Alinity i

HIV Ag/Ab Combo Reagent Kit

en
HIV Ag/Ab
08P07
G71155R02
B8P070

Revised March 2017.

REF 08P0722
REF 08P0732

Instructions must be carefully followed. Reliability of assay results cannot be guaranteed if there are any deviations from these instructions.

NAME

Alinity i HIV Ag/Ab Combo Reagent Kit (also referred to as HIV Ag/Ab).

INTENDED USE

The Alinity i HIV Ag/Ab Combo assay is a chemiluminescent microparticle immunoassay (CMIA) used 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) on the Alinity i analyzer.

The Alinity i HIV Ag/Ab Combo assay is 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 Alinity i 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 THE 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 Alinity i 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 Alinity i 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

This assay is a two-step immunoassay for the qualitative detection of HIV p24 antigen and antibodies to HIV-1 (group M and group O), and HIV-2 in human serum or plasma using chemiluminescent microparticle immunoassay (CMIA) technology.

Sample, HIV-1/HIV-2 antigen and HIV p24 monoclonal (mouse) antibody coated paramagnetic microparticles, assay diluent, and wash buffer are combined and incubated. The 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. The mixture is washed. HIV-1/HIV-2 antigens (recombinant), synthetic peptides, and HIV p24 antibody (mouse, monoclonal) acridinium-labeled conjugate is added to create a reaction mixture and incubated. Following another wash cycle, Pre-Trigger and Trigger solutions are added.

The resulting chemiluminescent reaction is measured as relative light units (RLUs). There is a direct relationship between the amount of HIV antigen and antibodies in the sample and the RLUs detected by the system optics.

The presence or absence of HIV p24 antigen or HIV-1/HIV-2 antibodies in the sample is determined by comparing the chemiluminescent RLU in the reaction to the cutoff RLU determined from an active calibration.

For additional information on system and assay technology, refer to the Alinity ci-series Operations Manual, Section 3.

Abbott

REAGENTS

Kit Contents

Alinity i HIV Ag/Ab Combo 08P07

NOTE: Some kit sizes are not available in all countries. Please contact your local distributor.

Volumes (mL) listed in the table below indicate the volume per cartridge.

REF	08P0722	08P0732
Tests per cartridge	100	600
Number of cartridges per kit	2	2
Tests per kit	200	1200
MICROPARTICLES	6.6 mL	32.1 mL
CONJUGATE	6.1 mL	31.6 mL
ASSAY DILUENT	6.3 mL	31.8 mL

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 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 HIV Ag/Ab Combo assay diluent containing TRIS buffer. Preservative: sodium azide.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use

Safety Precautions

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

The following warnings and precautions apply to: 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.
Disposal	
P501	Dispose of contents / container in accordance with local regulations.

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

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

For a detailed discussion of safety precautions during system operation, refer to the Alinity ci-series Operations Manual, Section 8.

Reagent Handling

- Upon receipt, gently invert the unopened reagent kit by rotating it over and back for a full 180 degrees, 5 times with green label stripe facing up and then 5 times with green label stripe facing down. This ensures that liquid covers all sides of the bottles within the cartridges. During reagent shipment, microparticles can settle on the reagent septum.
  - Place a check in the square on the reagent kit to indicate to others that the inversions have been completed.
- After mixing, place reagent cartridges in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.
- If a reagent cartridge is dropped, place in an upright position for 1 hour before use to allow bubbles that may have formed to dissipate.
- Reagents are susceptible to the formation of foam and bubbles. Bubbles may interfere with the detection of the reagent level in the cartridge and cause insufficient reagent aspiration that may adversely affect results.

For a detailed discussion of reagent handling precautions during system operation, refer to the Alinity ci-series Operations Manual, Section 7.

Reagent Storage

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	2 to 8°C	Until expiration date	Store in upright position. If cartridge does not remain upright, gently invert the cartridge 10 times and place in an upright position for 1 hour before use.
Onboard	System Temperature	30 days	
Opened	2 to 8°C	Until expiration date	Store in upright position. If cartridge does not remain upright during storage, discard the cartridge. Do not reuse original reagent caps or replacement caps due to the risk of contamination and potential to compromise reagent performance.

