Human T-Lymphotrophic Virus Types I and II

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

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

Key to Symbols

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Caution]</td>
<td>Consult instructions for use</td>
</tr>
<tr>
<td>![Conjugate]</td>
<td>Conjugate</td>
</tr>
<tr>
<td>![Conjugate Wash]</td>
<td>Conjugate Wash</td>
</tr>
<tr>
<td>![Contains Azide]</td>
<td>Contains Sodium Azide. Contact with acids liberates very toxic gas.</td>
</tr>
<tr>
<td>![Distributed By]</td>
<td>Distributed by</td>
</tr>
<tr>
<td>![EC REP]</td>
<td>Authorized Representative in the European Community</td>
</tr>
<tr>
<td>![HTLV-II Control]</td>
<td>HTLV-II Positive Assay Control</td>
</tr>
<tr>
<td>![In Vitro]</td>
<td>In Vitro Diagnostic Medical Device</td>
</tr>
<tr>
<td>![IVD]</td>
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<td>![Line Cleaner]</td>
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<tr>
<td>![Lot]</td>
<td>Lot Number</td>
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<tr>
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<td>Assay Kit Card</td>
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<tr>
<td>![Master Lot]</td>
<td>Master Lot</td>
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<tr>
<td>![Negative Calibrator]</td>
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<tr>
<td>![Microparticles]</td>
<td>Microparticles</td>
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<tr>
<td>![Positive Calibrator]</td>
<td>Positive Calibrator</td>
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<tr>
<td>![Prime/Purge Accessories]</td>
<td>Prime/Purge Accessories</td>
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<tr>
<td>![Prime/Purge accessories]</td>
<td>Prime/Purge Accessories</td>
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<tr>
<td>![Run Control Adapters]</td>
<td>Run Control Adapters</td>
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<tr>
<td>![Sample Cups]</td>
<td>Sample Cups</td>
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<tr>
<td>![Transfer Wash]</td>
<td>Transfer Wash</td>
</tr>
<tr>
<td>![Warning: May cause an allergic reaction]</td>
<td>Warning: May cause an allergic reaction</td>
</tr>
<tr>
<td>![Warning: Severe Irritant]</td>
<td>Warning: Severe Irritant</td>
</tr>
</tbody>
</table>

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

U.S. License No. 43
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 (HTLV-I) and/or human T-lymphotropic virus Type II (HTLV-II) in human serum and plasma. 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 specific tests are obtained while the donor’s heart is still beating. It is not intended for use on cord blood specimens.

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 HTLV-II antibodies present in the sample bind to the antigen(s) on the Microparticles.
- After this 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 and 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 Conjugate Wash.
- The Acidinium-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 negative for anti-HTLV-I and 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 tested in duplicate. Follow appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive. Customers outside the U.S. must follow their country’s government 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 (REF #650-68)

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

- **MICROPARTICLES** 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: 0.0381 units/mL. Preservative: 0.1% sodium azide. (Symbol: )

- **CONJUGATE** 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: )

- **CAL [+]** 3 Bottles (10.4 mL each) Positive Calibrator (Human). Recalibrated, 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: )

- **CAL [-]** 3 Bottles (10.4 mL each) Negative Calibrator (Human). Recalibrated, inactivated plasma reactive for anti-HTLV-I. Minimum Sample/Cutoff is 0.50. Positive Calibrator may be cross-reactive with HTLV-II antigens. Preservative: 0.1% sodium azide. (Symbol: )

- **HTLV-I/HTLV-II CONTROL** 3 Bottles (10.4 mL each) HTLV-I/II Positive Control (1) Human. Recalibrated, inactivated plasma reactive for anti-HTLV-I/II. Minimum Sample/Cutoff is 1.50. HTLV-I/II Positive Control (2) may be cross-reactive with HTLV-I antigens. Preservative: 0.1% sodium azide. (Symbol: )

- **PROBE** 1 Bottle (324 mL) Human T-Lymphotropic Virus Types I and II Biotinylated Probe. Biotinylated HTLV-I, HTLV-II, and HTLV-I/II Enzyme Linked 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-I/II Positive Control (1) as “Pos Assay CTL (1)”.

- **Transfer Wash** 1 Bottle (3342 mL) Transfer Wash, Phosphate buffered saline. Preservative: 0.1% sodium azide. (Symbol: )

- **Conjugate Wash** 1 Bottle (1725 mL) Conjugate Wash, MES (2-[N-morpholino)ethanesulfonic acid) buffered saline. Preservative: 0.1% ProClin 300. (Symbol: )

- **Probe Wash** 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 (REF 1A75-02 or 3L27-02)

- Contains sodium azide.

