ARCHITECT

SYSTEM

en

HIV Ag/Ab Combo

REF 4J27

B4J2S0

G45772R06

Read Highlighted Changes
Revised May 2019

HIV Ag/Ab Combo

Customer Service: Contact your local representative or find country-specific contact information on www.abbottdiagnostics.com

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

Key to symbols used

REF	List Number	CONTROL NO.	Control Number
IVD	*In Vitro* Diagnostic Medical Device	REAGENT LOT	Reagent Lot
		REACTION VESSELS	Reaction Vessels
LOT	Lot Number	SAMPLE CUPS	Sample Cups
SN	Serial Number	SEPTUM	Septum
	Expiration Date	REPLACEMENT CAPS	Replacement Caps
2°C 8°C	Store at 2-8°C	CONTAINS: AZIDE	Contains sodium azide. Contact with acids liberates very toxic gas.
	Consult instructions for use	GTIN	Global Trade Item Number
		PRODUCT OF GERMANY	Product of Germany
	Manufacturer	WARNING: SEVERE IRRITANT	Warning: Severe Irritant

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

Abbott

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 human immunodeficiency virus type 1 and/or type 2 (HIV-1/HIV-2) in human serum or plasma including specimens collected post-mortem (non-heart-beating). 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 to prevent transmission of HIV-1/HIV-2 to recipients of blood, blood components, cells, tissue and organs. An ARCHITECT HIV Ag/Ab Combo result does not distinguish between the detection of HIV p24 antigen, HIV-1 antibody, or HIV-2 antibody reactivity.

SUMMARY AND EXPLANATION OF TEST

Acquired immunodeficiency syndrome (AIDS) is caused by two types of human immunodeficiency viruses, collectively designated HIV.[1-7]

HIV is the etiologic agent of AIDS.[1,3,6,7] HIV is transmitted by sexual contact, exposure to blood or blood products, and prenatal infection of a fetus or perinatal infection of a newborn.[8] Antibodies against HIV are nearly always detected in AIDS patients and HIV infected asymptomatic individuals,[8,9] and HIV infection is always detected in AIDS patients and seropositive individuals by culture or amplification of viral RNA and/or proviral DNA.[8,10]

Phylogenetic analysis classifies HIV-1 into groups M (major), N (non-M, non-O), and O (outlier).[4,5] 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.[11-17] However, group O infections have been identified in Europe and the USA.[18-22] HIV-1 group M is composed of genetic subtypes (A, B, C, D, F, G, H, J, and K) and circulating recombinant forms (CRFs).[5,23] The geographic distribution and regional predominance of HIV-1 subtypes and CRFs 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.[23-28] 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.[29,30] In Asia, subtype C is found in India, and CRF01_AE (formerly called subtype E) and subtype B are in Thailand and southeast Asia.[31] South America predominantly has subtypes B and F.[32,33]

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.[6-8] However, 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.[34-37] 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.[31,37] HIV-2 is classified into genetic subtypes A-G with most infections caused by subtypes A and B.[38,39]

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.[9,40-44] 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.[9,40-44] TMPs from HIV-1 groups M and O and HIV-2 are represented in ARCHITECT HIV Ag/Ab Combo reagents by five recombinant antigens and two synthetic peptides derived from native TMP sequences. The rationale for including three pairs of TMPs is derived from the genetic diversity within HIV-1 and between HIV-1 and HIV-2.[4,5,45,46] Serologic studies indicate that although HIV-1 and HIV-2 share multiple common epitopes in their core antigens, the envelope glycoproteins are much less cross-reactive.[7,47-51] Antibodies elicited against the TMP (or portions of the TMP) of a viral strain within one group or type may react well, poorly, or not at all with the TMP (or portions of the TMP) from a viral strain of a different group or type.[15,52-57] An exception may be antibodies elicited against HIV-1 group N.[11,12]

Early after infection with HIV, but prior to seroconversion, HIV antigen(s) may be detected in serum or plasma specimens.[57-65] The HIV structural protein most often used as the marker of antigenemia is the core protein, p24. The ARCHITECT HIV Ag/Ab Combo uses anti-HIV p24 in the reagents to detect HIV p24 antigen prior to seroconversion, thereby decreasing the seroconversion window and improving early detection of HIV infection.