Reagents may be stored on or off the system. If removed from the system, store reagents with new replacement caps in an upright position at 2 to 8°C. For reagents stored off the system, it is recommended that they be stored in their original trays or boxes to ensure they remain upright.

For information on unloading reagents, refer to the Alinity ci-series Operations Manual, Section 5.

Indications of Reagent Deterioration

Deterioration of the reagents may be indicated when a calibration error occurs or a control value is out of the specified range. Associated test results are invalid, and samples must be retested. Assay recalibration may be necessary.

For troubleshooting information, refer to the Alinity ci-series Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The Alinity i HIV Ag/Ab Combo assay file must be installed on the Alinity i analyzer prior to performing the assay.

For detailed information on assay file installation and viewing and editing assay parameters, refer to the Alinity ci-series Operations Manual, Section 2.

For information on printing assay parameters, refer to the Alinity ci-series Operations Manual, Section 5.

For a detailed description of system procedures, refer to the Alinity ci-series Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen types listed below were verified for use with this assay on the ARCHITECT i System.

Other specimen types, collection tube types, and anticoagulants have not been verified with this assay.

Specimen Types	Collection Tubes
Serum	Serum
	Serum separator
Plasma	Potassium EDTA
	Sodium heparin
	Lithium heparin
	Plasma separator
	Sodium citrate
	ACD
	CPDA-1
	CPD
	Potassium oxalate

- 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.
- For cadaveric donors, serum and plasma, may be used; follow general standards and/or regulations for collection, storage and handling.
- The instrument does not provide the capability to verify specimen types. It is the responsibility of the operator to verify that the correct specimen types are used in the assay.

Specimen Conditions

- Do not use:
  - heat-inactivated specimens
  - pooled specimens
  - grossly hemolyzed specimens
  - specimens with obvious microbial contamination
  - 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.
- Specimens from heparinized patients may be partially coagulated and contain fibrin. Draw the specimen prior to heparin therapy.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

- Follow the tube manufacturer's processing instructions for collection tubes. Gravity separation is not sufficient for specimen preparation.
- Specimens should be free of bubbles. Remove bubbles with an applicator stick before analysis. Use a new applicator stick for each specimen to prevent cross-contamination.

To ensure consistency in results, recentrifuge specimens prior to testing if

- they contain fibrin, red blood cells, or other particulate matter
- they require repeat testing.

NOTE: If fibrin, red blood cells, or other particulate matter are observed, mix by low speed vortex or by inverting 10 times prior to recentrifugation.

Prepare frozen specimens as follows:

- Frozen specimens must be completely thawed before mixing.
- Mix thawed specimens thoroughly by low speed vortex or by inverting 10 times.
- Visually inspect the specimens. If layering or stratification is observed, mix until specimens are visibly homogeneous.
- If specimens are not mixed thoroughly, inconsistent results may be obtained.
- Recentrifuge specimens.

Prepare cadaveric blood specimens as follows:

- After initial centrifugation, recentrifuge specimens as described below.
- If specimens are not centrifuged directly after initial centrifugation, it is recommended to remove the supernatant from the clot, red blood cells, or separator gel until further processing.

Recentrifugation of Specimens

- Transfer specimens to a centrifuge tube and centrifuge at a minimum of 100 000 g-minutes.
- Examples of acceptable time and force ranges that meet this criterion are listed in the table below.

