Alinity s

HIV Ag/Ab Combo Reagent Kit
Human Immunodeficiency Virus Types 1 and 2 (E coli, B megaterium Recombinant) Antigen, Antibody (p24) and Synthetic Peptides

en
HIV Combo
06P01
G92052R02
B6P0Y0

Read Highlighted Changes: Revised March 2020.

REF 06P0160

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

NAME

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

Human Immunodeficiency Virus Types 1 and 2 (*E coli, B megaterium* Recombinant) Antigen, Antibody (p24) and Synthetic Peptides

INTENDED USE

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

The Alinity s HIV Ag/Ab Combo assay is intended to screen individual human donors, including volunteer donors of whole blood and blood components, and other living donors for the presence of anti-HIV-1/HIV-2 and HIV-1 p24 antigen. The assay is also intended for use in testing serum and plasma specimens to screen organ donors when specimens are obtained while the donor's heart is still beating, and in testing serum specimens to screen cadaveric (non-heart-beating) donors. It is not intended for use on cord blood specimens.

SUMMARY AND EXPLANATION OF THE TEST

Acquired immunodeficiency syndrome (AIDS) is caused by 2 types of human immunodeficiency viruses, HIV type 1 (HIV-1) and HIV type 2 (HIV-2). Collectively, these 2 types of human immunodeficiency virus are designated HIV.[1-4] HIV is a major global health issue, accounting for more than 32 million deaths globally to date. In 2018, there were approximately 37.9 million people living with HIV, 1.7 million people were newly infected, and 770 000 people died from HIV-related causes.[5]

HIV is a member of the genus lentivirus in the family *Retroviridae*.[1, 2, 6] Retroviruses use a viral encoded reverse transcriptase to transcribe viral RNA into DNA. The use of an error prone reverse transcriptase for viral replication leads to high mutation rates and recombination which are the drivers of HIV genetic diversity.[6, 7]

HIV-1 is classified into 4 groups: M (major), N (non-M, non-O), O (outlier), and P.[8-12] HIV-1 group M is composed of genetic subtypes (A, B, C, D, F, G, H, J, K, and L), circulating recombinant forms (CRFs), and unique recombinant forms (URFs).[7, 10, 13, 14]

HIV-1 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, CRFs, and URFs vary.[13, 15] HIV-1 subtype B is globally widespread in most parts of the world.[13, 15, 16] The prevalence of non-subtype B strains is on the rise across the USA, and a significant percentage of new HIV-1 infections in Europe are caused by non-B subtype strains.[16-18] HIV-1 groups N, O, and P are endemic to west central Africa and are relatively rare.[8, 9, 11, 12, 19, 20] However, group O infections have been identified in Europe and the USA.[18, 21, 22]

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 composed of 8 genetic subtypes (A, B, C, D, E, F, G and H).[23]

HIV-2 infections have lower transmission rates, lower viral titers, and a longer latency period with slower disease progression than HIV-1.[24] HIV-2 is endemic to West Africa, and international spread has been limited.[24-26] HIV-2 infections have been identified in North America and Europe at a low prevalence compared to HIV-1.[18, 24-26]

HIV is transmitted by sexual contact, exposure to blood or blood products, and prenatal or perinatal infection of a fetus or newborn.[25]

During early infection, the first marker to be detected in HIV infected individuals is the HIV RNA followed several days later by the HIV-1 core protein p24 antigen. Several days after the appearance of the HIV-1 p24 antigen, antibodies against HIV are detectable.[27] HIV RNA levels peak prior to antibody seroconversion, and then decline to steady state levels. HIV-1 p24 antigen levels also peak prior to seroconversion and then become undetectable consistent with the immune complexing of the antigen with the emerging antibodies.[27] After seroconversion, antibodies against HIV are nearly always detected in HIV infected asymptomatic individuals and AIDS patients.[27, 28]

HIV antigen and antibody combination assays are used to identify individuals infected with HIV and to prevent transmission of the virus to recipients of blood, blood components, cells, tissues, and organs. In addition, these assays are used as an aid in the diagnosis of HIV infection. Alinity s HIV Ag/Ab Combo uses HIV-1 p24 antibodies as reagents to detect HIV-1 p24 antigen prior to seroconversion, thereby decreasing the seroconversion window and improving early detection of HIV infection. The assay also detects antibodies to HIV-1 groups M and O, and HIV-2.

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

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

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

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

The presence or absence of HIV-1 p24 antigen and/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 s System Operations Manual, Section 3.

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REAGENTS

Kit Contents

Alinity s HIV Ag/Ab Combo Reagent Kit 06P01

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

REF	06P0160
Tests per cartridge	500
Number of cartridges per kit	10
Tests per kit	5000
MICROPARTICLES	27.0 mL
CONJUGATE	26.5 mL
ASSAY DILUENT	26.7 mL

MICROPARTICLES HIV-1/HIV-2 antigen and HIV-1 p24 antibody (mouse IgG, monoclonal) coated microparticles in TRIS buffered saline. Minimum concentration: 0.07% solids. Preservative: sodium azide.

