



Trypanosoma cruzi (E coli, Recombinant) Antigen



Customer Service
United States: 1-877-4ABBOTT

FOR REFERENCE USE ONLY

Key to symbols used	
REF List Number	LOT Lot Number
IVD In Vitro Diagnostic Medical Device	ASSAY KIT CARD Assay Kit Card
Store at 2-8°C	MASTER LOT Master Lot
Store at 15-30°C	CALIBRATORS Calibrators
Caution, consult accompanying documents	REACTION TRAYS Reaction Trays
Consult instructions for use	PIPETTE TIPS Pipette Tips
ACTIVATOR DILUENT Activator Diluent	REAGENT COMPONENTS Reagent Components
ACTIVATOR CONCENTRATE Activator Concentrate	RUN CONTROL ADAPTERS Run Control Adapters
Expiration Date	SAMPLE CUPS Sample Cups
	Manufacturer
	EC REP Authorized Representative

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

US License No. 43

NAME AND INTENDED USE

The ABBOTT PRISM Chagas assay is an *in vitro* chemiluminescent immunoassay (ChLIA) for the qualitative detection of antibodies to *Trypanosoma cruzi* (*T. cruzi*), the causative agent of Chagas disease, in human serum and plasma specimens. The ABBOTT PRISM Chagas assay is intended to screen individual human donors, including volunteer donors of whole blood and blood components and other living donors, for the presence of antibodies to *T. cruzi*. The assay is also intended for use in testing serum and plasma specimens to screen organ donors when specimens are obtained while the donor's heart is still beating, and in testing blood specimens to screen cadaveric (non-heart-beating) donors. It is not intended for use on cord blood specimens.

SUMMARY AND EXPLANATION OF THE TEST

Chagas disease or American trypanosomiasis is caused by the parasite *T. cruzi*. There are 3 morphologic forms in the life cycle of *T. cruzi*: epimastigote (multiplying form found in the midgut of insect vectors); amastigote (multiplying intracellular form in mammalian hosts); and trypomastigote (nondividing extracellular form in mammalian blood and insect feces).¹ The majority of *T. cruzi* proteins are expressed in all 3 morphologic forms. The ABBOTT PRISM Chagas assay is based on recombinant proteins FP3, FP6, FP10, and TcF.²⁻⁵ In aggregate, these 4 hybrid recombinant proteins represent at least 14 distinct antigenic regions that broadly represent all 3 morphologic forms. Moreover, these recombinant proteins also contain antigens recognized by antibodies present in persons with acute *T. cruzi* infection as well as those with chronic Chagas disease.⁶

BIOLOGICAL PRINCIPLES OF THE PROCEDURE

The ABBOTT PRISM Chagas assay is a two-step sandwich ChLIA. The reactions occur within the ABBOTT PRISM System in the following sequence:

- Microparticles coated with *T. cruzi* recombinant antigens (FP3, FP6, FP10, and TcF) are incubated with sample (either plasma, serum, calibrator, or control) and specimen diluent in the incubation well of the reaction tray. During incubation, antibodies to *T. cruzi* 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.
- The mouse anti-human CPSP-acridinium conjugate is added to the microparticles on the matrix and incubated to bind any antibody to *T. cruzi* that is present. After this second 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 antibody to *T. cruzi* in the sample. The presence or absence of antibodies to *T. cruzi* 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 antibody to *T. cruzi* by the criteria of the ABBOTT PRISM Chagas 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 antibody to *T. cruzi* by the criteria of the ABBOTT PRISM Chagas assay.

Specimens that are initially reactive must be handled as described in the **Preparation for Analysis** section of this package insert and retested in duplicate. Reactivity in either or both of these duplicated tests (*i.e.*, repeatedly reactive) is highly predictive of the presence of antibodies to *T. cruzi*. Follow the 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 that follows 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 Chagas Assay Kit (No. 7K35-68)

NOTE: Do not mix reagents from different bottles. Do not mix or interchange reagents from different ABBOTT PRISM Chagas Assay Kits.