ABBOTT PRISM Activator Diluent (REF 1A75-01 or 3L27-01)

- Contains sodium azide.

Or

ABBOTT PRISM Positive Run Control Kit (REF 3E60-11)

NOTE: Each batch MUST end in a release control (ABBOTT PRISM Positive Control). The ABBOTT PRISM Positive Control (included in Kit REF 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.

WARNINGS AND PRECAUTIONS

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

Safety Precautions

**CAUTION:** This product 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 or inactivated microorganisms will not transmit infection. Therefore, all human sourced materials should be considered potentially infectious. It is recommended that these reagents and human specimens be 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. 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.**
- **Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local, state, and federal regulations.**

- The human plasma used in the Negative Calibrator is nonreactive for HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, and anti-HCV.
- The human plasma used in the Positive Calibrator is reactive for anti-HTLV-I, anti-HTLV-II, and anti-HIV-1/HIV-2.
- The human plasma used in the Positive Control (1) and anti-HIV-1/HIV-2.

- **Any lot of ABBOTT PRISM HTLV-I/HTLV-II Wash Kit may be used with any lot of ABBOTT PRISM HTLV-I/HTLV-II Assay Kit.**
- **Any lot of ABBOTT PRISM HTLV-I/HTLV-II Wash Kit may 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 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 (REF 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.

Storage Instructions

- **Store the ABBOTT PRISM HTLV-I/HTLV-II Assay Kit, ABBOTT PRISM Run Control Kit, and ABBOTT PRISM Positive Run Control Kit, 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
- For the software versions that may be used to perform the assay, refer to the ABBOTT PRISM Assay / Software Version Matrix located in the Supplemental Information tab of the ABBOTT PRISM Operations Manual.
- 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-I 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 direct bilirubin (≤ 20 mg/dL), hemoglobin (≤ 500 mg/dL), red blood cells (≤ 0.4% v/v), triglycerides (≤ 3000 mg/dL), or protein (≤ 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 used with the ABBOTT PRISM HTLV-I/HTLV-II assay.
- Specimens collected by plasmapheresis that have not been frozen do not require recentrifugation. Specimens retested within 24 hours of initial centrifugation, must be recentrifuged from 30,000 to 75,000 g-minutes (excluding non-frozen plasmapheresis) not tested within 24 hours.

NOTE: If custom tube adapters (i.e., adapters not defined by the centrifuge manufacturer) are used, then the radius (r) operating within the centrifuge should be manually measured in millimeters and the RCF calculated.

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
- ABBOTT PRISM HTLV-I/HTLV-II Wash Kit
- ABBOTT PRISM HTLV-I/HTLV-II Assay Kit
- ABBOTT PRISM HTLV-I/HTLV-II Run Control Kit

Materials Required but Not Provided
- ABBOTT PRISM HTLV-I/HTLV-II Wash Kit
- ABBOTT PRISM HTLV-I/HTLV-II Assay Kit
- ABBOTT PRISM HTLV-I/HTLV-II Run Control Kit

Additional Materials Available
- ABBOTT PRISM Sample Cups
- ABBOTT PRISM Run Control Kit
- ABBOTT PRISM Line Cleaners

Centrifugation
- The time should be measured from the time the rotor reaches the required RCF or rpm to the time it begins decelerating.

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, rmax 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, rmax is a 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 (rmax) operating within the centrifuge should be manually measured in millimeters and the RCF calculated.

<table>
<thead>
<tr>
<th>g-minutes</th>
<th>RCF (x g)</th>
<th>Centrifugation Time (minutes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>12,000</td>
<td>15</td>
</tr>
<tr>
<td>20</td>
<td>9,000</td>
<td>20</td>
</tr>
<tr>
<td>25</td>
<td>7,500</td>
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</table>

Table II

<table>
<thead>
<tr>
<th>Table I</th>
<th>Table II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centrifugation Time (minutes)</td>
<td>RCF (x g)</td>
</tr>
<tr>
<td>10</td>
<td>5,000</td>
</tr>
<tr>
<td>15</td>
<td>2,000 - 3,000</td>
</tr>
<tr>
<td>20</td>
<td>1,500 - 3,000</td>
</tr>
<tr>
<td>25</td>
<td>1,300 - 3,000</td>
</tr>
</tbody>
</table>

Convert rpm to RCF as follows: RCF = 1.12 x rmax x (rpm/1000)^2

The unit of measurement for the product of RCF (x g) and centrifugation time (minutes).
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, Section 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 homogeneous solution. Additional gentle inversion may be required to thoroughly resuspend microparticles. Avoid foaming.