CONJUGATE HIV-1 antigens, HIV-1/HIV-2 synthetic peptides, and HIV-1 p24 antibody (mouse IgG, monoclonal) acridinium-labeled conjugate in phosphate buffer with protein (bovine) stabilizer and surfactant. Minimum concentration: 61.518 ng/mL. Preservative: sodium azide.

ASSAY DILUENT TRIS buffer with protein (mouse serum and IgG) stabilizer and surfactant. Preservative: sodium azide.

Warnings and Precautions

- IVD
- For *In Vitro* Diagnostic Use
- Performance characteristics of this product have not been established for laboratory diagnosis of HIV-1/HIV-2 infection.

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.[29-32]

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.
P332+P313	If skin irritation occurs: Get medical advice / attention.
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.transfusion.abbott or contact your local representative.

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

Reagent Handling

- Do not invert reagent cartridges.
- Upon receipt, reagent cartridges can be used immediately or stored in an upright position.
- 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 s System Operations Manual, Section 7.

Reagent Storage

- Do not freeze.

	Storage Temperature	Maximum Storage Time	Additional Storage Instructions
Unopened	2 to 8°C	Until expiration date	Store in upright position.
Opened	2 to 15°C	15 days after opening*	Store in upright position. Discard after 15 days. If cartridge does not remain upright during storage off the system, discard the cartridge. Do not reuse original reagent caps or replacement caps due to the risk of contamination and the potential to compromise reagent performance.

* Includes time on board the system.

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 15°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 s System 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 s System Operations Manual, Section 10.

INSTRUMENT PROCEDURE

The Alinity s HIV Ag/Ab Combo Assay File must be installed on the Alinity s System prior to performing the assay.

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

For information on printing assay parameters, refer to the Alinity s System Operations Manual, Section 5.

For a detailed description of system procedures, refer to the Alinity s System Operations Manual.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

Specimen Types

The specimen types listed below were verified for use with this assay.

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

Specimen Types	Anticoagulants
Serum (including serum separator tubes)	Not Applicable
Plasma	Dipotassium EDTA (including plasma preparation tubes)
	Tripotassium EDTA
	Lithium heparin (including plasma separator tubes)
	Sodium citrate
	Sodium heparin
	ACD-A
	ACD-B
	CP2D
	CPD
	CPDA-1

- Liquid anticoagulants may have a dilution effect resulting in lower S/CO values for individual specimens.
- Performance has not been established for the use of umbilical cord blood or bodily fluids such as urine, saliva, semen, amniotic fluid, cerebrospinal fluid, or pleural fluid.
- Performance has been established for the use of cadaveric serum specimens (including specimens collected post-mortem, non-heart-beating) that have been collected up to 24 hours after death.[33] Follow general standards and/or regulations for collection, storage, and handling.
- Performance has not been established for the use of cadaveric plasma specimens.
- Testing of cadaveric serum 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 has not been verified.
- The system 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 with the assay.

Specimen Conditions

- Do not use:
  - heat-inactivated specimens
  - pooled specimens
  - grossly hemolyzed specimens
  - specimens with obvious microbial contamination
  - specimens with fungal growth
- For accurate results, serum and plasma specimens should be free of fibrin, red blood cells, and other particulate matter.
- To prevent cross contamination, use of disposable pipettes or pipette tips is recommended.

Preparation for Analysis

Failure to follow the specified centrifugation procedure may give erroneous or inconsistent test results.

- Clear, nonhemolyzed specimens should be used when possible. Specimens containing visible particulate matter may give erroneous or inconsistent test results.
- 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.
- Prior to centrifugation, previously frozen specimens (including previously frozen plasmapheresis specimens) must be mixed gently and thoroughly after thawing.
- Specimens collected by plasmapheresis, which have not been frozen, do not require centrifugation. All other specimens (including previously frozen plasmapheresis specimens) must be centrifuged between 30 000 - 75 000 g-minutes.
- All specimens must be tested or retested within 48 hours of initial centrifugation. After 48 hours, these specimens need to be recentrifuged between 30 000 - 75 000 g-minutes.

The acceptable time and force ranges that meet this criterion are listed in the table below.

Centrifugation Time (Minutes)	RCF (x g)	g-Minutes
10	3000	30 000
15	2000 - 3000	30 000 - 45 000
20	1500 - 3000	30 000 - 60 000
25	1300 - 3000	32 500 - 75 000

Convert rpm to RCF as follows: $RCF = 1.12 \times r_{max} (rpm/1000)^2$

Convert RCF to rpm as follows:

$$rpm = 1000 \times \sqrt{\frac{RCF}{1.12 \times r_{max}}}$$

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. The radius measured is dependent on whether the rotor is a fixed angle rotor or a swinging bucket rotor. This value is typically provided with the rotor by the manufacturer. For the fixed angle rotor, r_{max} is the measure of the distance from the rotor axis (center) to the bottom of the specimen tube in the rotor or rotor adapter. For the swinging bucket rotor, r_{max} is the measure of the distance from the rotor axis (center) to the bottom of the specimen tube in the rotor adapter or bucket at full extension.