  Centrifugation time using alternate RCF values can be calculated using the following formula:

$$\text{Minimum Centrifugation time (minutes)} = \frac{\text{100 000 g-minutes}}{\text{RCF}}$$

Recentrifugation Time (Minutes)	RCF (x g)	g-Minutes
10	10 000	100 000
20	5000	100 000
40	2500	100 000

$$RCF = 1.12 \times r_{max}\ (rpm/1000)^2$$

RCF -	The relative centrifugal force generated during centrifugation.
rpm -	The revolutions per minute of the rotor on which the specimens are being spun (usually the digital readout on the centrifuge will indicate the rpm).
Centrifugation Time -	The time should be measured from the time the rotor reaches the required RCF or rpm to the time it begins decelerating.
r_{max} -	Radius of the rotor in millimeters. NOTE: If custom tube adapters (i.e., adapters not defined by the centrifuge manufacturer) are used, then the radius (rmax) should be manually measured in millimeters and the RCF calculated.
g-minutes -	The unit of measure for the product of RCF (× g) and centrifugation time (minutes).

- Transfer clarified specimen to a sample cup or secondary tube for testing. For centrifuged specimens with a lipid layer, transfer only the clarified specimen and not the lipemic material.

Specimen Storage

Specimen storage conditions were verified on the ARCHITECT i System.

Specimen Type	Temperature	Maximum Storage Time	Special Instructions
Serum/ Plasma	Room temperature (15 to 30˚C)	3 days	Specimens may be stored on or off the clot, red blood cells, or separator gel.
	2 to 8˚C	14 days	Specimens may be stored on or off the clot, red blood cells, or separator gel.
Cadaveric	Room temperature (15 to 30˚C)	3 days	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.
	2 to 8˚C	14 days	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.

Specimens may be stored for up to 3 days at room temperature (15 to 30˚C) or 14 days refrigerated at 2-8˚C prior to being tested. If testing will be delayed more than 14 days, the specimens should be removed from the clot, red blood cells, or separator gel and store frozen (-20˚C or colder).

Avoid more than 6 freeze/thaw cycles.

No qualitative differences were observed for cadaveric blood specimens (nonreactive or spiked reactive) when subjected to up to 3 freeze/thaw cycles.

For cadaveric specimens, most antibodies are considered stable for years when stored at -20˚C.[71]

Specimen Shipping

Package and label specimens in compliance with applicable state, federal, and international regulations covering the transport of clinical specimens and infectious substances.

PROCEDURE

Materials Provided

08P07 Alinity i HIV Ag/Ab Combo Reagent Kit

Materials Required but not Provided

- Alinity i HIV Ag/Ab Combo assay file
- 08P0701 Alinity i HIV Ag/Ab Combo Calibrator
- 08P0710 Alinity i HIV Ag/Ab Combo Controls or other control material
- 06P1160 Alinity Trigger Solution
- 06P1265 Alinity Pre-Trigger Solution
- 06P1368 Alinity i-series Concentrated Wash Buffer

For information on materials required for operation of the instrument, refer to the Alinity ci-series Operations Manual, Section 1.

For information on materials required for maintenance procedures, refer to the Alinity ci-series Operations Manual, Section 9.

Assay Procedure

For a detailed description of how to run an assay, refer to the Alinity ci-series Operations Manual, Section 5.

- If using primary or aliquot tubes, refer to the Alinity ci-series Operations Manual, Section 4 to ensure sufficient specimen is present.
- To minimize the effects of evaporation, verify adequate sample cup volume is present prior to running the test.
- Maximum number of replicates sampled from the same sample cup: 10
  - Priority:
    - Sample volume for first test: 150 µL
    - Sample volume for each additional test from same sample cup: 100 µL
  - ≤ 3 hours on the reagent and sample manager:
    - Sample volume for first test: 150 µL
    - Sample volume for each additional test from same sample cup: 100 µL
  - > 3 hours on the reagent and sample manager:
    - Replace with a fresh aliquot of sample.
- Refer to the Alinity i HIV Ag/Ab Combo calibrator package insert and/or Alinity i HIV Ag/Ab Combo control package insert for preparation and usage.
- For general operating procedures, refer to the Alinity ci-series Operations Manual, Section 5.
- For optimal performance, it is important to perform routine maintenance as described in the Alinity ci-series Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Sample Dilution Procedures

Samples cannot be diluted for the Alinity i HIV Ag/Ab Combo assay.

