactive Specimens (%)	Number of Repeatedly Reactive Specimens (%)	Number of Nonreactive Specimens (%)	Number of Repeatedly Reactive Specimens (%)	
2 to 5 Years	Female	6 (100.00)	0 (0.00)	6 (100.00)	0 (0.00)	0 (0.00)
	Male	5 (100.00)	0 (0.00)	5 (100.00)	0 (0.00)	0 (0.00)
6 to 10 Years	Female	7 (100.00)	0 (0.00)	7 (100.00)	0 (0.00)	0 (0.00)
	Male	13 (100.00)	0 (0.00)	13 (100.00)	0 (0.00)	0 (0.00)
11 to 15 Years	Female	14 (100.00)	0 (0.00)	14 (100.00)	0 (0.00)	0 (0.00)
	Male	12 (100.00)	0 (0.00)	12 (100.00)	0 (0.00)	0 (0.00)
16 to 21 Years	Female	358 (99.17)	3 (0.83)	356 (98.61)	5 (1.39)	2 (0.55)
	Male	172 (99.42)	1 (0.58)	172 (99.42)	1 (0.58)	1 (0.58)
	Total	**587 (99.32)**	**4 (0.68)**	**585 (98.98)**	**6 (1.02)**	**3 (0.51)** [a]

[a] Includes individuals in the following categories: two (2) individuals at increased risk for HIV from an HIV-2 endemic area confirmed positive by HIV Western blot, and one (1) individual at low risk for HIV confirmed positive by HIV-1 Western blot.

Specificity

Specificity was determined using the 588 presumed negative specimens based on the FDA-licensed HIV-1/2/O Antibody assay and supplemental testing. The specificity of the ARCHITECT HIV Ag/Ab Combo assay in a pediatric population in this study was 99.83% (587/588) with an exact 95% confidence interval of 99.06% to 100.00%.

Sensitivity

Sensitivity was determined from 64 specimens, which included 61 specimens known to be HIV-1 positive by HIV-1 Western blot (Table 17), 1 specimen from the low risk for HIV population (refer to Table 3), and 2 specimens from the increased risk for HIV populations confirmed positive by supplemental testing (Table 18). The sensitivity of ARCHITECT HIV Ag/Ab Combo in a pediatric population in this study was 100.00% (64/64) with an exact 95% confidence interval of 94.40% to 100.00%.

The distribution of the results by age and gender for the 61 pediatric subjects known to be HIV-1 positive is presented in Table 17.

The reactivity in pediatric subjects at increased risk for infection with HIV-1 and HIV-2 is presented in Table 18. There were no specimens that were repeatedly reactive on the FDA-licensed Antibody assay and confirmed positive that were non-reactive on the ARCHITECT HIV Ag/Ab Combo.

Table 17: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Pediatric Subjects Known To Be Infected with HIV

Age Range	Gender	ARCHITECT HIV Ag/Ab Combo Number of Repeatedly Reactive Specimens (%)	Number of HIV-1 Western Blot Confirmed Specimens (%)
2 to 5 Years	Female	5 (8.20)	5 (100.00)
	Male	5 (8.20)	5 (100.00)
6 to 10 Years	Female	6 (9.84)	6 (100.00)
	Male	14 (22.95)	14 (100.00)
11 to 15 Years	Female	16 (26.23)	16 (100.00)
	Male	3 (4.92)	3 (100.00)
16 to 21 Years	Female	3 (4.92)	3 (100.00)
	Male	9 (14.75)	9 (100.00)
Total		**61 (100.00)**	**61 (100.00)**

Table 18: Reactivity of the ARCHITECT HIV Ag/Ab Combo Assay in Pediatric Subjects at Increased Risk for Infection with HIV

Specimen Category	Number Tested	ARCHITECT HIV Ag/Ab Combo	FDA-Licensed HIV-1/2/O Antibody Assay	Repeatedly Reactive Specimens (Number Reactive/Positive by Method)			
		Number of Repeatedly Reactive Specimens (%)	Number of Repeatedly Reactive Specimens (%)	HIV-1 Western Blot (%)	HIV-2 Western Blot (%)	HIV-1 p24 Antigen (%)	HIV-1 RNA PCR (%)
Individuals at Increased Risk for HIV Infection - US Population	7	0 (0.00)	1 (14.29)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Individuals at Increased Risk for HIV Infection - HIV-2 Endemic Area	49	2 (4.08)	2 (4.08)	2 [a] (4.08)	1 [a] (2.04)	0 (0.00)	0 (0.00)
Pregnant Females at Increased Risk for HIV Infection	38	0 (0.00)	1 (2.63)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)
Pediatric Population at Risk for HIV Infection	88	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)	0 (0.00)

[a] One specimen was positive by both HIV-1 and HIV-2 Western blot and further differentiated as HIV-1 by an FDA-approved HIV-/HIV-2 immunoassay.