NOTE: If custom tube adapters (i.e., adapters not defined by the centrifuge manufacturer) are used, then the radius (r_{max}) 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).

Specimen Storage

Specimen Type	Temperature	Maximum Storage Time	Special Instructions
Living Donor Serum/ Plasma	Room temperature (15 to 30°C)	7 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.
	-20°C or colder	3 months	Remove serum or plasma from the clot, red blood cells, or separator gel.

- Living donor specimens stored at -20°C or colder for greater than 3 months may be used for informational purposes (*e.g.*, lookback testing, discordant sample testing, clinical and validation testing).
- Storage at a combination of 15 to 30°C and 2 to 8°C may not exceed 14 days (inclusive of shipping time) and cannot exceed the maximum durations listed in the table above.
- Performance has not been established for living donor specimens that have undergone more than 6 freeze/thaw cycles.

Specimen Type	Temperature	Maximum Storage Time	Special Instructions
Cadaveric Serum	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.
	-20°C or colder	3 months	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.

- Performance has not been established using cadaveric specimens stored at -20°C or colder for greater than 3 months.
- Storage at a combination of 15 to 30°C and 2 to 8°C may not exceed 14 days (inclusive of shipping time) and cannot exceed the maximum durations listed in the table above.
- Performance has not been established for cadaveric specimens that have undergone more than 6 freeze/thaw cycles.

Specimen Shipping

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

PROCEDURE

Materials Provided

06P01 Alinity s HIV Ag/Ab Combo Reagent Kit

Materials Required but not Provided

- Alinity s HIV Ag/Ab Combo Assay File
- 06P0103 Alinity s HIV Ag/Ab Combo Calibrator Kit
- 06P0120 Alinity s HIV Ag/Ab Combo Assay Control Kit
- 06P0124 Alinity s HIV Ag/Ab Combo Release Control Kit
- Alinity Trigger Solution
- Alinity Pre-Trigger Solution
- Alinity s Concentrated Wash Buffer

For information on materials required for operation of the system, refer to the Alinity s System Operations Manual, Section 1.

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

Assay Procedure

For a detailed description of how to run an assay, refer to the Alinity s System Operations Manual, Section 5.

- Primary tubes may be on board the system for up to 10 hours.
- If using primary or aliquot tubes, refer to the Alinity s System 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

  ≤ 3 hours on the reagent and sample manager:
  - Sample volume for first test: 300 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 s HIV Ag/Ab Combo Calibrator Kit, Assay Control Kit, and/or Release Control Kit package inserts for preparation and usage.
- For general operating procedures, refer to the Alinity s System Operations Manual, Section 5.
- For optimal performance, it is important to perform routine maintenance as described in the Alinity s System Operations Manual, Section 9. Perform maintenance more frequently when required by laboratory procedures.

Calibration

For instructions on performing a calibration, refer to the Alinity s System Operations Manual, Section 5.

Three replicates of Alinity s HIV Ag/Ab Combo Calibrator 1 are automatically tested by the system. The calibrator must be priority loaded.

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

Once a calibration is accepted and stored, it may be used for 14 days. During this time, 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 quality control limits used to monitor and control system performance.

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

Quality Control Procedures

Assay Controls

The Alinity s HIV Ag/Ab Combo Assay Controls must be tested once every 24 hours when the system is being used.

Assay control values must be within the ranges specified in the Alinity s HIV Ag/Ab Combo Assay Control Kit package insert. When the assay control values are within range, sample results are generated, and a valid release control result is required to release test results. If an assay control value is not within range, sample results are not generated for in-process or scheduled samples. For troubleshooting information, refer to the Alinity s System Operations Manual, Section 10.

Release Controls

The Alinity s HIV Ag/Ab Combo Release Control must be tested in order to release test results.

The release control is tested at user-defined intervals. For configuring the release control, refer to the Alinity s System Operations Manual, Section 2. For manually ordering the release control, refer to the Alinity s System Operations Manual, Section 5.

The release control must meet specifications defined in the Alinity s HIV Ag/Ab Combo Release Control Kit package insert in order to validate the system functionality and release test results. If the release control does not meet specifications, refer to the Alinity s System Operations Manual, Section 10, for additional information.

Other Controls

Additional controls may be tested at operator's discretion in accordance with local, state, and/or federal regulations or accreditation requirements and your laboratory's quality control policy. For additional information on configuring customer controls, refer to the Alinity s System Operations Manual, Section 2.

Invalidate controls: Additional controls may be tested anywhere within a run as an invalidate control. Specifications may be assigned to invalidating controls. If an invalidate control fails to meet assigned specifications, no sample results are calculated or provided by the system. When an invalidate control meets assigned specifications, sample processing continues, and a valid release control result is required to release test results.

Non-validating controls: Additional controls may be tested anywhere within a run as a non-validating control. Specifications may be assigned to non-validating controls. A valid release control result is required to release test results. If the user-assigned specifications for the non-validating control(s) are not met and the release control specifications are met, there will be no effect on sample processing. In this case, reactive sample results must not be considered invalid.

