Human T-Lymphotropic Virus Types I and II

ABBOTT PRISM

Customer Service
United States: 1-877-4ABBOTT

Key to symbols used

REF	List Number
LOT	Lot Number
	Expiration Date
IVD	*In Vitro* Diagnostic Medical Device
2°C – 8°C	Store at 2-8°C
15°C – 30°C	Store at 15-30°C
	Consult instructions for use
	CAUTION: Consult accompanying documents
	Abbott Laboratories Diagnostics Division Abbott Park, IL 60064 USA — Manufacturer
ACTIVATOR DILUENT	Activator Diluent
ACTIVATOR CONCENTRATE	Activator Concentrate
EC REP	Authorized Representative

U.S. License No. 43

ABBOTT LABORATORIES
Diagnostics Division
Abbott Park, IL 60064

List No. 6E50
Printed in U.S.A.

NAME AND INTENDED USE

The ABBOTT PRISM HTLV-I/HTLV-II assay is an *in vitro* chemiluminescent immunoassay (ChLIA) for the qualitative detection of antibodies to human T-lymphotropic virus Type I and/or human T-lymphotropic virus Type II (anti-HTLV-I/HTLV-II) in human serum and plasma specimens. The ABBOTT PRISM HTLV-I/HTLV-II (ChLIA) 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-HTLV-I/HTLV-II. It is also intended for use in testing blood and plasma specimens to screen organ donors when specimens are obtained while the donor's heart is still beating. It is not intended for use on cord blood specimens.

SUMMARY AND EXPLANATION OF THE TEST

HTLV-I, a human Type-C retrovirus,[1,2] has been etiologically associated with neoplastic conditions and demyelinating neurologic disorders including: adult T-cell leukemia (ATL),[3] and HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP).[4-7] HTLV-I is also associated with uveitis,[8] and linked to infective dermatitis, polymyositis, and arthritis.[9-12] Antibodies to HTLV-I are found with high frequency in persons afflicted with these disorders. However, it is well established in studies from viral endemic areas that HTLV-I antibody-negative ATL and HAM/TSP are seen.[13-16]

HTLV-I infection is endemic in the Caribbean,[16] Japan,[15] in some areas of Africa,[17] Central and South America,[18,19] in Melanesia,[20,21] the Middle East,[22] and central and northern Australia.[23,24,12] In the United States, HTLV-I has been identified in ATL patients, intravenous drug users, and in healthy individuals.[25-29] Transmission of HTLV-I (and HTLV-II) infection to transfusion recipients of infected cellular blood products is well documented.[30-35] Transmission can also occur via breast feeding,[36-39] sexual contact,[40] and sharing of contaminated needles and syringes by intravenous drug users.[26,41]

HTLV-I causes ATL in less than 4% of infected individuals and typically only after long latency periods.[42,43] The ATL syndrome appears to result from exposure early in life as occurs during maternal transmission via breast milk and may be dependent on maternal antibody titer and proviral load.[43,38] Approximately 10 to 15% of children exposed to HTLV-I through breast feeding develop antibodies to HTLV-I.[37-39] Perinatal transmission of HTLV-I occurs in approximately 5% of non-breast fed children born to infected mothers.[39] Following transfusion of cellular blood components in HTLV-I endemic areas, 44 to 63% of recipients seroconvert;[44,31] however, lower seroconversion rates (approximately 13%) have been reported in recipients of contaminated blood in the U.S.[45] In most cases, infection with HTLV-I during adult life results in HAM/TSP-like illness, and not in ATL.[14,43] The lifetime risk for HAM/TSP for those who live in an endemic area is estimated at less than 1%.[46,47] The presence of HTLV-I antibodies in an asymptomatic person indicates that the individual may be infected with the virus and should not donate blood,[41,48,49] but does not mean the individual has ATL or HAM/TSP or will develop ATL or HAM/TSP.[41,47-50] Consultation with appropriate medical personnel is recommended for discussion of additional concerns related to viral infection and its transmission.

HTLV-II was first isolated in 1982 from a patient having T-lymphocytic-hairy cell leukemia.[51,52] Association of HTLV-II with leukemia pathogenesis is not established; however, some cases of neurologic diseases resembling HAM/TSP have been reported to be associated with HTLV-II infection.[53-56] Epidemiologic data suggest that HTLV-II is a new-world virus common among Amerindians in North, Central, and South America.[53,57]

Transmission of HTLV-II, like HTLV-I, occurs via transfusion of cellular blood components, between needle-sharing intravenous drug users, and through sexual contact.[58,29,59-61] Mother-to-child transmission of HTLV-II has recently been reported.[62] At least one-half of U.S. blood donors who are positive by supplemental testing for antibody following HTLV-I screening have been identified as HTLV-II positive rather than HTLV-I positive.[29,34,48,49,53,63]

Neither HTLV-I nor HTLV-II causes acquired immunodeficiency syndrome (AIDS), and the HTLV-I and HTLV-II viruses are only remotely related to the AIDS virus, HIV. No cross-reactivity with antibodies to HIV-1 or HIV-2 has been demonstrated for this assay. The finding of antibodies to HTLV-I/HTLV-II by this assay has no relationship to the presence of antibodies to HIV and does not imply any risk of AIDS.

The ABBOTT PRISM HTLV-I/HTLV-II assay has been developed to detect antibodies to HTLV-I and HTLV-II in human serum or plasma. This detection is accomplished through the presence of HTLV-I and HTLV-II viral antigens on the solid phase. The ABBOTT PRISM HTLV-I/HTLV-II assay does not discriminate between antibody reactivity to HTLV-I and HTLV-II.