Calibration

For instructions on performing a calibration, refer to the Alinity ci-series Operations Manual, Section 5.

Each assay control must be tested to evaluate the assay calibration.

Once a 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.
- Daily quality control results are outside of statistically-based quality control limits used to monitor and control system performance, as described in the Quality Control Procedures section of this package insert.
  - If statistically-based quality control limits are not available then the calibration should not exceed a 30-day limit for recalibration frequency.

This assay may require recalibration after maintenance to critical parts or subsystems or after service procedures have been performed.

Quality Control Procedures

The recommended control requirement for the Alinity i HIV Ag/Ab Combo assay is that a single sample of each control level 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.

To establish statistically-based control limits, each laboratory should establish its own concentration target and ranges for new control lots at each clinically relevant control level. This can be accomplished by assaying a minimum of 20 replicates over several (3-5) days and using the reported results to establish the expected average (target) and variability about this average (range) for the laboratory. Sources of variation that should be included in this study in order to be representative of future system performance include:

- Multiple stored calibrations
- Multiple reagent lots
- Multiple calibrator lots
- Multiple processing modules (if applicable)
- Data points collected at different times of the day

Refer to published guidelines for information or general control recommendation, for example Clinical and Laboratory Standards Institute (CLSI) Document C24-A3 or other published guidelines, for general quality control recommendations.[72]

- If more frequent control monitoring is required, follow the established quality control procedures for your laboratory.
- If quality control results do not meet the acceptance criteria defined by your laboratory, sample results may be suspect. Follow the established quality control procedures for your laboratory. Recalibration may be necessary. For troubleshooting information, refer to the Alinity ci-series Operations Manual, Section 10.
- Review quality control results and acceptance criteria following a change of reagent or calibrator lot.

Quality Control Guidance

Refer to "Basic QC Practices" by James O Westgard, Ph.D. for guidance on laboratory quality control practices.[73]

Verification of Assay Claims

For protocols to verify package insert claims, refer to Verification of Assay Claims in the Alinity ci-series Operations Manual.

RESULTS

Calculation

The Alinity i analyzer calculates results for the Alinity i HIV Ag/Ab Combo assay using the ratio of the sample RLU to the cutoff RLU (S/CO) for each specimen and control.

Cutoff RLU = Calibrator 1 Mean RLU x 0.40

The cutoff RLU is stored for each reagent lot calibration.

S/CO = Sample RLU/Cutoff RLU

Interpretation of Results

The cutoff is 1.00 S/CO.

Initial Results

S/CO	Instrument Interpretation	Retest Procedure
< 1.00	Nonreactive	No retest required.
≥ 1.00	Reactive	Retest in duplicate.

Final Interpretation

Initial Interpretation	Results with Retest	Final Interpretation
Nonreactive	No retest required.	Nonreactive. HIV p24 Ag and/or HIV-1/HIV-2 Ab not detected.
Reactive	If both retest results are < 1.00	Nonreactive. HIV p24 Ag and/or HIV-1/HIV-2 Ab not detected
	If one or both retest results are ≥ 1.00	Reactive. Presumptive evidence of HIV p24 Ag and/or HIV-1/ HIV-2 Ab; perform a supplemental assay

Reactive specimens should be further tested by a supplemental method.

The Interpretation of Results for specimens with a final result of reactive by the Alinity i 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.

Alinity i HIV Ag/Ab Combo and supplemental assay results should be interpreted in conjunction with the patient's clinical presentation, history, and other laboratory results.

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 Alinity ci-series 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. Alinity i 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.[74, 75]
- Heterophilic antibodies in human serum can react with reagent immunoglobulins, interfering with *in vitro* immunoassays. 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.[76]

SPECIFIC PERFORMANCE CHARACTERISTICS

Representative performance data are provided in this section. Results obtained in individual laboratories may vary.

The Alinity i analyzer and the ARCHITECT i System utilize the same reagents and sample/reagent ratios.