Quality Control Guidance

Refer to "Basic QC Practices" by James O Westgard, Ph.D. for guidance on laboratory quality control practices.[34]

RESULTS

Calculation

The Alinity s System calculates results for the Alinity s 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

Initial Result (S/CO)	Interpretation	Retest Procedure
< 1.00	Nonreactive	No retest required. Specimen considered negative for HIV-1 p24 antigen and antibodies to HIV-1 and HIV-2.
≥ 1.00	Reactive	Retest in duplicate.

Final Interpretation

Retest Results (S/CO)	Final Results	Final Interpretation
Both results < 1.00	Nonreactive	Specimen considered negative for HIV-1 p24 antigen and antibodies to HIV-1 and HIV-2.
One or both results ≥ 1.00	Repeatedly Reactive	Specimen should be further tested by supplemental methods.

Supplemental methods should follow appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive.

Customers outside the US must follow their country's government recommendations and regulations for specimens found to be repeatedly reactive.

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 s System Operations Manual, Section 5.

LIMITATIONS OF THE PROCEDURE

- Potential interference has not been evaluated for substances other than those described in the **SPECIFIC PERFORMANCE CHARACTERISTICS - Interference** section of this package insert.
- False reactive results can be expected with any test kit. Falsely elevated results may be observed due to non-specific interactions (refer to the **SPECIFIC PERFORMANCE CHARACTERISTICS** section of this package insert).
- The Alinity s HIV Ag/Ab Combo assay does not discriminate between HIV-1 p24 antigen and HIV-1 or HIV-2 antibody reactivity.
- The presence of HIV-1 p24 antigen or HIV-1/HIV-2 antibodies is not a diagnosis of AIDS. It is recommended that repeatedly reactive specimens be investigated by supplemental testing. Individuals who are repeatedly reactive should be referred for medical evaluation which may include additional testing.
- Although the association of infectivity and the presence of HIV-1 p24 antigen or HIV-1/HIV-2 antibodies is strong, it is recognized that presently available methods for HIV-1 p24 antigen and HIV-1/HIV-2 antibody detection are not sensitive enough to detect all potentially infectious units of blood or possible cases of HIV infection. A nonreactive test result does not exclude infection.

Refer to the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert for specimen limitations.

SPECIFIC PERFORMANCE CHARACTERISTICS

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

Reproducibility

A study was performed based on guidance from CLSI EP15-A2.[35] Testing was conducted using 3 lots of the Alinity s HIV Ag/Ab Combo Reagent Kit, Calibrator Kit, Assay Control Kit, and Release Control Kit. Panel members and controls were tested twice a day for 5 days in replicates of 4 at 3 sites.

		Mean	Within-Run		Between-Run		Between-Day		Within-Laboratory[a]		Between-Site		Between-Lot		Reproducibility[b]	
Sample	N	S/CO	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
Low HIV-1 Group M Antibody	360	1.69	0.060	3.5	0.029	1.7	0.024	1.4	0.071	4.2	0.089	5.2	0.057	3.3	0.127	7.5
High HIV-1 Group M Antibody	360	8.92	0.305	3.4	0.107	1.2	0.000	0.0	0.323	3.6	0.498	5.6	0.320	3.6	0.676	7.6
Low HIV-2 Antibody	360	1.71	0.058	3.4	0.000	0.0	0.024	1.4	0.063	3.7	0.086	5.1	0.162	9.5	0.194	11.4
High HIV-2 Antibody	360	9.07	0.300	3.3	0.000	0.0	0.118	1.3	0.322	3.5	0.442	4.9	0.808	8.9	0.976	10.8
Low HIV-1 Group O Antibody	360	1.64	0.055	3.4	0.002	0.2	0.030	1.8	0.063	3.8	0.063	3.8	0.178	10.9	0.199	12.2
Low HIV-1 p24 Antigen	360	1.76	0.047	2.7	0.000	0.0	0.012	0.7	0.049	2.8	0.035	2.0	0.011	0.6	0.061	3.5
High HIV-1 p24 Antigen	360	8.89	0.222	2.5	0.084	0.9	0.000	0.0	0.238	2.7	0.195	2.2	0.042	0.5	0.311	3.5
Positive Control 1	359[c]	2.99	0.103	3.4	0.025	0.8	0.028	0.9	0.109	3.6	0.118	3.9	0.127	4.3	0.205	6.8
Positive Control 2	360	2.30	0.071	3.1	0.000	0.0	0.026	1.2	0.076	3.3	0.076	3.3	0.219	9.5	0.244	10.6
Positive Control 3	360	2.72	0.077	2.8	0.020	0.7	0.016	0.6	0.081	3.0	0.025	0.9	0.030	1.1	0.090	3.3
Positive Control 4	360	1.92	0.076	3.9	0.000	0.0	0.014	0.7	0.077	4.0	0.045	2.3	0.183	9.6	0.204	10.6
Negative Control	360	0.08	0.013	NA	0.003	NA	0.000	NA	0.014	NA	0.007	NA	0.008	NA	0.018	NA

%CV = Coefficient of Variation expressed as a percentage; N = Number of Replicates; NA = Not Applicable: %CVs are not meaningful when S/CO approaches zero; SD = Standard Deviation

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

[b] Includes within-run, between-run, between-day, between-site, between-lot and the site-lot interaction variability.