Specimens that are not reactive by the ABBOTT PRISM HTLV-I /HTLV-II assay are considered negative for antibodies to HTLV-I and HTLV-II. These specimens need not be tested further. Specimens that are initially reactive should be retested in duplicate. Reactivity in either or both of these duplicate tests (*i.e.*, repeatedly reactive) is highly predictive of the presence of HTLV-I and/or HTLV-II antibodies in people at risk for HTLV infection. However, as for enzyme immunoassays, the ABBOTT PRISM HTLV-I/HTLV-II assay may yield nonspecific reactions due to other causes, particularly when testing low prevalence populations (*e.g.*, blood donors). Additional, more specific tests, such as the Western blot assay and the radioimmunoprecipitation assay (RIPA), are supportive in determining if repeatedly reactive specimens are positive for antibodies to HTLV.[48,49,64] A combination of such tests must be capable of identifying antibodies to HTLV core (*gag*) proteins (p24) and envelope (*env*) proteins (native gp46, gp61/68).[30,64]

An HTLV-I, HTLV-II, or dual infection can only be differentiated serologically by parallel testing using antigens from HTLV-I and HTLV-II in specific immunoassays.[65,66] Tests based on reactivities to HTLV-I and HTLV-II type specific proteins may enable viral typing. Nonserologic tests based on the presence of infected cells, or HTLV-I /HTLV-II DNA probe testing (*e.g.*, polymerase chain reaction [PCR]) may also be used in discrimination.[67,68] Recommendation for appropriate use of additional more specific tests may be issued periodically by the U.S. Public Health Service.[48,49]

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ABBOTT PRISM HTLV-I/HTLV-II assay is a three-step sandwich ChLIA. The reactions occur within the ABBOTT PRISM System in the following sequence:

- Microparticles coated with sonicated and detergent-inactivated HTLV-I and HTLV-II antigens are incubated with sample (either plasma, serum, calibrator, or control) in the incubation well of the reaction tray. During incubation, HTLV-I and/or HTLV-II antibodies present in the sample bind to the antigen(s) on the Microparticles.
- After this first incubation is complete, the reaction mixture is transferred to the glass fiber matrix (matrix) of the reaction tray using the Transfer Wash. The Microparticles are captured by the matrix, while the remaining mixture flows through to the absorbent blotter.
- A Probe consisting of biotinylated HTLV-I and HTLV-II proteins is added to the Microparticles on the matrix and incubated. The Probe binds to the HTLV-I/HTLV-II Microparticle-antibody complex created during the first incubation process. After the second incubation, the unbound Probe is washed into the blotter with the Probe Wash.
- The Acridinium-Labeled Anti-Biotin Conjugate is added to the Microparticles on the matrix to bind any Probe that is present and then incubated. After this incubation, the unbound Conjugate is washed into the blotter with the Conjugate Wash.
- The chemiluminescent signal is generated by addition of an alkaline hydrogen peroxide solution. The resultant photons are counted.

The amount of light emitted is proportional to the amount of anti-HTLV-I and/or anti-HTLV-II in the sample. The presence or absence of anti-HTLV-I/HTLV-II in the sample is determined by comparing the number of photons collected from the sample to a cutoff value determined from a calibration performed in the same batch. If the number of photons collected from a test sample is less than the cutoff value, the sample is considered nonreactive for anti-HTLV-I and/or anti-HTLV-II by the criteria of the ABBOTT PRISM HTLV-I/HTLV-II assay. These specimens need not be further tested. If the number of photons collected from a test sample is greater than or equal to the cutoff value, the sample is considered reactive for anti-HTLV-I and/or anti-HTLV-II by the criteria of the ABBOTT PRISM HTLV-I/HTLV-II assay. Specimens which are initially reactive must be handled according to the table in the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert and retested in duplicate. Follow appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive. For further information regarding ChLIA technology, refer to the ABBOTT PRISM Operations Manual, Section 3.

REAGENTS

NOTE: Each specific component description noted below is accompanied by a unique symbol. These symbols appear on both the component labels and on corresponding instrument tubing identifier labels. They are meant to facilitate identification and installation of reagent bottles within the ABBOTT PRISM System ambient reagent bay and refrigerator.

ABBOTT PRISM HTLV-I/HTLV-II Assay Kit (No. 6E50-68)

NOTE: Do not mix reagents from different bottles. Do not mix or interchange reagents from different ABBOTT PRISM HTLV-I/HTLV-II Assay Kits.

- 1 Bottle (319 mL) Human T-Lymphotropic Virus Types I and II Coated Microparticles in phosphate buffer with Tween®* 20 and protein stabilizers. Minimum concentration: 0.038% solids. Preservative: 0.1% sodium azide. (Symbol: ●)
- 1 Bottle (331 mL) Anti-Biotin (Mouse Monoclonal):Acridinium Conjugate in phosphate buffered saline with Triton®** X-100 and protein stabilizers. Minimum concentration: 0.05 µg/mL. Preservative: 0.1% sodium azide. (Symbol: ▲)
- 3 Bottles (10.4 mL each) Negative Calibrator (Human). Recalcified plasma. Preservative: 0.1% sodium azide. (Symbol: NC)
- 3 Bottles (10.4 mL each) Positive Calibrator (Human). Recalcified, inactivated plasma reactive for anti-HTLV-I. Minimum Sample/Cutoff is 2.00. Positive Calibrator may be cross-reactive with HTLV-II antigens. Preservative: 0.1% sodium azide. (Symbol: PC)
- 3 Bottles (10.4 mL each) HTLV-II Positive Assay Control (1) (Human). Recalcified, inactivated plasma reactive for anti-HTLV-II. Minimum Sample/Cutoff is 1.50. HTLV-II Positive Assay Control (1) may be cross-reactive with HTLV-I antigens. Preservative: 0.1% sodium azide. (Symbol: PC2)
- 1 Bottle (324 mL) Human T-Lymphotropic Virus Types I and II Biotinylated Probe. Biotinylated HTLV-I, HTLV-II, and HTLV-I Envelope Enriched Viral Lysate in TRIS buffered saline with calf serum and protein stabilizers. Minimum concentration: 0.034 mg/L protein. Preservative: 0.1% ProClin®*** 300. (Symbol: ■)

  NOTE: The ABBOTT PRISM Calibration Report identifies the ABBOTT PRISM HTLV-II Positive Assay Control (1) as "Pos Assay CTL (1)".

Other Reagents Required

ABBOTT PRISM HTLV-I/HTLV-II Wash Kit (No. 6E50-58)

- 1 Bottle (3342 mL) Transfer Wash. Phosphate buffered saline. Preservative: 0.1% sodium azide. (Symbol: ~)
- 1 Bottle (1725 mL) Conjugate Wash. MES {2-(N-morpholino) ethanesulfonic acid} buffered saline. Preservative: 0.1% ProClin*** 300. (Symbol: ★)

- 1 Bottle (1718 mL) Probe Wash. TRIS buffered saline with Triton** X-100. Preservatives: 0.1% ProClin*** 300 and 0.1% sodium azide. (Symbol: →)

ABBOTT PRISM Activator Concentrate (No. 1A75-02)

- 4 Bottles (900 mL each) Activator Concentrate. 0.4% hydrogen peroxide/0.06% diethylenetriaminepentaacetic acid.