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, ARCHITECT *i* Wash Buffer, 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 (mouse) 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 antigens [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 *i* 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 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 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

Reagent Kit, 100 Tests, 500 Tests, 4 x 100 Tests, 4 x 500 Tests

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

ARCHITECT 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

ARCHITECT *i* Pre-Trigger Solution

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

ARCHITECT *i* Trigger Solution

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

ARCHITECT *i* Wash Buffer

- **WASH BUFFER** Wash Buffer containing phosphate buffered saline solution. Preservatives: Antimicrobial Agents.

WARNINGS AND PRECAUTIONS

- IVD
- For *In Vitro* Diagnostic Use

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

Safety Precautions

- **CAUTION:** This product requires the handling of human specimens. It is recommended that all human sourced materials are considered potentially infectious and be handled in accordance with the OSHA Standard on Bloodborne Pathogens.[66] Biosafety Level 2[67] or other appropriate biosafety practices[68,69] should be used for materials that contain or are suspected of containing infectious agents.

The following warnings and precautions apply to this component:

- Assay Diluent

WARNING: Contains Polyethylene glycol octylphenyl ether (Triton X-100) and Sodium Azide

H319 Causes serious eye irritation.
EUH032 Contact with acids liberates very toxic gas.

Prevention
P264 Wash hands thoroughly after handling.
P280 Wear protective gloves / protective clothing / eye protection.

Response
P305+P351 +P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P337+P313 If eye irritation persists: Get medical advice / attention.

This material and its container must be disposed of in a safe way.

- 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.
- Safety Data Sheets are available at www.abbottdiagnostics.com or contact your local representative.
- 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 8.

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

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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.** 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

- Before performing the assay, the ARCHITECT HIV Ag/Ab Combo assay file must be installed on the ARCHITECT *i* System obtained from an ARCHITECT *i* System Assay CD-ROM. For detailed information on assay file installation and on 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

Verified Specimen Types

- Human serum (including serum collected in serum separator tubes)
- Plasma collected in:
  - potassium EDTA
  - sodium heparin
  - lithium heparin
  - plasma separator tubes
  - sodium citrate
  - ACD, CPDA-I, CPD
  - potassium oxalate
- 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.
- Performance has been established for the use of cadaveric blood specimens (specimens collected post-mortem, non-heart-beating), for details refer to section **TESTING OF CADAVERIC BLOOD SPECIMENS.**

Specimen Conditions

- Do not use specimens with the following conditions:
  - heat-inactivated
  - pooled
  - grossly hemolyzed (> 500 mg/dL)
  - obvious microbial contamination
  - body fluids other than human serum and plasma
- 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

- Serum or plasma specimens should be stored for no longer than 3 days at room temperature (15 to 30°C) or 14 days at 2 to 8°C following specimen collection. If a storage period greater than 3 days at room temperature or 14 days at 2 to 8°C 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 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).