[c] One replicate was missing due to a wash zone aspiration failure.

Specificity

A total of 7347 fresh serum specimens and 6511 fresh plasma specimens from volunteer whole blood donors were collected at 3 distinct blood centers. A total of 3138 specimens from plasmapheresis donors were collected at one additional blood center. The initial and repeat reactive rates for the serum specimens were 0.08% (6/7347) and 0.07% (5/7347), respectively. The initial and repeat reactive rates for the plasma specimens were 0.09% (6/6511) and 0.09% (6/6511), respectively. The initial and repeat reactive rates for the plasmapheresis donor specimens were 0.10% (3/3138) and 0.10% (3/3138), respectively. Repeatedly reactive specimens were further tested using the following supplemental assays: HIV-1 qualitative RNA assay, HIV-1 Western blot/HIV-1 IFA, HIV-2 EIA, and HIV-1/2 immunochromatographic assay. Based on supplemental test results, 13 specimens were negative, and 1 specimen was indeterminate.

Specificity based on assumed zero prevalence of antigen/antibody to HIV in whole blood and plasmapheresis donors was estimated in this study to be 99.92% (16 981/16 994) with a 95% confidence interval of 99.87% to 99.96%.

Specimen Category	Number Tested	IR (% of Total) (95% CI)	RR (% of Total) (95% CI)	Number Positive by Supplemental Testing (% of RR)	Specificity (%)[a] (95% CI)
Volunteer Blood Donors - Serum	7347	6 (0.08) (0.03 - 0.18)	5 (0.07) (0.02 - 0.16)	0 (0.00)	99.93 (7342/7347) (99.84 - 99.98)
Volunteer Blood Donors - Plasma	6511	6 (0.09) (0.03 - 0.20)	6 (0.09) (0.03 - 0.20)	0 (0.00)	99.91 (6504/6510) (99.80 - 99.97)
Total Volunteer Blood Donors	**13 858**	**12 (0.09) (0.04 - 0.15)**	**11 (0.08) (0.04 - 0.14)**	**0 (0.00)**	**99.92 (13 846/13 857) (99.86 - 99.96)**
Plasmapheresis Donors	3138	3 (0.10) (0.02 - 0.28)	3 (0.10) (0.02 - 0.28)	0 (0.00)	99.94 (3135/3137) (99.77 - 99.99)
Total Donors	**16 996**	**15 (0.09) (0.05 - 0.15)**	**14 (0.08) (0.05 - 0.14)**	**0 (0.00)**	**99.92 (16 981/16 994) (99.87 - 99.96)**

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

[a] Based on supplemental test results for the 14 repeatedly reactive specimens, 1 specimen was indeterminate (plasmapheresis donor) and 13 specimens were negative (5 blood donor serum, 6 blood donor plasma, and 2 plasmapheresis donors). The 1 repeatedly reactive specimen found to be indeterminate by supplemental testing was excluded from the specificity calculations. One additional Alinity s HIV Ag/Ab Combo nonreactive specimen was indeterminate (blood donor plasma) by supplemental testing and was excluded from the specificity calculations.

For total donors, the IR rate not reactive on retest was estimated to be 0.01% (1/16 982) with a 95% confidence interval of 0.00% to 0.03%.

IR Rate Not Reactive on Retest = 100% x (Number of IR – Number of RR) / (Number Tested – Number of RR)

Sensitivity

A total of 2476 specimens from the categories shown in the table below were tested using the Alinity s HIV Ag/Ab Combo assay at 3 clinical sites. Repeatedly reactive specimens from individuals at increased risk of HIV-1/2 infection and individuals at increased risk of HIV infection from HIV-2 endemic areas were tested using the following supplemental assays: HIV-1 qualitative RNA assay, HIV-1 IFA, and HIV-1/2 immunochromatographic assay.

Sensitivity was estimated to be 100.00% (1336/1336) with a 95% confidence interval of 99.72% to 100.00% for preselected positive specimens and HIV-1 viral isolates.

			Alinity s HIV Ag/Ab Combo		
Specimen Category	Number Tested	Number Positive	Number RR (% of Total)	Number RR that were Positive (% of RR)	Sensitivity (%) (95% CI)
Preselected Anti-HIV-1 Positive[a]	1016	1016	1016 (100.00)	1016 (100.00)	100.00 (1016/1016) (99.64 - 100.00)
Preselected Anti-HIV-2 Positive[b]	232	232	232 (100.00)	232 (100.00)	100.00 (232/232) (98.42 - 100.00)
Preselected HIV-1 Antigen Positive[c]	35	35	35 (100.00)	35 (100.00)	100.00 (35/35) (90.00 - 100.00)
HIV-1 Viral Isolates[d]	53	53	53 (100.00)	53 (100.00)	100.00 (53/53) (93.28 - 100.00)
Subtotal	**1336**	**1336**	**1336 (100.00)**	**1336 (100.00)**	**100.00 (1336/1336) (99.72 - 100.00)**
Individuals at Increased Risk of HIV-1/2 Infection[g]	605	21	23 (3.80)	21 (91.30)	NA[i]
Individuals at Increased Risk of HIV Infection from HIV-2 Endemic Areas[f]	535	49[g]	61[h] (11.40)	49 (80.33)	100.00 (49/49) (92.75 - 100.00)
Total	**2476**	**1406**	**1420 (57.35)**	**1406 (99.01)**	**100.00 (1406/1406) (99.74 - 100.00)**