ABBOTT PRISM Activator Diluent (No. 1A75-01)

- 4 Bottles (900 mL each) Activator Diluent. 0.3 N sodium hydroxide.

ABBOTT PRISM Run Control Kit (No. 3E60-10)

Or

ABBOTT PRISM Positive Run Control Kit (No. 3E60-11)

NOTE: Each batch **MUST** end in a release control (ABBOTT PRISM Positive Control). The ABBOTT PRISM Positive Control (included in Kit No. 3E60-10 or 3E60-11) must be used as the release control which has been configured to validate system functionality and release sample results. Refer to the ABBOTT PRISM Run Control Kit package insert or the ABBOTT PRISM Positive Run Control Kit package insert for detailed handling and use instructions.

* Tween is a registered trademark of ICI Americas.

** Triton is a registered trademark of Union Carbide Co., Inc.

*** ProClin is a registered trademark of Rohm & Haas.

WARNINGS AND PRECAUTIONS

For *In Vitro* Diagnostic Use.

The performance characteristics of this product have not been established for the laboratory diagnosis of HTLV-I/HTLV-II infection.

Safety Precautions

CAUTION: This product contains human sourced and/or potentially infectious components. Refer to the REAGENTS section of this package insert. No known test method can offer complete assurance that products derived from human sources will not transmit infection. Therefore, all human sourced materials must be considered potentially infectious. It is recommended that these reagents and human specimens be handled in accordance with the OSHA Standard on Bloodborne Pathogens.[68] Biosafety Level 2[69] or other appropriate biosafety practices[70,71] should be used for materials that contain or are suspected of containing infectious agents. These precautions include, but are not limited to the following:

- Wear gloves when handling specimens or reagents.
- Do not pipette by mouth.
- Do not eat, drink, smoke, apply cosmetics, or handle contact lenses in areas where specimens or reagents are handled.
- Clean and disinfect all spills of specimens or reagents using an appropriate disinfectant, such as 0.1% sodium hypochlorite, or other suitable disinfectants.[70,71,72]
- Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local, state, and federal regulations.[73,74]
- The human plasma used in the Negative Calibrator is nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, anti-HCV and anti-HTLV-I/HTLV-II.
- The human plasma used in the Positive Calibrator is reactive for anti-HTLV-I, and nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2, and anti-HCV.
- The human plasma used in HTLV-II Positive Assay Control (1) is reactive for anti-HTLV-II and nonreactive for HBsAg, HIV-1 Ag or HIV-1 RNA, anti-HIV-1/HIV-2 and anti-HCV.

- The ABBOTT PRISM Line Cleaner (No. 7A03-31) containing 2% tetraethylammonium hydroxide (TEAH) may cause mild eye irritation. If this solution comes in contact with eyes, rinse immediately with water. For additional information, refer to the ABBOTT PRISM Operations Manual, Section 8.
- This product contains sodium azide; for a specific listing, refer to the **REAGENTS** section of this package insert. Contact with acids liberates very toxic gas. This material and its container must be disposed of in a safe way.
- The ABBOTT PRISM HTLV I/HTLV-II Conjugate Wash, Probe Wash and Biotinylated Probe contain methylisothiazolones (which are components of ProClin) and are classified per applicable European Community (EC) Directives as: Irritant (Xi). The following are the appropriate Risk (R) and Safety (S) phrases.

R43	May cause sensitization by skin contact.
S24	Avoid contact with skin.
S35	This material and its container must be disposed of in a safe way.
S37	Wear suitable gloves.
S46	If swallowed, seek medical advice immediately and show this container or label.

Handling Precautions

- Do not use kits beyond the expiration date.
- **Gently** invert each component several times prior to loading the original container on the ABBOTT PRISM System to ensure a homogenous solution. Additional gentle inversion may be required to thoroughly resuspend microparticles. Avoid foaming. Each component of the ABBOTT PRISM HTLV-I/HTLV-II Wash Kit should be at room temperature (15-30˚C) and then mixed before loading onto the ABBOTT PRISM System.
- Do not mix reagents from different bottles. Do not mix or interchange reagents from different ABBOTT PRISM HTLV-I/HTLV-II Assay Kits.
- Any lot of ABBOTT PRISM HTLV-I/HTLV-II Wash Kit can be used with any lot of ABBOTT PRISM HTLV-I/HTLV-II Assay Kit.
- Any lot of ABBOTT PRISM Activator Concentrate, ABBOTT PRISM Activator Diluent, and Control from ABBOTT PRISM Run Control Kit or ABBOTT PRISM Positive Run Control Kit may be used with any lot of any ABBOTT PRISM Assay Kit.
- Treat Negative and Positive Calibrators and Controls as specimens.
- Avoid microbial and chemical contamination of samples, reagents, and equipment. The use of disposable pipette tips is recommended for any preliminary sample transfer.
- Use accurately calibrated equipment.
- Do not freeze reagents.
- Failure to adhere to instructions in the ABBOTT PRISM Operations Manual or package insert may result in erroneous test results.
- Use caution when handling samples, reagent bottles, and reagent caps to prevent cross contamination.

Additional safety and handling precautions and limitations for the assay kit, calibrators, specimens, controls, and other reagents are described in the ABBOTT PRISM Operations Manual, Sections 7 and 8.