- **MICROPARTICLES** 1 Bottle (340 mL) *T. cruzi* (*E. coli*, recombinant) antigen coated microparticles in phosphate buffer. Minimum concentration: 0.036% solids. Preservative: 0.1% ProClin 300. (Symbol: ●)

- **CONJUGATE** 1 Bottle (335 mL) Anti-human (mouse monoclonal):CPSP-acridinium conjugate in MOPS buffer with protein (bovine) stabilizers and detergent. Minimum concentration: 5 ng/mL. Preservative: 0.1% ProClin 300. (Symbol: ▲)
- **CAL-** 3 Bottles (10.4 mL each) Negative Calibrator. Recalcified, human plasma. Preservative: 0.1% ProClin 300 and 0.01% gentamicin sulfate. (Symbol: NC)
- **CAL+** 3 Bottles (10.4 mL each) Positive Calibrator containing *T. cruzi* (mouse/human chimeric monoclonal) antibody in recalcified, human plasma. Minimum activity: 3.53 S/CO. Preservative: 0.1% ProClin 300 and 0.01% gentamicin sulfate. (Symbol: PC)
- **SPECIMEN DILUENT** 1 Bottle (340 mL) Specimen Diluent containing borate buffer, surfactants, and urea. Preservative: 0.1% ProClin 300. (Symbol: X)

Other Reagents Required

ABBOTT PRISM Chagas Wash Kit (No. 7K35-58)

- **TRANSFER WASH** 1 Bottle (3422 mL) Transfer Wash. Borate buffered saline with surfactant. Preservative: 0.1% ProClin 300. (Symbol: ♯)
- **CONJUGATE WASH** 1 Bottle (2811 mL) Conjugate Wash. TRIS buffer with detergent. Preservative: 0.15% ProClin 950. (Symbol: ★)

ABBOTT PRISM Activator Concentrate (No. 1A75-02 or 3L27-02)

- **ACTIVATOR CONCENTRATE** 4 Bottles (900 mL each) Activator Concentrate. 0.4% hydrogen peroxide/0.06% diethylenetriamine-pentaacetic acid.

ABBOTT PRISM Activator Diluent (No. 1A75-01 or 3L27-01)

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

ABBOTT PRISM Chagas Run Control Kit (No. 6L86-10)


NOTE: Each batch **MUST** end in a release control (ABBOTT PRISM Chagas Positive Control). The ABBOTT PRISM Chagas Positive Control (included in Kit No. 6L86-10) must be used as a release control, which has been configured to validate the system functionality and release sample results. Refer to the ABBOTT PRISM Chagas Run Control Kit package insert for detailed handling and use instructions.

WARNINGS AND PRECAUTIONS

For *In Vitro* Diagnostic Use.

The performance characteristics of this product have not been established for the laboratory diagnosis of *T. cruzi* 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 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 Pathogens⁷. Biosafety Level 2⁸ or other appropriate biosafety practices^{9,10} 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 disinfectant.^{11,12}
- Decontaminate and dispose of all specimens, reagents, and other potentially contaminated materials in accordance with local, state, and federal regulations.^{13,14}
- The human plasma used in the negative calibrator is nonreactive for antibodies to *T. cruzi*, HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, and anti-HCV.
- The positive calibrator contains *T. cruzi* (mouse/human chimeric monoclonal) antibody added to human plasma that is nonreactive for antibodies to *T. cruzi*, HBsAg, HIV-1 RNA or HIV-1 Ag, anti-HIV-1/HIV-2, and anti-HCV.

- All the components of this kit contain methylisothiazolones, which are components of ProClin. These components 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

- Avoid microbial and chemical contamination of samples, reagents, and equipment. The use of disposable pipette tips is recommended for any preliminary sample transfer.**
- 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 homogeneous solution. Additional gentle inversion may be required to thoroughly resuspend microparticles. Avoid foaming. Each component of the ABBOTT PRISM Chagas 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 Chagas Assay Kits.
- Any lot of ABBOTT PRISM Chagas Wash Kit can be used with any lot of ABBOTT PRISM Chagas Assay Kit.
- Any lot of ABBOTT PRISM Activator Concentrate, ABBOTT PRISM Activator Diluent, and Control from an ABBOTT PRISM Chagas Run Control Kit may be used with any lot of ABBOTT PRISM Chagas Assay Kit.
- Treat Negative and Positive Calibrators and Controls as potentially infectious.
- Use accurately calibrated equipment.
- Do not freeze reagents.
- Failure to adhere to instructions in the ABBOTT PRISM Operations Manual or this 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, **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 (No. 6A36-60). Cover the bottle opening securely with the cap provided and invert gently 5 to 10 times to mix. Load the activator solution on the ABBOTT PRISM System. Refer to the ABBOTT PRISM Operations Manual, Section 5, **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 Chagas Assay Kit, the ABBOTT PRISM Chagas Run Control Kit and the ABBOTT PRISM Activator Concentrate at 2-8°C.
- Store the ABBOTT PRISM Chagas Wash Kit and the ABBOTT PRISM Activator Diluent at room temperature (15-30°C).
 - The activator solution must be stored at 15-30°C and used within 24 hours of preparation.
- When stored and handled as directed, assay and wash kit components are stable until the expiration date.
- Store ABBOTT PRISM Pipette Tips and ABBOTT PRISM Reaction Trays in their original packaging until use.