NA = Not Applicable; RR = Repeatedly Reactive; CI = Confidence Interval

[a] Specimens were confirmed positive for HIV-1 antibody by HIV-1 Western blot. The preselected anti-HIV-1 positive category included 488 specimens from individuals with stage 1 HIV infection, 427 specimens from individuals with stage 2 HIV infection and 101 specimens from individuals with stage 3 HIV infection.

[b] The preselected anti-HIV-2 positive specimens were confirmed positive for HIV-2 antibody by HIV-2 Western blot and differentiated by a rapid enzyme immunoassay that differentiates HIV-1 and HIV-2.

[c] All 35 specimens were HIV-1 p24 antigen positive; 32 were Western blot negative and 3 were Western blot indeterminate.

[d] 53 unique viral isolates that were propagated in cell culture and classified as HIV-1 group M (subtypes A, B, C, D, F, G, H, J, CRF01, CRF02, CRF06, and URFs), HIV-1 group N, HIV-1 group O, and HIV-1 group P.

[e] The following risk factors were included: diagnosed or treated for a sexually transmitted disease, heterosexual contact with a high-risk individual, heterosexual contact with an infected individual, history of incarceration, intravenous drug user, men who have sex with men, multiple sex partners, and sexual contact with HIV infected individual.

[f] The following risk factors were included: intravenous drug user, multiple sex partners, and unprotected sex with an HIV infected individual. Individuals from HIV-2 endemic areas included specimens from the following areas: Ivory Coast (285) and Sierra Leone (250).

[g] The 49 specimens that were positive by supplemental testing included 32 anti-HIV-1 positive specimens, 2 anti-HIV-2 positive specimens, 6 anti-HIV-2 positive with anti-HIV-1 cross-reactivity specimens, and 9 undifferentiated anti-HIV positive specimens.

[h] Of the 61 repeatedly reactive specimens, 49 were positive, 10 were indeterminate, and 2 were negative by supplemental testing.

[i] The sensitivity calculation and confidence interval are not meaningful due to the small number of specimens.

Group and Subtype Detection

A total of 532 specimens known to be positive for anti-HIV-1 and HIV-1 p24 antigen were evaluated using the Alinity s HIV Ag/Ab Combo assay. All anti-HIV-1 subtype positive (subtypes A-D, F-H, and J-[illegible]), anti-HIV-1 groups (N, O, P), and anti-HIV-1 URF subtype samples were detected by the Alinity s HIV Ag/Ab Combo assay. Additionally, all HIV-1 antigen subtype positive (subtypes B, C, and CRF02) samples (human) and a panel of 100 antigen samples from viral isolates derived from tissue culture supernatants were tested and were detected. The panel of viral isolates represented HIV-1 group M (subtypes A-D, F-H, and J, URFs, and CRFs) and groups N, O, and P.

Analytical Sensitivity

Analytical sensitivity was evaluated using dilutions of the WHO 1st International Standard for HIV-1 p24 Antigen, NIBSC code: 90/636. The dilutions ranged from 0.50 to 4.00 IU/mL. The dilutions were tested across 3 lots of the Alinity s HIV Ag/Ab Combo Reagent Kit on 1 Alinity s System. The analytical sensitivity results on the Alinity s HIV Ag/Ab Combo assay ranged from 0.80 to 0.83 IU/mL.

Seroconversion Sensitivity

To determine the seroconversion sensitivity, 20 seroconversion panels obtained from commercial vendors were tested on the Alinity s System using the Alinity s HIV Ag/Ab Combo assay. The results were compared to a commercially available HIV-1/HIV-2 assay and representative data from 5 panels are summarized in the following table.

Panel ID	Days Since 1st Bleed	Alinity s HIV Ag/Ab Combo Reactive ≥ 1.00 S/CO	Commercially-Available Anti-HIV-1/HIV-2 Assay Reactive ≥ 1.00 S/CO
PRB953	0	0.14	0.41
	3	0.66	0.63
	7	**9.51**	0.86
	10	**33.97**	**20.59**
PRB955	0	0.12	0.36
	3	**1.78**	0.31
	7	**13.53**	0.71
	12	**28.71**	**41.73**
	14	**37.99**	**55.95**
PRB958	0	0.27	0.30
	2	0.09	0.32
	7	**2.89**	0.29
	9	**8.12**	0.33
	15	**33.61**	**10.79**
	17	**39.14**	**29.92**
HIV 9018	0	0.10	0.36
	4	0.10	0.37
	7	0.11	0.36
	11	0.10	0.34
	14	0.11	0.38
	18	0.10	0.33
	21	0.11	0.34
	25	0.86	0.52
	28	**7.88**	0.54
	32	**21.32**	**6.00**
	35	**38.66**	**26.45**