Preparation of Activator Solution

Activator Solution must be prepared by mixing equal parts of ABBOTT PRISM Activator Concentrate and ABBOTT PRISM Activator Diluent. The Activator Solution expires 24 hours from preparation. The ABBOTT PRISM Activator Concentrate may be used immediately after removing from the refrigerator. The volume of Activator Solution required for multiple tests is calculated by the ABBOTT PRISM System software. Refer to the ABBOTT PRISM Operations Manual, Section 5, under **PLAN WORK LOAD**, for additional information. Use clean pipettes and/or metal-free containers (such as plasticware or acid-washed and purified or equivalent water-rinsed glassware) to measure. Refer to the ABBOTT PRISM Operations Manual Glossary for the definition of purified water. Prepare the Activator Solution in the bottle provided in the ABBOTT PRISM Accessory Kit (List No. 6A36-60). Cover the bottle opening securely with the cap provided and invert gently five to ten times to mix. Load the Activator Solution on the ABBOTT PRISM System. Refer to the ABBOTT PRISM Operations Manual, Section 5, under **PREPARE AND LOAD ACTIVATOR SOLUTION**, for additional information.

NOTE: The Activator Solution must be used within 24 hours of preparation.

Storage Instructions

- Store the ABBOTT PRISM HTLV-I/HTLV-II Assay Kit, ABBOTT PRISM Run Control Kit, ABBOTT PRISM Positive Run Control Kit, and ABBOTT PRISM Activator Concentrate at 2-8˚C.
- Store the ABBOTT PRISM HTLV-I/HTLV-II Wash Kit and ABBOTT PRISM Activator Diluent at room temperature (15-30˚C).
- Store ABBOTT PRISM Pipette Tips and ABBOTT PRISM Reaction Trays in their original packaging until use.
- The Activator Solution must be stored at 15-30˚C and used within 24 hours of preparation.

Indications of Instability or Deterioration of Reagents

The ABBOTT PRISM System will not continue to process samples when calibrator or positive assay control values do not meet specifications. This may indicate either deterioration or contamination of reagents, or instrument failure. Refer to the ABBOTT PRISM Operations Manual, Section 10, for additional information.

INSTRUMENT PROCEDURE

- ABBOTT PRISM software version 3.12 or higher must be used to perform the assay.
- Refer to the ABBOTT PRISM Operations Manual for a detailed description of Instrument Procedures.
- Refer to the ABBOTT PRISM Operations Manual, Section 7, for limitations associated with test management.
- Solutions required for instrument cleaning and maintenance are described in detail in the ABBOTT PRISM Operations Manual, Sections 5 and 9.
- For optimal performance, it is important to follow the routine maintenance procedures defined in the ABBOTT PRISM Operations Manual, Section 9.

SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS

- Serum (including serum collected in serum separator tubes), plasma collected in EDTA, potassium oxalate, sodium citrate, ACD-A, ACD-B, CP2D, CPD, or CPDA-1 anticoagulants, or plasma collected from segmented tubing may be used with the ABBOTT PRISM HTLV-I/HTLV-II assay. Follow the manufacturer's processing instructions for serum and plasma collection tubes.

  CAUTION: Do not use specimens collected in heparin. Use of heparin as an anticoagulant may cause a reduction in Sample Net Counts and in Sample Net Counts/Cutoff Value (S/CO) for ABBOTT PRISM HCV; therefore, heparin is not recommended for any ABBOTT PRISM assay.

- This assay was designed and validated for use with individual human serum and plasma specimens. This assay has not been validated for use with pooled specimens.
- Do not use heat-inactivated specimens.
- Do not use specimens with obvious microbial contamination.
- When shipped, specimens must be packaged and labeled in compliance with applicable regulations covering the transport of clinical specimens and infectious substances. Specimens may be shipped at 30°C or colder for a period not to exceed 7 days. Prior to freezing, the serum or plasma should be removed from the clot or red blood cells.
- Specimens may be stored for up to 14 days at 2-8°C. If storage periods greater than 14 days are anticipated, the serum or plasma should be removed from the clot or red blood cells to avoid hemolysis. Store the serum or plasma frozen (-20°C or colder).
- Previously frozen specimens must be mixed gently and thoroughly after thawing and centrifuged according to Table II in this section.
- Twenty nonreactive and 40 low-level reactive specimens showed no qualitative performance differences when subjected to 6 freeze-thaw cycles. However, some specimens that have undergone multiple freeze-thaw cycles or have been stored frozen for prolonged periods may give erroneous or inconsistent test results.

  NOTE: Some specimens nonreactive for anti-HTLV-I and/or anti-HTLV-II that have been subjected to frozen storage have exhibited nonspecific reactivity in the ABBOTT PRISM HTLV-I/HTLV-II assay.
- Clear, non-hemolyzed specimens should be used when possible. Specimens containing visible particulate matter may give erroneous or inconsistent test results.
- No qualitative performance differences were observed when 20 nonreactive and 40 low-level reactive specimens were spiked with elevated levels of bilirubin ($\leq$ 20 mg/dL), hemoglobin ($\leq$ 500 mg/dL), red blood cells ($\leq$ 0.4% v/v), triglycerides ($\leq$ 3000 mg/dL), or protein ($\leq$ 12 g/dL). However, specimens that contain greater concentrations of these potentially interfering substances have not been tested. The impact of greater concentrations of these potentially interfering substances on the ABBOTT PRISM HTLV-I/HTLV-II assay is unknown.
- Performance has not been established using cadaveric specimens, umbilical cord blood, or body fluids such as urine, saliva, semen, amniotic fluid, cerebrospinal fluid, or pleural fluid. These specimens should not be tested using the ABBOTT PRISM HTLV-I/HTLV-II assay.
- Specimens collected by plasmapheresis that have not been frozen do not require centrifugation. All other specimens (including previously frozen plasmapheresis specimens) must be centrifuged as follows:

  Non-frozen specimens (excluding non-frozen plasmapheresis specimens) must be centrifuged such that g-minutes is between 30,000 and 75,000. A refrigerated or non-refrigerated centrifuge is acceptable for use. The acceptable time and force ranges that meet this criterion are listed in Table I.

Table I

Centrifugation Time (minutes)	RCF (x g)	g-minutes
10	3,000	30,000
15	2,000 - 3,000	30,000 - 45,000
20	1,500 - 3,000	30,000 - 60,000
25	1,300 - 3,000	32,500 - 75,000

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

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 a measure of the distance from the rotor axis (center) to the bottom of the tube cavity. For the swinging bucket rotor, r_{max} is a measure of the distance from the rotor axis (center) to the bottom of the tube bucket while it is extended during rotation.

g-minutes - The unit of measure for the product of RCF (x g) and centrifugation time (minutes).