Gently invert calibrators and assay control in the calibrator pack several times prior to each use. 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. Gently invert calibrators and assay control in the calibrator pack several times. 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 the QA/QC procedures. The ABBOTT PRISM HTLV-I/HTLV-II assay is a three-step ChIAJ 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). Invalid controls: Additional controls may be run anywhere within a batch as an invalid/valid control. Specifications may be assigned to invalidating controls. If an invalid control fails to meet assigned specifications, sample processing is shutdown and no sample results are calculated or provided by the instrument. When an invalid 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 run control adapter.

If 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

1. 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.

2. 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 re centrifugation.

3. 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.

4. 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.

5. Follow appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive. Customers outside the U.S. must follow their country’s government recommendations and regulations for specimens found to be repeatedly reactive.

6. 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 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 prior to 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 recalculated 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 for 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.\(^b\) for a mixed model\(^c\) (Table II).

ASSAY SPECIFICITY

A total of 21,943 serum and plasma specimens from volunteer whole blood donors were collected and tested at five geographically distinct blood centers using three lots of PRISM HTLV-I/HTLV-II Reagent Kit (Tables IV and V). 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%.

Table IV

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Number Tested</th>
<th>% of Total (95% CI)</th>
<th>% of RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>4,066</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
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<tr>
<td>Plasma</td>
<td>5,967</td>
<td>2 (0.03)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Total Donors</td>
<td>10,033</td>
<td>2 (0.02)</td>
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</tr>
</tbody>
</table>

SPECIMEN CONTAINING POTENTIALLY INTERFERING SUBSTANCES

Table V

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Number Tested</th>
<th>% of Total (95% CI)</th>
<th>% of RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum</td>
<td>2,085</td>
<td>0 (0.00)</td>
<td>0 (0.00)</td>
</tr>
<tr>
<td>Plasma</td>
<td>3,785</td>
<td>5 (0.13)</td>
<td>5 (0.04 - 0.21)</td>
</tr>
<tr>
<td>Total Donors</td>
<td>6,870</td>
<td>5 (0.08)</td>
<td>5 (0.03 - 0.27)</td>
</tr>
</tbody>
</table>

Abbreviations: 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-BV positive (100), anti-HIV positive (12); anti-MHV positive (12), HBsAg positive (12), anti-HIV positive (12), anti-HIV 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 bison positive (5).
c The four repeatedly reactive specimens included the following categories: anti-HIV 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 VI). 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-I/HTLV-II 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 VII). 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-I/HTLV-II positive but not typeable.

### Table VI

<table>
<thead>
<tr>
<th>Category</th>
<th>Number Tested</th>
<th>Number Positive by Research Use Only (%)</th>
<th>Number Positive by Supplemental Test (%)</th>
<th>HTLV Type Differentiation of Supplemental Test-Positive Specimens</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Positive</td>
<td>601</td>
<td>100.00</td>
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<tr>
<td>Suspected HTLV-II Associated Diseases</td>
<td>114</td>
<td>100.00</td>
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<tr>
<td>Total</td>
<td>715</td>
<td>100.00</td>
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</table>

### Table VII

<table>
<thead>
<tr>
<th>Category</th>
<th>Number Tested</th>
<th>Number Positive by Research Use Only (%)</th>
<th>Number Positive by Supplemental Test (%)</th>
<th>HTLV Type Differentiation of Supplemental Test-Positive Specimens</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increased Risk for HTLV-I and/or HTLV-II Infection</td>
<td>1,256</td>
<td>100.00</td>
<td>(8.44)</td>
<td>(94.34)</td>
</tr>
<tr>
<td>HTLV-I and/or HTLV-II Endemic Areas</td>
<td>1,049</td>
<td>29.00</td>
<td>(4.39)</td>
<td>(63.04)</td>
</tr>
<tr>
<td>Total</td>
<td>2,305</td>
<td>129.00</td>
<td>(6.69)</td>
<td>(84.65)</td>
</tr>
</tbody>
</table>

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BIBLIOGRAPHY