Panel ID	Days Since 1st Bleed	Alinity s HIV Ag/Ab Combo Reactive ≥ 1.00 S/CO	Commercially-Available Anti-HIV-1/HIV-2 Assay Reactive ≥ 1.00 S/CO
HIV 9022	0	0.07	0.34
	3	0.09	0.33
	7	0.08	0.32
	10	0.12	0.34
	15	0.07	0.35
	17	0.09	0.32
	23	0.89	0.49
	25	8.81	0.35
	32	292.67	8.01

Other Specimen Conditions or Disease States

A total of 242 specimens from individuals with other specimen conditions or disease states unrelated to HIV infection were evaluated. All 242 specimens were nonreactive using the Alinity s HIV Ag/Ab Combo assay.

Category	Number Tested	IR (% of Total)	RR (% of Total)	Number Positive by Supplemental Testing (% of Repeatedly Reactive)
Other Specimen Conditions or Disease States[a]	242	0 (0.00)	0 (0.00)	Not applicable

IR = Initially Reactive; RR = Repeatedly Reactive

[a] The specimens included the following: Anti-HTLV I/II Positive (10), Anti-HCV Positive (10), HBV Positive (10), Anti-HAV Positive (10), Co-infected CMV/EBV/HSV (10), Anti-*T pallidum* Positive (10), Rheumatoid Factor Positive (10), Anti-ds DNA Positive (10), Pregnant Females (14), Multiparous Females (10), Hyper IgG/IgM (10), Influenza Vaccine Recipient (10), Hemodialysis Patients (10), HAMA Positive (10), *E coli* Infection (10), Heterophilic Antibody Positive (8), Anti-gonococcus Positive (10), Anti-*C trachomatis* Positive (10), Anti-*T gondii* Positive (10), Fungal (Yeast) Infection (10), Anti-nuclear Antibody Positive (10), Crohn's Disease (10), Anti-VZV Positive (10), and Anti-rubella Positive (10).

Interference

Potentially Interfering Endogenous Substances

A study was performed based on guidance from CLSI EP07-A2.[36]

No interference was observed using the Alinity s HIV Ag/Ab Combo assay from potentially interfering substances at the levels shown below.

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

In addition, a negative control, an anti-HIV-1 positive control, and an HIV-1 antigen positive control were spiked with biotin to a concentration of 4250 ng/mL. No interference was observed using the Alinity s HIV Ag/Ab Combo assay.

The effect of potentially interfering substances has only been evaluated for those listed in this package insert.

PERFORMANCE CHARACTERISTICS OF CADAVERIC SPECIMEN TESTING

Reproducibility

Twenty-three cadaveric donor serum specimens and 23 living donor serum specimens were spiked with human plasma reactive for anti-HIV-1 group M, anti-HIV-1 group O, anti-HIV-2, or HIV-1 p24 antigen to create low-level reactive specimens.

Each specimen was tested once per day for 6 days using each of 3 lots of the Alinity s HIV Ag/Ab Combo Reagent Kit. Total %CV values were determined.

Analyte	Specimen Category	Number of Replicates	Mean S/CO	Total[a] SD	Total[a] %CV
Anti-HIV-1 Group M	Cadaveric[b]	414	5.28	0.439	8.3
	Living Donor	414	4.86	0.442	9.1
Anti-HIV-1 Group O	Cadaveric[b]	414	4.36	0.551	12.6
	Living Donor	414	4.31	0.583	13.5
Anti-HIV-2	Cadaveric[b]	414	3.49	0.228	6.5
	Living Donor	414	3.52	0.213	6.0
HIV-1 p24 Antigen	Cadaveric[b]	414	3.94	0.286	7.3
	Living Donor	414	4.00	0.175	4.4

[a] Total variability contains within-specimen, between-lot and lot-specimen interaction variance components.

[b] Cadaveric serum specimens were collected up to 21.6 hours after death.

Specificity

Specificity was determined by testing 55 cadaveric serum specimens and 55 living donor serum specimens. Each specimen was tested once using each of 3 lots of the Alinity s HIV Ag/Ab Combo Reagent Kit.

Specimen Category	Lot	Nonreactive	Repeatedly Reactive	Specificity (%) (95% CI)
Cadaveric[a]	Lot 1	55	0	100.00 (93.51 - 100.00)
	Lot 2	55	0	100.00 (93.51 - 100.00)
	Lot 3	55	0	100.00 (93.51 - 100.00)
Living Donor	Lot 1	55	0	100.00 (93.51 - 100.00)
	Lot 2	55	0	100.00 (93.51 - 100.00)
	Lot 3	55	0	100.00 (93.51 - 100.00)

CI = Confidence Interval

[a] Cadaveric serum specimens were collected up to 23.7 hours after death.