Previously frozen specimens must be centrifuged such that g-minutes is between 180,000 and 300,000. A refrigerated or non-refrigerated centrifuge is acceptable for use. The acceptable time and force ranges that meet this criterion are listed in Table II.

Table II

Centrifugation Time (minutes)	RCF (x g)	g-minutes
15	12,000	180,000
20	9,000 - 12,000	180,000 - 240,000
25	7,200 - 12,000	180,000 - 300,000

ANY specimen (excluding non-frozen plasmapheresis) not tested within 24 hours of initial centrifugation, must be recentrifuged from 30,000 to 75,000 g-minutes as defined for non-frozen specimens.

NOTE: Specimens retested within 24 hours of initial centrifugation do not require recentrifugation.

FAILURE TO FOLLOW THE SPECIFIED CENTRIFUGATION PROCEDURE MAY GIVE ERRONEOUS OR INCONSISTENT TEST RESULTS.

Specimen Volume

The specimen volume required to perform a single assay on the ABBOTT PRISM System varies according to the number and type of assays, and the different specimen containers. The ABBOTT PRISM HTLV-I/HTLV-II assay requires 100 µL sample dispense. For ABBOTT PRISM Sample Cups, the minimum specimen volume required for one ABBOTT PRISM HTLV-I/HTLV-II assay is 400 µL. For primary or aliquot tubes, or additional assay volume requirements, refer to the ABBOTT PRISM Operations Manual, Section 5.

PROCEDURE

Materials Provided

- No. 6E50-68 ABBOTT PRISM HTLV-I/HTLV-II Assay Kit

Materials Required but Not Provided

- No. 6E50-58 ABBOTT PRISM HTLV-I/HTLV-II Wash Kit
- No. 1A75-02 ABBOTT PRISM Activator Concentrate
- No. 1A75-01 ABBOTT PRISM Activator Diluent
- No. 5A07-01 ABBOTT PRISM Reaction Trays
- No. 5A07-10 ABBOTT PRISM Pipette Tips
- No. 6A36-60 ABBOTT PRISM Accessory Kit
- No. 3E60-10 ABBOTT PRISM Run Control Kit

  or

- No. 3E60-11 ABBOTT PRISM Positive Run Control Kit
- No. 6A36-31 ABBOTT PRISM Run Control Adapters
- Protective Disposable Gloves
- Disinfectant
- Purified Water-rinsed or Clean Disposable Measuring Equipment

Additional Materials Available

- No. 7B36-01 ABBOTT PRISM Sample Cups

ABBOTT PRISM HTLV-I/HTLV-II ASSAY PROCEDURE

Key procedures for the process of testing samples that require operator interaction are listed below as reminders. For detailed information concerning batch time, maximum batch size, reagent handling and loading, and associated procedural steps, refer to the ABBOTT PRISM Operations Manual, Sections 2, 5, and 7.

- Enter a Plan Work Load (refer to the ABBOTT PRISM Operations Manual, Section 5).
- Replace reagents as needed (refer to the ABBOTT PRISM Operations Manual, Sections 5 and 7).

  NOTE: Gently invert each component several times prior to loading on the ABBOTT PRISM System to ensure a homogenous solution. Additional gentle inversion may be required to thoroughly resuspend microparticles. Avoid foaming. Each component of the ABBOTT PRISM HTLV-I/HTLV-II Wash Kit should be at room temperature (15-30°C) and then mixed before loading onto the ABBOTT PRISM System.

- Verify that all tubing label symbols match the symbols on each reagent label. (Refer to the symbol key in the **REAGENTS** section of this package insert, and the ambient reagent bay and refrigerator diagrams provided with the ABBOTT PRISM System.)
- **Verify that all tubing is securely fastened to the corresponding wash and reagent bottles.**
- Inspect the waste containers. Empty and clean as defined in the ABBOTT PRISM Operations Manual, Section 9, if necessary.
- Prepare Activator Solution (refer to the **Preparation of Activator Solution** section of this package insert) and load into the ABBOTT PRISM System.
- Verify adequate number of ABBOTT PRISM Reaction Trays are in the Tray Loader.
- Verify adequate number of ABBOTT PRISM Pipette Tips are in the Pipette Tip Racks.
- Perform the prime procedure (refer to the ABBOTT PRISM Operations Manual, Section 5).
- Initiate sample processing. Open the bottles in the calibrator pack and place in the calibrator rack. Load the calibrator rack and sample racks, including the run controls. Refer to the **QUALITY CONTROL PROCEDURES**, Control Handling Procedure, under **Controls** in this package insert.
- After the calibrators and positive assay control have been automatically pipetted, remove the calibrator rack. Close the calibrator and positive assay control bottles and return them to 2-8˚C storage.
- Each specimen is initially tested once, unless the operator overrides this automatic function of the ABBOTT PRISM System.
- Sample racks may be removed after the samples have been pipetted.

NOTE: No operator interaction is required for the following steps, which are automatically carried out by the ABBOTT PRISM System: reaction tray transport, calibrator/assay control/sample/release control pipetting, incubation, reagent dispense, sample reading, data reduction, run validity and result determination.

- After specimen processing is complete, perform the purge procedure. (Refer to the ABBOTT PRISM Operations Manual, Section 5.)

Refer to the ABBOTT PRISM Operations Manual, Section 3, for a detailed description of ChLIA procedures. The ABBOTT PRISM HTLV-I/HTLV-II assay is a three-step ChLIA procedure.

QUALITY CONTROL PROCEDURES

Calibration

The ABBOTT PRISM HTLV-I/HTLV-II Negative and Positive Calibrators and HTLV-II Positive Assay Control (1) are automatically tested in triplicate at the beginning of each batch. The ABBOTT PRISM System will not generate results when calibrator or positive assay control values do not meet specifications. This may indicate either deterioration or contamination of reagents, or instrument failure.