Potentially Interfering Substances

A study was performed to evaluate the susceptibility of the ARCHITECT HIV Ag/Ab Combo assay to elevated levels of potentially interfering substances based on guidance from the CLSI document EP7-A2.[39]

Each potential interferent was evaluated in both serum and plasma. Serum and plasma samples were prepared with no analyte and with four positive analyte types (anti-HIV-1, anti-HIV-1 group O, anti-HIV-2, and HIV-1 p24 antigen) at a level of approximately 3 S/CO (S/CO range: 2 to 4). These prepared specimens were supplemented with potential interferents as described below:

- Bilirubin test samples were prepared by adding bilirubin (conjugated and unconjugated) to a final concentration of $\geq$ 20 mg/dL to serum and plasma tubes containing no analyte (n = 43) and each positive analyte type (n = 177).
- Hemoglobin test samples were prepared by adding hemolysate containing hemoglobin to a final concentration of $\geq$ 500 mg/dL to serum and plasma tubes containing no analyte (n = 48) and each positive analyte type (n = 185).
- Triglycerides test samples were prepared by adding triglyceride stock solution to a final concentration of $\geq$ 1250 mg/dL to serum and plasma tubes containing no analyte (n = 47) and each positive analyte type (n = 191).
- Total Protein test samples were prepared by adding human serum protein to a final concentration of $\geq$ 12 g/dL to serum and plasma tubes containing no analyte (n = 49) and each positive analyte type (n = 174).

A mean S/CO change of no more than –20% for HIV-1 antigen, HIV-1 group M, HIV-1 group O, and HIV-2 antibody positive samples (S/CO range: 2 to 4) and a mean change of no more than 0.20 S/CO for nonreactive samples (S/CO range: < 1.00) were observed when serum and plasma specimens were spiked with elevated levels of bilirubin, hemoglobin, triglycerides, or total protein.

Summary of Results for Potentially Cross-Reacting Specimens

The ARCHITECT HIV Ag/Ab Combo assay was evaluated for potential cross-reactivity for specimens from individuals with medical conditions unrelated to HIV infection as summarized in Table 19. The specimens were tested using the ARCHITECT HIV Ag/Ab Combo assay and the FDA-licensed HIV-1/2/O Antibody Assay. The results for all 290 specimens were nonreactive with both assays.

Table 19: List of Potentially Cross-Reacting Specimens Tested

Category	n	Category	n	Category	n
Chlamydia	10	Hepatitis A Virus (anti-HAV positive)	10	Pregnancy Second Trimester	9
Common Cold	10	Hepatitis B Virus (anti-HBV positive)	10	Pregnancy Third Trimester	10
Crohn's Disease	10	Hepatitis C Virus (anti-HCV positive)	10	Rheumatoid Factor positive	10
Cytomegalovirus (anti-CMV positive)	9	Herpes Simplex Virus (anti-HSV positive)	9	Rubella IgG	9
Elevated IgG	7	Human Anti-Mouse Antibodies (HAMA) positive	10	Smallpox vaccine recipient	10
Elevated IgM	10	Human T-Lymphotropic Virus (HTLV)	6	Syphilis (positive serology)	10
Epstein-Barr Virus (anti-EBV positive)	10	IgM Monoclonal Gammopathy	9	Systemic Lupus Erythematosus (SLE & ANA)	14
Fungal Infections	10	Influenza vaccine recipient	10	Varicella Zoster Virus (anti-VZV positive)	10
Graves Disease	10	Multiparous Pregnancies	10	Viral Diarrheal Illness	10
Hemodialysis	8	Pregnancy First Trimester	10	Anti-*Escherichia coli* (anti-*E.coli* positive)	10

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

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