Indications of Instability or Deterioration of Reagents

The ABBOTT PRISM System will not continue to process samples when calibrator or positive 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.
- ABBOTT PRISM software version 3.2 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

Specimen Types

- For living donors, 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 Chagas assay. Follow the manufacturer's specimen collection 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 the ABBOTT PRISM HCV assay; therefore, heparin is not recommended for any ABBOTT PRISM assay.

- For cadaveric donors, only **serum** may be used; follow general standards and/or regulations for collection.
- Do not use cadaveric **plasma** specimens.

Specimen Conditions

- 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.
- For living donors and cadaveric (non-heart-beating) donors, serum from heparinized patients may be incompletely coagulated, resulting in potential instrument errors such as drain time errors due to the presence of fibrin. To prevent this phenomenon, draw specimen prior to heparin therapy or after heparin therapy is discontinued and activated partial thromboplastin time (aPTT) levels return within normal range.
- Do not use heat-inactivated specimens.
- Do not use specimens with obvious microbial contamination.
- Performance has not been established using plasmapheresis 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 Chagas assay.
- Clear, nonhemolyzed specimens should be used when possible. Specimens containing visible particulate matter may give erroneous or inconsistent test results.

Potential Interfering Substances

Spiking studies performed with potential interfering substances did not demonstrate interference with the assay either for negative or low level positive donor samples. Interference with detection of low levels of added antibodies to *T. cruzi* was seen in some diagnostic patient samples with abnormally high levels of bilirubin and serum proteins.

- No qualitative performance differences were observed when a minimum of 27 nonreactive donor specimens and 27 reactive donor specimens, which were created by spiking with *T. cruzi* antibody to low-level reactivity, were spiked with potentially interfering substances, creating samples with artificially elevated levels of bilirubin (≤ 20 mg/dL), hemoglobin in plasma (≤ 500 mg/dL), red blood cells ($\leq 0.4\%$ v/v), triglycerides ($\leq 3,000$ mg/dL), or protein (≤ 12 g/dL).

- Additional studies were performed on diagnostic specimens with various levels of potentially interfering substances. Twenty specimens from patients with elevated levels of endogenous hemoglobin in whole blood (16.3 to 18.0 g/dL) and 18 specimens with elevated levels of endogenous triglycerides (1,003 to 2,094 mg/dL) were spiked with *T. cruzi* antibody to target a low level of reactivity. All of these specimens prior to spiking were nonreactive. All of the spiked hemoglobin and triglyceride specimens became reactive.

Twenty seven specimens from individuals within the normal range of endogenous total protein (6.5 to 8.1 g/dL) yielded expected S/CO values when spiked with low levels of *T. cruzi* antibody. Sixteen specimens from patients with elevated levels of endogenous total protein (9.1 to 14.4 g/dL) and 7 specimens with elevated levels of endogenous total bilirubin (7.2 to 38.6 mg/dL) were spiked with *T. cruzi* antibody to target a low level of reactivity. All of these specimens prior to spiking were nonreactive. Ten of the sixteen specimens with elevated total protein (9.3 to 14.4 g/dL) did not become reactive. Two of the 7 specimens with elevated total bilirubin did not become reactive (with levels of 20.1 and 37.4 mg/dL total bilirubin). The impact of abnormally high concentrations of these potentially interfering substances on the ABBOTT PRISM Chagas assay is unknown as the clinical status for the diagnostic patient samples used in the high concentration endogenous studies is not known and therefore the patients may not represent typical blood donors.

Preparation for Analysis

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

Nonfrozen specimens must be centrifuged such that g-minutes are between 30,000 and 75,000. A refrigerated or nonrefrigerated centrifuge is acceptable for use. The acceptable time and force ranges that meet this criterion are listed in **Table I**.

Any specimen that is not tested or retested within 24 hours of initial centrifugation must be recentrifuged as described in **Table I**.