Controls

1. The ABBOTT PRISM Positive Control **MUST** be included as the last sample in each batch as a release control. The operator is prompted to include this control as the last sample in every batch, and the ABBOTT PRISM Positive Control is then automatically tested as a single replicate. This control must meet specifications defined in the ABBOTT PRISM Run Control Kit package insert or the ABBOTT PRISM Positive Run Control Kit package insert in order to validate system functionality and release sample results. If this control does not meet specifications defined in the ABBOTT PRISM Run Control Kit package insert or the ABBOTT PRISM Positive Run Control Kit package insert, refer to the ABBOTT PRISM Operations Manual, Section 10, for additional information.
2. Additional controls may be run at the operator's discretion (refer to the ABBOTT PRISM Operations Manual, Section 3). **Invalidate controls:** Additional controls may be run anywhere within a batch as an invalidate control. Specifications may be assigned to invalidating controls. If an invalidate control fails to meet assigned specifications, sample processing is shutdown and no sample results are calculated or provided by the instrument. When an invalidate control meets assigned specifications, sample processing continues and a valid release control (ABBOTT PRISM Positive Control) result is required to release data. **Non-validating controls:** Additional controls may be run anywhere within a batch as a non-validating control. Specifications may be assigned to non-validating controls. A valid release control (ABBOTT PRISM Positive Control) result is required to release data. 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.
3. Control Handling Procedure
   a. Place run control adapters into the sample rack. **The adapters can be placed in any rack position except 1, 2, 27 or 28.**
   b. Place each run control bottle into an adapter in the sample rack such that when the bottle flip-top cap is opened, it can be snapped into an open position within the adapter.
   c. As mentioned above, place an ABBOTT PRISM Positive Control after the last sample tested in the batch. **The controls can be placed in any rack position except 1, 2, 27, or 28.**

Refer to the ABBOTT PRISM Operations Manual, Section 3, for additional information on calibrators, assay controls and run controls.

ASSAY PARAMETER SPECIFICATIONS

The ABBOTT PRISM HTLV-I/HTLV-II assay parameter specifications have been factory set. These parameters cannot be printed, displayed, or edited.

RESULTS

Calculation of Cutoff and S/CO Values

The ABBOTT PRISM System calculates the ABBOTT PRISM HTLV-I/HTLV-II assay cutoff value using the following formula:

Cutoff Value = Mean Negative Calibrator (NC) Net Counts + (0.15 x Mean Positive Calibrator [PC] Net Counts)

Example:
Mean NC Net Counts = 1,100
Mean PC Net Counts = 6,900
1,100 + (0.15 x 6,900) = 2,135
Cutoff Value = 2,135

The ABBOTT PRISM System calculates the ABBOTT PRISM HTLV-I/HTLV-II assay S/CO for each sample and control using the following formula:

S/CO = Sample Net Counts ÷ Cutoff Value

Example:
Sample Net Counts = 3,000
Cutoff Value = 2,135
3,000 ÷ 2,135 = 1.41
S/CO = 1.41

Interpretation of Results

- In the ABBOTT PRISM HTLV-I/HTLV-II assay, specimens with Net Counts less than the cutoff value are nonreactive and need not be tested further. Nonreactive specimens are considered negative for anti-HTLV-I/HTLV-II by the criteria of the ABBOTT PRISM HTLV-I/HTLV-II assay.
- Specimens with Net Counts greater than or equal to the cutoff value are considered initially reactive by the criteria of the ABBOTT PRISM HTLV-I/HTLV-II assay. All specimens (excluding non-frozen plasmapheresis specimens) that are reactive on initial testing must be centrifuged prior to retesting according to the table in the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert. Initially reactive specimens must be retested in duplicate using the ABBOTT PRISM HTLV-I/HTLV-II Assay Kit.

  NOTE: Specimens retested within 24 hours of initial centrifugation do not require recentrifugation.
- If the sample Net Counts for both retests are less than the cutoff value, the specimen is nonreactive. Nonreactive specimens are considered negative for anti-HTLV-I/HTLV-II by the criteria of the ABBOTT PRISM HTLV-I/HTLV-II assay.
- If the sample Net Counts for either duplicate retest are greater than or equal to the cutoff value, the specimen is considered repeatedly reactive. Repeatedly reactive results indicate the presence of anti-HTLV-I/HTLV-II by the criteria of the ABBOTT PRISM HTLV-I/HTLV-II assay.
- Follow appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive.
- Individuals who are repeatedly reactive may be referred for medical evaluation and additional testing.

Reading Results

Some S/CO values may be flagged with "<" or ">" symbols. For more information on sample reports, refer to the ABBOTT PRISM Operations Manual, Section 5: Operating Instructions, Reports. The ABBOTT PRISM System reports sample results in Net Counts and S/CO. Net Counts are used by the ABBOTT PRISM System to interpret results. The S/CO value is provided in reports to show reactivity relative to the cutoff value. In the ABBOTT PRISM HTLV-I/HTLV-II assay, specimens with S/CO values of less than 1.00 are considered nonreactive. Specimens with an S/CO value of greater than or equal to 1.00 are considered reactive.

System Errors

For a description of the error codes that appear on ABBOTT PRISM System reports, refer to the ABBOTT PRISM Operations Manual, Section 10.

LIMITATIONS OF THE PROCEDURE

- This assay was designed and validated for use with individual human serum and plasma specimens. This assay has not been validated for use with pooled specimens.
- The ABBOTT PRISM HTLV-I/HTLV-II assay does not discriminate between HTLV-I and HTLV-II antibody reactivity.
- A test result that is negative does not exclude the possibility of exposure to or infection with HTLV-I and/or HTLV-II. Negative results in this assay in individuals with prior exposure to HTLV-I and/or HTLV-II may be due to antibody levels below the limit of detection of this assay or lack of antibody reactivity to the HTLV antigens used in this assay.