Unless otherwise specified, all studies were performed on the Alinity i analyzer.

Precision

Within-Laboratory Precision

A study was performed based on guidance from CLSI document EP05-A2.[77] Testing was conducted using 3 lots of the Alinity i HIV Ag/Ab Combo Reagent Kit, 3 lots of Alinity i HIV Ag/Ab Combo Calibrator, and 3 lots of Alinity i HIV Ag/Ab Combo Controls and 1 instrument. Four controls and 12 human plasma panels were assayed in a minimum of 2 replicates at 2 separate times per day on 20 different days.

			Within-Run (Repeatability)		Within-Laboratory (Total)[a]	
Sample	n	Mean (S/CO)	SD	%CV	SD (Range[b])	%CV (Range[b])
Negative Control	360	0.07	0.008	11.6	0.015 (0.012-0.018)	21.8 (19.6-23.0)
Positive Control 1	360	4.44	0.108	2.4	0.141 (0.114-0.166)	3.2 (2.6-3.6)
Positive Control 2	359	3.43	0.077	2.2	0.173 (0.111-0.254)	5.0 (3.1-7.6)
Positive Control 3	358	3.14	0.062	2.0	0.087 (0.081-0.095)	2.8 (2.6-2.9)
HIV-1 High Negative Panel	357	0.76	0.024	3.1	0.031 (0.028-0.035)	4.1 (3.8-4.4)
HIV-1 Low Positive Panel	358	1.21	0.033	2.7	0.047 (0.045-0.050)	3.9 (3.8-4.0)

Sample	n	Mean (S/CO)	Within-Run (Repeatability) SD	Within-Run (Repeatability) %CV	Within-Laboratory (Total)[a] SD (Range[b])	Within-Laboratory (Total)[a] %CV (Range[b])
HIV-1 High Positive Panel	357	11.12	0.450	4.1	0.498 (0.472-0.541)	4.5 (4.4-4.6)
HIV-2 High Negative Panel	353	0.75	0.019	2.5	0.029 (0.028-0.031)	3.9 (3.4-4.3)
HIV-2 Low Positive Panel	359	1.09	0.030	2.7	0.044 (0.041-0.047)	4.0 (3.7-4.5)
HIV-2 High Positive Panel	358	13.30	0.359	2.7	0.450 (0.426-0.467)	3.4 (3.2-3.7)
HIV p24 High Negative Panel	360	0.75	0.018	2.4	0.026 (0.025-0.027)	3.5 (3.4-3.5)
HIV p24 Low Positive Panel	360	1.16	0.030	2.6	0.036 (0.031-0.040)	3.1 (2.7-3.3)
HIV p24 Moderate Positive Panel	359	2.48	0.093	3.7	0.104 (0.071-0.148)	4.2 (2.8-6.1)
HIV p24 High Positive Panel	360	10.04	0.195	1.9	0.224 (0.216-0.237)	2.2 (2.1-2.3)
HIV-1 gO High Negative Panel	357	0.75	0.025	3.4	0.036 (0.033-0.038)	4.8 (4.7-4.9)
HIV-1 gO Low Positive Panel	360	1.11	0.037	3.3	0.052 (0.045-0.056)	4.7 (4.3-4.8)

[a] Includes within-run, between-run, and between-day variability.

[b] Maximum and minimum SD or %CV for each reagent lot and instrument combination.

Specificity

A total of 5340 blood donor specimens and 213 hospitalized patient specimens were tested using the Alinity i HIV Ag/Ab Combo assay. Repeatedly reactive samples were further tested by confirmation testing. Seven blood donor specimens were initially reactive, of which 4 were repeat reactive, but could not be confirmed by supplemental testing. The specimens were also tested using commercially-available HIV Ag/Ab assay.

Of the 213 hospitalized patient specimens (HP), 2 specimens were confirmed as HIV positive by supplemental testing. These specimens were excluded from specificity calculation. There was one specimen confirmed falsely reactive for the hospitalized patient specimens.