TESTING OF CADAVERIC BLOOD SPECIMENS

- Performance has been established for the use of cadaveric blood specimens (specimens collected post-mortem, non-heart-beating) that have been collected up to 17.5 hours after death. Performance was established using 50 spiked and 50 non-spiked cadaveric blood specimens[70].
- Testing of cadaveric blood specimens from patients with plasma dilution due to transfusions of > 2000 mL of blood or colloids within 48 hours, or > 2000 mL of crystalloids within 1 hour (or any combination thereof) prior to collection of the specimens have not been validated.
- Follow general standards and/or regulations for collection, storage and handling.
- Follow the tube manufacturer's processing instructions for serum or plasma collection tubes. After initial centrifugation, transfer the supernatant to a centrifuge tube and centrifuge at 10,000 RCF (Relative Centrifugal Force) for 10 minutes. If specimens are not processed directly after initial centrifugation, it is recommended to remove the supernatant from the clot, red blood cells or separator gel until further processing.
- Cadaveric blood specimens can be stored for up to 14 days at 2-8°C or up to 3 days at 15-30°C following collection.
- No qualitative differences were observed for cadaveric blood specimens (nonreactive or spiked reactive) when subjected to up to 3 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 *i* System
- ARCHITECT HIV Ag/Ab Combo Assay file, may be obtained from:
  - ARCHITECT *i* System e-Assay CD-ROM found on www.abbottdiagnostics.com
  - ARCHITECT *i* System Assay CD-ROM
- 4J27-03 ARCHITECT HIV Ag/Ab Combo Calibrator
- 4J27-12 ARCHITECT HIV Ag/Ab Combo Controls
- ARCHITECT *i* **PRE-TRIGGER SOLUTION**
- ARCHITECT *i* **TRIGGER SOLUTION**
- ARCHITECT *i* **WASH BUFFER**
- ARCHITECT *i* **REACTION VESSELS**
- ARCHITECT *i* **SAMPLE CUPS**
- ARCHITECT *i* **SEPTUM**
- ARCHITECT *i* **REPLACEMENT CAPS**
- Pipettes or pipette tips (optional) to deliver the volumes specified on the Patient or Control order screen.

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

Assay Procedure

- Before loading the ARCHITECT 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 *i* 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 *i* 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 *i* 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

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

- 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 *i* 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 PROCEDURE

- 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.[71,72] 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.[73] 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[74] using a mixed analysis of variance model.[75] The data from the study are summarized in Table 1.*

Table 1
ARCHITECT HIV Ag/Ab Combo Precision

Panel			Intra-assay		Inter-assay[a]	
Member (units)	n	Mean	SD	%CV	SD	%CV
Calibrator 1 (RLUs)	432	5629	201.8	3.6	235.7	4.2
NC[b] (S/CO)	1224	0.09	0.019	20.23	0.022	24.11
PC[c] 1 (S/CO)	1224	3.96	0.155	3.91	0.155	3.91
PC[c] 2 (S/CO)	1224	3.57	0.115	3.22	0.161	4.51
PC[c] 3 (S/CO)	1224	3.19	0.107	3.34	0.141	4.41
PM[d] 1 (S/CO)	432	2.57	0.098	3.82	0.137	5.33
PM[d] 2 (S/CO)	432	2.44	0.116	4.76	0.146	6.01
PM[d] 3 (S/CO)	432	2.36	0.075	3.16	0.097	4.12
PM[d] 4 (S/CO)	432	1.44	0.054	3.78	0.054	3.78

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

[b] Negative Control

[c] Positive Control

[d] 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 2
ARCHITECT HIV Ag/Ab Combo Specificity of Blood Donor Specimens

Specimen Type	n	Initially Reactive	Repeat Reactive	Specificity (%)	Specificity 95% CI[a]
Plasma	2747	3	3	99.89	99.68 - 99.98
Serum	3618	6	4	99.89	99.72 - 99.97
Total	6365	9	7	99.89	99.77 - 99.96

[a] Confidence Interval

* 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.*

Table 3
ARCHITECT HIV Ag/Ab Combo Specificity of Hospitalized Patients and Interfering Substances

Specimen Type	n	Initial Reactive	Repeat Reactive	Specificity (%)
HP	2841	11	11	99.61
IS[a]	310	1	1	99.68
Total	3151	12	12	99.62

[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.

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.* The specimens from patients at increased risk for HIV infection belonged to the following categories: Intravenous drug users, homosexual males, and sexually transmitted diseases.