- Guidelines published by the U.S. Public Health Service recommend that repeatedly reactive specimens be investigated by additional more specific tests such as Western blot and radioimmunoprecipitation assay (RIPA). These supplemental tests should be used in addition to type-specific peptide or probe tests for HTLV-I and HTLV-II discrimination. Interpretation of such tests should be consistent with these published guidelines.
- False-reactive test results can be expected with any test kit. False-reactive test results have been observed due to nonspecific interactions. Refer to the **SPECIFIC PERFORMANCE CHARACTERISTICS** section of this package insert for assay performance characteristics.
- **Do not use specimens collected in heparin. Use of heparin as an anticoagulant may cause a reduction in Sample Net Counts and in S/CO for ABBOTT PRISM HCV; therefore, heparin is not recommended for any ABBOTT PRISM assay.**
- Serum from heparinized patients may be incompletely coagulated. Erroneous or inconsistent test results may occur due to the presence of fibrin. To prevent this phenomenon, draw specimen prior to heparin therapy.
- Do not use heat-inactivated specimens.
- Some specimens that have undergone multiple freeze-thaw cycles or have been stored frozen for prolonged periods may result in erroneous or inconsistent test results.
- Previously frozen specimens must be centrifuged per the **SPECIMEN COLLECTION AND PREPARATION FOR ANALYSIS** section of this package insert prior to running the assay.
- Performance has not been established using cadaveric specimens, umbilical cord blood, or body fluids such as urine, saliva, semen, amniotic fluid, cerebrospinal fluid, or pleural fluid. These specimens should not be tested using the ABBOTT PRISM HTLV-I/HTLV-II assay.
- Do not use specimens with obvious microbial contamination, gross lipemia, or gross hemolysis.

SPECIFIC PERFORMANCE CHARACTERISTICS

Assay Reproducibility

Assay reproducibility was determined by testing a seven-member panel consisting of three diluted specimens reactive or borderline reactive for anti-HTLV-I (panel members 1, 2, and 3), three diluted specimens reactive or borderline reactive for anti-HTLV-II (panel members 4, 5, and 6) and one specimen nonreactive for anti-HTLV-I and anti-HTLV-II (panel member 7). Panel members were prepared in recalcified human plasma. Each panel member was tested in replicates of four in five runs over five days with each of three reagent lots at five sites. In addition, each panel member was tested in replicates of four in five runs over five days with one of the three reagent lots at four of the five sites. The Negative, Positive, and Supplemental Positive Controls were tested once at the beginning and end of each run on each subchannel. The Negative and Positive Calibrators and the HTLV-II Positive Assay Control (1) were automatically tested in triplicate at the beginning of each run on each subchannel. The intra-assay and inter-assay standard deviation (SD) and percent coefficient of variation (%CV) were determined with a variance component analysis,[75] for a mixed model[76] (Table III).

Table III

ABBOTT PRISM HTLV-I/HTLV-II Assay Reproducibility

Panel Member or Control	Number of Replicates	Mean S/CO*	Intra-assay SD	Intra-assay %CV	Inter-assay[a] SD	Inter-assay[a] %CV
1	379[b]	6.95	0.325	4.7	0.406	5.8
2	380	2.38	0.105	4.4	0.141	5.9
3	380	0.79	0.042	5.4	0.051	6.5
4	380	8.50	0.381	4.5	0.422	5.0
5	380	2.95	0.139	4.7	0.160	5.4
6	380	0.88	0.042	4.8	0.051	5.8
7	380	0.34	0.024	7.0	0.024	7.0
Negative Control	378[c]	0.30	0.030	10.1	0.030	10.1
Positive Control	380	2.57	0.136	5.3	0.136	5.3
Supplemental Positive Control	380	2.67	0.147	5.5	0.151	5.7

*Cutoff Value = Mean Negative Calibrator Net Counts + (0.15 x Mean Positive Calibrator Net Counts)

Calibrator	Number of Replicates	Mean Net Counts	Intra-assay SD	Intra-assay %CV	Inter-assay SD	Inter-assay %CV
Negative	570	609	46.8	7.7	46.8	7.7
Positive	570	8,217	375.7	4.6	375.7	4.6
HTLV-II Positive Assay Control (1)	570	5,600	251.1	4.5	251.1	4.5

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

[b] One replicate was invalid due to instrument detection of a sample dispense error.

[c] Two replicates were invalid due to instrument detection of low net counts for a sample.

Assay Specificity

A total of 21,943 fresh serum and plasma specimens from volunteer whole blood donors were collected and tested at five geographically distinct blood centers (Table IV). Two sites tested a total of 8,244 serum specimens with initial and repeat reactive rates of 0.04% (3/8,244) and 0.02% (2/8,244), respectively. Three sites tested a total of 13,699 plasma specimens with initial and repeat reactive rates of 0.20% (28/13,699) and 0.09% (13/13,699), respectively. A total of 15 specimens were repeatedly reactive. Based on supplemental test results from a research use only Western blot and/or RIPA, five of the 15 specimens were negative, nine specimens were indeterminate, and the results of one specimen could not be interpreted due to the presence of nonspecific background.

Specificity based on assumed zero prevalence of antibody to HTLV-I and/or HTLV-II in blood donors was estimated in these studies to be 99.93% (21,928/21,943) with a 95% confidence interval of 99.89% to 99.96%.

Two sites evaluated 407 serum or plasma repository specimens collected from 407 individuals with medical conditions unrelated to HTLV-I/HTLV-II infection or containing potentially interfering substances (Table IV). Four of the 407 specimens (0.98%) were initially and repeatedly reactive. One of the four specimens (25.00%) was anti-HTLV-II positive by supplemental tests, two specimens were indeterminate, and the results of one specimen could not be interpreted.

Table IV

Reactivity of the ABBOTT PRISM HTLV-I/HTLV-II Assay in Whole Blood Donors, in Specimens from Individuals with Medical Conditions Unrelated to HTLV-I/HTLV-II Infection and in Specimens Containing Potentially Interfering Substances

Category	Number Tested	IR (% of Total) (95% CI)	RR (% of Total) (95% CI)	Number Positive By Supplemental Tests[a] (% of RR)
Volunteer Blood Donors				
Serum	8,244	3 (0.04) (0.01 - 0.11)	2 (0.02) (0.00 - 0.09)	0 (0.00)
Plasma	13,699	28 (0.20) (0.14 - 0.30)	13 (0.09) (0.05 - 0.16)	0 (0.00)
Total Donors	21,943	31 (0.14) (0.10 - 0.20)	15 (0.07) (0.04 - 0.11)	0 (0.00)
Medical Conditions Unrelated to HTLV-I/HTLV-II Infection and/or Specimens Containing Potentially Interfering Substances[b]	407	4 (0.98)	4[c] (0.98)	1[d] (25.00)

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

[a] A positive result was defined by the presence of antibodies to both *gag* (p24) and *env* (native gp46 or gp61/67) antigens using research use only Western blot and/or RIPA.