Category	n	Alinity i HIV Ag/Ab Combo IR (% of Total)	RR (% of Total)	Number Positive by Supplemental Testing (% of RR)	Specificity [a] (95% CI)	Commercially-available HIV Ag/Ab Assay n	Specificity [a] (95% CI)
Blood Donors - Serum	2647	6 (0.23)	3 (0.11)	0 (0.00)	99.89% (2644/2647) (99.67 - 99.98)	2639	99.85% (2635/2639) (99.61 - 99.96)
Blood Donors - Plasma	2693	1 (0.04)	1 (0.04)	0 (0.00)	99.96% (2692/2693) (99.79 - 100.00)	2730	99.96% (2729/2730) (99.80 - 100.00)
Total	5340	7 (0.13)	4 (0.07)	0 (0.00)	99.93% (5336/5340) (99.81 - 99.98)	5369[b]	99.91% (5364/5369) (99.78 - 99.97)
Hospitalized Patients	213	3 (1.41)	3 (1.41)	2 (66.67)	99.53% (210/211) (97.39 - 99.99)	213	99.53% (210/211) (97.39 - 99.99)

IR = Initially Reactive, RR = Repeatedly Reactive, CI = Confidence Interval

[a]Repeatedly reactive specimens determined to be positive by supplemental testing were excluded from these calculations.

[b]None of the 29 specimens additionally tested on the commercially-available HIV Ag/Ab assay were initial reactive.

Sensitivity

A total of 635 positive specimens for HIV-1 group M including subtypes, HIV-1 circulating recombinant forms (CRFs), HIV-1 unique recombinant forms (URFs), HIV-1 group O, and HIV-2 antibodies were tested using the Alinity i HIV Ag/Ab Combo assay and the commercially-available HIV Ag/Ab assay.

Specimen Category	n	Number Reactive	Alinity i HIV Ag/Ab Combo Sensitivity	Commercially-available HIV Ag/Ab Assay Sensitivity
Anti-HIV-1 gM (subtypes A-J, CRF's) [a]	389	389	100.00%	100.00%
Anti-HIV gO	43	43	100.00%	100.00%
Anti-HIV-2	115	115	100.00%	100.00%
HIV-1 Antigen Positive	17	17	100.00%	100.00%
Lysates of Cell Culture Supernatants [b]	71	71	100.00%	100.00%
Total	635	635	100.00%	100.00%

[a] The group/subtype was not determined for 21 specimens.

[b] Includes HIV-1 gM (subtypes A-J, CRF's, and URF's) and gN, gO and gP specimens.

The analytical sensitivity of the Alinity i HIV Ag/Ab Combo assay was evaluated on the Alinity i analyzer. Antigen sensitivity was conducted across 3 lots of Alinity i HIV Ag/Ab Combo Reagent Kit with the WHO International Standard HIV-24 Ag (NIBSC code: 90/636) and the Bio-Rad HIV-1 Antigen Standard. For the HIV-1 p24 Ag, the sensitivity results ranged from 0.53 IU/mL to 0.74 IU/mL. For the Bio-Rad HIV-1 antigen standard, the sensitivity results ranged from 20.41 pg/mL to 20.81 pg/mL.

Seroconversion Sensitivity

To determine the seroconversion sensitivity, 37 seroconversion panels obtained from commercial vendors were tested on the Alinity i analyzer using the Alinity i HIV Ag/Ab Combo assay. Representative data from 5 panels are summarized in the following table. The Alinity i HIV Ag/Ab Combo assay demonstrated acceptable seroconversion detection for the remaining 32 panels.