* These are representative performance data. 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
ARCHITECT HIV Ag/Ab Combo Sensitivity

Antibody Type	Total n	Reactive n	Sensitivity (%)
Anti-HIV-1	520	520	100.0
Anti-HIV-2	111	111	100.0
Anti-HIV gO[a]	6	6	100.0

[a] 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 of the ARCHITECT HIV Ag/Ab Combo assay to detect p24 antigen and anti-HIV-1 was evaluated by testing sequential specimens from 31 seroconversion panels. These panels are commercially available and precharacterized for HIV antigen and antibodies. Table 5 shows data from 5 seroconversion panel members.*

Table 5
ARCHITECT HIV Ag/Ab Combo Seroconversion Sensitivity

Panel	Days Since 1st Bleed	ARCHITECT HIV Ag/Ab Combo (S/CO)	Western Blot[a]	HIV Ag[a] (S/CO)	PCR[a] Copies/mL
BBI	0	0.12	Neg[b]	0.1	4,000
PRB953	3	**1.04**	Neg	0.6	80,000
	7	**11.71**	Neg	**8.8**	700,000
	10	**31.79**	Neg	**19.3**	1,000,000
BBI	0	0.17	IND[c] (f24[d])	0.3	1,000
PRB955	3	**1.86**	IND (f24)	**1.8**	70,000
	7	**17.48**	IND (f24)	**14.0**	400,000
	12	**24.62**	IND (f24)	**22.4**	> 800,000
	14	**34.17**	IND (24)	**21.3**	700,000
BBI	0	**1.09**	Neg	**2.3**	80,000
PRB959	7	**323.59**	Neg	> **40.5**	> 500,000
	9	**192.13**	Neg	> **40.5**	> 500,000
	14	**75.41**	p24, gp160	**14.4**	> 500,000
	19	**66.38**	p24, gp160	0.7	200,000
	21	**66.29**	p24, gp160	0.7	200,000
	26	**68.46**	p24, gp160	**1.1**	300,000
BCP	0	0.10	p24	0.255	< 400
6247	2	0.09	p24	0.373	< 400
	7	0.09	p24	0.343	< 400
	9	0.09	p24	0.343	< 400
	14	0.09	p24	0.294	< 400
	16	0.09	p24	0.275	< 400
	21	**1.11**	p24	**1.265**	23,600
	23	**7.65**	p24	**8.598**	124,000
	28	**155.50**	p24	**37.618**	675,000
	30	**129.37**	Neg	**39.941**	> 750,000
NABI	0	0.12	IND[c] (p24)	0.45	2,326
SV404	8	0.13	IND (p24)	0.48	2,672
	11	0.13	IND (p24)	0.56	3,079
	15	0.23	IND (p24)	0.52	7,190
	18	**1.33**	IND (p24)	**1.48**	54,380
	22	**6.51**	IND (p24)	**4.84**	279,800

[a] Data from the vendor.

[b] Neg = no band or bands being observed.

[c] IND = indeterminant

[d] f24 = faint p24 antigen band

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

The ARCHITECT HIV Ag/Ab Combo assay has an analytical sensitivity of < 50 pg/mL to HIV-1 p24 Ag. Antigen sensitivity was evaluated with the HIV Ag 2003 AFSSAPS panel across three lots of ARCHITECT HIV Ag/Ab Combo reagents. The results demonstrated an average sensitivity to HIV-1 p24 Ag of 18.06 pg/mL.* In addition, sensitivity was assessed using the HIV-1 p24 Antigen, First International Reference Reagent, NIBSC code: 90/636. The results demonstrated an average sensitivity of 0.87 IU/ml.*

The WRAIR (Walter Reed Army Institute of Clinical Research, Rockville, MD) Clade Panel consisting of 32 members with the following subtypes was tested: A, B, B/A/B, C, D, G, F, Group O, CRF02_AG, CRF01_AE. For all panel members, the ARCHITECT HIV Ag/Ab Combo antigen sensitivity was better than antigen sensitivity of a comparative HIV antigen/antibody combo assay.*

* These are representative performance data. Results obtained at individual laboratories may vary.

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

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