[b] Specimens from individuals with medical conditions unrelated to HTLV-I/HTLV-II infection and specimens containing potentially interfering substances included the following categories: anti-CMV positive (12), anti-EBV positive (100), anti-HSV positive (12), anti-HAV positive (12), HBsAg positive (12), anti-HIV-1 positive (12), anti-HIV-2 positive (5), anti-HCV positive (12), rubella antibody positive (12), toxoplasma antibody positive (12), *E. coli* infections (5), syphilis serology positive (12), anti-nuclear antibody positive (12), rheumatoid factor positive (12), influenza vaccine recipients (52), elevated IgG and elevated IgM (24), elevated triglycerides (12), elevated bilirubin (12), elevated hemoglobin (12), multiple myeloma (11), non-Hodgkin's lymphoma (20), non-HTLV leukemia/lymphoma (17), and biotin positive (5).

[c] The four repeatedly reactive specimens included the following categories: anti-HIV-1 positive (2) and non-Hodgkin's lymphoma (2).

[d] One non-Hodgkin's lymphoma specimen tested anti-HTLV-II positive by research use only Western blot and/or RIPA.

Assay Sensitivity

A total of 715 serum and plasma specimens from 601 individuals known to be positive for HTLV-I or HTLV-II antibodies and 114 individuals with HTLV-I and/or suspected HTLV-II associated diseases were tested with the ABBOTT PRISM HTLV-I/HTLV-II assay (Table V). Of the 715 specimens tested, 715 (100.00%) specimens were repeatedly reactive. Of the 715 repeatedly reactive specimens, 714 (99.86%) specimens tested positive by research use only Western blot and/or RIPA, of which 412 specimens were anti-HTLV-I positive, 298 specimens were anti-HTLV-II positive, and 4 specimens were anti-HTLV positive but not typeable. The overall sensitivity was estimated in these studies to be 100.00% (714/714) with a 95% confidence interval of 99.48% to 100.00%. In addition, 2,305 serum and plasma specimens from 1,256 individuals at increased risk for HTLV-I and/or HTLV-II infection and 1,049 individuals from HTLV-I and/or HTLV-II endemic areas were tested with the ABBOTT PRISM HTLV-I/HTLV-II assay (Table VI). Of the 2,305 specimens tested, 152 (6.59%) specimens were repeatedly reactive, of which 129 (84.87%) specimens tested positive by research use only Western blot and/or RIPA. Thirty four of the 129 specimens were anti-HTLV-I positive, 84 specimens were anti-HTLV-II positive, and 11 specimens were anti-HTLV positive but not typeable.

Table V

Reactivity of the ABBOTT PRISM HTLV-I/HTLV-II Assay in Individuals Known to be Positive for HTLV-I/HTLV-II Antibodies and Individuals with HTLV-I and/or Suspected HTLV-II Associated Diseases

Category	Number Tested	Number Repeatedly Reactive (% of Total)	Number Positive By Supplemental Tests[a] (% of Repeatedly Reactive)	HTLV Type Differentiation of Supplemental Test-Positive Specimens[b]		
				HTLV-I	HTLV-II	Not Typeable
Preselected anti-HTLV-I/HTLV-II Positive	601	601[c] (100.00)	601 (100.00)	303	298	0
HTLV-I and/or Suspected HTLV-II Associated Diseases[d]	114	114 (100.00)	113[e] (99.12)	109	0	4
TOTAL	715	715 (100.00)	714 (99.86)	412	298	4

[a] A positive result was defined by the presence of antibodies to both *gag* (p24) and *env* (native gp46 or gp61/67) antigens using research use only Western blot and/or RIPA.

[b] HTLV type differentiation was determined by reactivity to recombinant gp46-I or gp46-II peptides on a research use only Western blot, or by research use only HTLV-I and HTLV-II peptide EIAs.

[c] Specimens from the preselected anti-HTLV-I/HTLV-II positive category were only tested once.

[d] Individuals with HTLV-I and/or suspected HTLV-II associated diseases included ATL patients (52) and HAM/TSP patients (62).

[e] The remaining repeatedly reactive specimen (ATL patient) was indeterminate by supplemental testing.

Table VI

Reactivity of the ABBOTT PRISM HTLV-I/HTLV-II Assay in Individuals at Increased Risk for HTLV-I and/or HTLV-II Infection, and from HTLV-I and/or HTLV-II Endemic Areas

Category	Number Tested	Number Repeatedly Reactive (% of Total)	Number Positive By Supplemental Tests[a] (% of Repeatedly Reactive)	HTLV Type Differentiation of Supplemental Test-Positive Specimens[b]		
				HTLV-I	HTLV-II	Not Typeable
Increased Risk for HTLV-I and/or HTLV-II Infection[c]	1,256	106 (8.44)	100[d] (94.34)	8	83	9
HTLV-I and/or HTLV-II Endemic Areas[e]	1,049	46 (4.39)	29[f] (63.04)	26	1	2
TOTAL	2,305	152 (6.59)	129[g] (84.87)	34	84	11

[a] A positive result was defined by the presence of antibodies to both *gag* (p24) and *env* (native gp46 or gp61/67) antigens using research use only Western blot and/or RIPA.

[b] HTLV type differentiation was determined by reactivity to recombinant gp46-I or gp46-II peptides on a research use only Western blot.

[c] Individuals at increased risk for HTLV-I and/or HTLV-II infection included intravenous drug users (1,125) and STD clinic patients (131).

[d] The 100 supplemental test-positive specimens were all intravenous drug users (IVDU). Five of the six remaining repeatedly reactive specimens (IVDU) were indeterminate and one was negative by supplemental testing.

[e] Individuals from HTLV-I and/or HTLV-II endemic areas included specimens from the following areas: Caribbean (200), West Africa (200), Japan (200), and Central Africa (449).

[f] The 29 supplemental test-positive specimens included two from West Africa, 18 from Japan, and nine from Central Africa. The remaining repeatedly reactive specimens were indeterminate (16) or could not be interpreted by supplemental testing (1).

[g] All 129 of these specimens were repeatedly reactive on a licensed anti-HTLV-I/HTLV-II reference test. An additional 93 specimens out of the 2,305 tested were repeatedly reactive on the licensed reference test and negative on the PRISM HTLV-I/HTLV-II assay. None of these 93 specimens were positive by supplemental testing.

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