Panel	Days Since 1st Bleed	Alinity i HIV Ag/Ab Combo (S/CO)	Western Blot[a]	HIV Ag[a] (S/CO)	PCR[a] Copies/mL
PRB941	0	0.10	Neg[b]	0.0	BLD[c]
	4	0.16	Neg	0.0	3000
	9	**1.07**	Neg	**1.4**	50 000
	18	**11.93**	IND[d] (24)	**2.3**	70 000
	21	**11.10**	IND (24)	0.2	10 000
	25	**9.82**	IND (24)	0.1	900
PRB944	0	0.36	Neg[b]	0.0	7000
	2	**1.61**	Neg	0.9	80 000
	7	**15.96**	Neg	**10.9**	> 800 000
	9	**14.72**	Neg	**12.6**	> 800 000
	14	**22.13**	IND[d] (24)	**8.7**	600 000
	16	**28.24**	Pos (24, 160)	**3.3**	300 000
PRB961	0	0.09	IND[d] (f24[e])	0.3	< 50
	5	0.09	IND (f24)	0.3	< 50
	7	0.08	IND (f24)	0.3	< 50
	12	0.07	IND (f24)	0.3	< 50
	14	0.08	IND (f24, f160)	0.3	< 50
	19	0.09	IND (f24)	0.4	< 50
	21	0.10	IND (f24)	0.5	480
	27	**7.55**	IND (f24)	**11.4**	150 000
	29	**24.25**	IND (f24)	**28.4**	200 000
PRB966	0	0.07	Neg[b]	0.2	< 50
	2	0.07	Neg	0.3	< 50
	20	0.06	Neg	0.3	< 50
	22	0.07	Neg	0.2	< 50
	30	0.06	Neg	0.2	< 50
	35	0.09	Neg	0.2	340
	37	0.09	Neg	0.3	1900
	44	**1.39**	Neg	**4.3**	280 000
	48	**2.33**	Neg	**1.8**	48 000
	51	**14.90**	Neg	**2.2**	82 000
9016	0	0.08	Neg	0.05	< 50
	31	0.07	Neg	0.79	< 50
	36	0.07	Neg	0.05	< 50
	38	0.07	Neg	0.05	< 50
	44	0.07	Neg	0.07	< 50
	47	0.08	Neg	0.08	< 50
	52	0.06	Neg	0.05	< 50
	56	0.28	Neg	0.32	7473
	59	**1.94**	Neg	**3.36**	69 010
	63	**11.03**	Neg	**13.22**	286 400

[a] Data from the vendor.

[b] Neg = no band or bands being observed

[c] BLD = Below Limit of Detection

[d] IND = indeterminant

[e] f24 = faint p24 antigen band

Other Disease States

This study was performed on the ARCHITECT i System.

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 322 specimens containing interfering substances (IS), 12 IS specimens were confirmed as having HIV infection by confirmation testing. These specimens were excluded from the study. Of the remaining 310 specimens, 1 was a repeat reactive by ARCHITECT HIV Ag/Ab Combo. The results demonstrated a specificity of 99.68%. 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).

Interference

This study was performed on the ARCHITECT i System.

Potentially Interfering Endogenous Substances

No qualitative performance differences were observed between experimental controls and more than 20 nonreactive or more than 20 spiked reactive specimens when tested with elevated levels of the compounds listed in the table below.

Potentially Interfering Substance	Interferent Level
Bilirubin	≤ 20 mg/dL
Triglycerides	≤ 3000 mg/dL
Protein	≤ 12 g/dL
Hemoglobin	≤ 500 mg/dL

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Note for number formatting:

- A space is used as thousands separator (example: 10 000 specimens).
- A period is used to separate the integer part from the fractional part of a number written in decimal form (example: 3.12%).

Key to Symbols

	Consult instructions for use
	Manufacturer
	Sufficient for
	Temperature limitation
	Use by/Expiration date
ASSAY DILUENT	Assay Diluent
CONJUGATE	Conjugate
CONTAINS: AZIDE	Contains Sodium Azide. Contact with acids liberates very toxic gas.
INVERSIONS PERFORMED	Inversions Performed
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRODUCT OF GERMANY	Product of Germany
REAGENT LOT	Reagent Lot
REF	List Number
SN	Serial number

Abbott GmbH & Co. KG
Max-Planck-Ring 2
65205 Wiesbaden
Germany
+49-6122-580

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