Analytical Sensitivity

Cadaveric serum specimens and living donor serum specimens were spiked with human plasma reactive for anti-HIV-1 group M, anti-HIV-1 group O, anti-HIV-2, or HIV-1 p24 antigen to create low-level reactive specimens. Each specimen was tested once, within 24 hours of spiking, using each of 3 lots of the Alinity s HIV Ag/Ab Combo Reagent Kit. All specimens were reactive on all 3 reagent lots.

Analyte	Specimen Category	Lot	Number of Specimens	Mean S/CO	Sensitivity (%) (95% CI)
Anti-HIV-1 Group M	Cadaveric[a]	Lot 1	55	4.84	100.00 (93.51 - 100.00)
		Lot 2	55	5.31	100.00 (93.51 - 100.00)
		Lot 3	55	5.24	100.00 (93.51 - 100.00)
	Living Donor	Lot 1	55	4.44	100.00 (93.51 - 100.00)
		Lot 2	55	5.03	100.00 (93.51 - 100.00)
		Lot 3	55	4.95	100.00 (93.51 - 100.00)
Anti-HIV-1 Group O	Cadaveric[a]	Lot 1	55	3.84	100.00 (93.51 - 100.00)
		Lot 2	55	4.28	100.00 (93.51 - 100.00)
		Lot 3	55	4.30	100.00 (93.51 - 100.00)
	Living Donor	Lot 1	55	3.74	100.00 (93.51 - 100.00)
		Lot 2	55	4.25	100.00 (93.51 - 100.00)
		Lot 3	55	4.23	100.00 (93.51 - 100.00)
Anti-HIV-2	Cadaveric[a]	Lot 1	52	3.27	100.00 (93.15 - 100.00)
		Lot 2	52	3.25	100.00 (93.15 - 100.00)
		Lot 3	52	3.35	100.00 (93.15 - 100.00)
	Living Donor	Lot 1	55	3.01	100.00 (93.51 - 100.00)
		Lot 2	55	3.09	100.00 (93.51 - 100.00)
		Lot 3	55	3.17	100.00 (93.51 - 100.00)
HIV-1 p24 Antigen	Cadaveric[a]	Lot 1	55	3.96	100.00 (93.51 - 100.00)
		Lot 2	55	3.90	100.00 (93.51 - 100.00)
		Lot 3	55	4.19	100.00 (93.51 - 100.00)
	Living Donor	Lot 1	55	3.77	100.00 (93.51 - 100.00)
		Lot 2	55	3.73	100.00 (93.51 - 100.00)
		Lot 3	55	3.98	100.00 (93.51 - 100.00)

CI = Confidence Interval

[a] Cadaveric serum specimens were collected up to 26.5 hours after death.

Cadaveric Specimen Storage

Cadaveric specimen storage was determined by testing a minimum of 12 low-level reactive specimens, prepared by spiking nonreactive cadaveric serum specimens to a target S/CO value near the cutoff with human plasma reactive for anti-HIV-1 group M, anti-HIV-1 group O, anti-HIV-2, or HIV-1 p24 antigen, and a minimum of 12 nonreactive cadaveric serum specimens. Each specimen was tested at Day 0, and then subjected to either 2 to 8°C storage for 14 days, room temperature (15 to 30°C) storage for 3 days, −20°C or colder storage for 3 months, or 6 freeze/thaw cycles. Nonreactive specimens were evaluated by calculating the differences between the mean S/CO of Day 0 and the mean S/CO of each storage condition and related timepoint. Reactive specimens were evaluated by calculating the percent differences between the mean S/CO of Day 0 and the mean S/CO of each storage condition and related timepoint. There were no changes to the interpretation; the data demonstrate that cadaveric serum specimens can be stored at the following conditions when tested using the Alinity s HIV Ag/Ab Combo assay.

		Nonreactive Specimens	Reactive Specimens Lower Limit of 2-sided 95% CI of % Differences			
Storage Condition	Timepoint	Upper Limit of 2-sided 95% CI of Differences	Anti-HIV-1 Group M	Anti-HIV-1 Group O	Anti-HIV-2	HIV-1 p24 Antigen
Room Temperature (15 to 30°C)[a]	3 days	0.00 S/CO	10.1%	14.3%	21.8%	-2.0%
2 to 8°C[a]	14 days	-0.01 S/CO	-1.2%	-1.2%	2.1%	-2.9%
-20°C or colder[b]	3 months	0.00 S/CO	-1.0%	-7.6%	-4.3%	2.3%
Freeze/Thaw[a]	6 cycles	0.00 S/CO	-6.9%	-5.9%	-6.0%	-7.9%

CI = Confidence Interval

[a] Cadaveric serum specimens were collected up to 32.1 hours after death.

[b] Cadaveric serum specimens were collected up to 21.4 hours after death.

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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.
DISTRIBUTED IN THE USA BY	Distributed in the USA by
INFORMATION FOR USA ONLY	Information needed for United States of America only
IVD	*In Vitro* Diagnostic Medical Device
LOT	Lot Number
MICROPARTICLES	Microparticles
PRODUCT OF GERMANY	Product of Germany
REF	List Number
SN	Serial number

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