NOTE: Filtered cadaveric serum specimens that are not tested within 24 hours of initial centrifugation must be recentrifuged, but do not need to be refiltered.

Table I: Nonfrozen Specimens

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

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

ANY previously frozen specimen that is not tested or retested within 24 hours of initial centrifugation and not refrozen must be recentrifuged at 30,000 to 75,000 g-minutes.

Table II: Previously Frozen Specimens

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

Additional Centrifugation Information

Convert rpm to RCF as follows: $RCF = 1.12 \times r_{max} (rpm/1,000)^2$

Convert RCF to rpm as follows: $rpm = 1000 \times \sqrt{\frac{RCF}{1.12 \times r_{max}}}$

RCF - The relative centrifugal force generated during centrifugation.

rpm - The revolutions per minute of the rotor on which the specimens are being spun (usually the digital readout on the centrifuge will indicate the rpm).

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

r_{max} - Radius of the rotor in millimeters. The radius measured is

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

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

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

Filtration of Centrifuged Cadaveric SERUM Specimens

Failure to adhere to the following instructions may result in erroneous or inconsistent test results.

Wear personal protective equipment, including eyewear.

After centrifugation, filter each cadaveric specimen through a Millipore GV Filter as follows:

1. Label an empty tube with the specimen identification number matching the original tube.

2. Remove the plunger from a sterile 10 cc syringe.

NOTE: Do not use a syringe smaller than 10 cc because excess pressure may build up, potentially causing damage to the filter unit or personal injury.

3. Remove the sterile filter from the package.

4. Securely screw the syringe to the filter.

NOTE: Do not touch the tip of the filter to avoid possible contamination.

5. Pour a minimum of 1 mL of the centrifuged cadaveric serum into the syringe.

NOTE: Additional volume may be required based on the number of PRISM assays performed. Refer to the **Specimen Volume** section of this package insert.

6. While holding the filter syringe unit over the tube, insert the plunger and slowly apply pressure to deliver the filtered cadaveric serum.

NOTE: A clogged filter will resist pressure and no additional sample volume will pass through.

7. If necessary, replace the clogged filter as follows:

a. Remove the sterile filter from the package.

b. Carefully invert the syringe to a filter-side-up position with the syringe plunger intact to prevent sample leakage. Gently remove the clogged filter and dispose of it in a potentially infectious waste container.

c. Securely screw the syringe to the filter.

d. Slowly apply pressure on the plunger to deliver the filtered cadaveric serum into the tube.

e. Repeat this step as needed to successfully complete the filtration process.

NOTE: Filtered cadaveric specimens that are not tested within 24 hours of initial centrifugation must be recentrifuged, but do not need to be refiltered.

Storage and Shipping

- Living donor specimens may be stored at 2-8°C or -20°C or colder for up to 14 days, or 30°C or colder for up to 7 days (inclusive of shipping time). Storage at a combination of these temperatures may not exceed 14 days.

- Cadaveric serum specimens may be stored at 2-8°C or -20°C or colder for up to 14 days, or 30°C or colder for up to 2 days (inclusive of shipping time). Storage at a combination of these temperatures may not exceed 14 days.

- Prior to freezing, the serum or plasma should be removed from the clot or red blood cells to avoid hemolysis.

- Living donor specimens and cadaveric donor serum stored at -20°C or colder for greater than 14 days may be used for informational purposes (e.g., lookback testing, discordant sample testing, clinical and validation testing).

- For collection of specimens from cadaveric donors, follow general standards and/or regulations.

- When shipping specimens, package and label specimens in compliance with applicable regulations covering the transport of clinical specimens and infectious substances.

- Thirty nonreactive and 30 low-level reactive living donor 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.
- Twenty-seven nonreactive and 28 low-level reactive cadaveric specimens that were received frozen showed no qualitative performance differences when subjected to 6 additional freeze/thaw cycles. However, some cadaveric specimens that have undergone multiple freeze/thaw cycles, or have been stored frozen for prolonged periods, may give erroneous or inconsistent test results.

Specimen Volume

The specimen volume required to test a single sample on the ABBOTT PRISM System varies according to the number of assays configured, which assays are selected, and the type (size) of specimen container used. The ABBOTT PRISM Chagas assay requires a 50 µL sample dispense. For ABBOTT PRISM Sample Cups, the minimum specimen volume required for one ABBOTT PRISM Chagas assay is 350 µL. For either primary or aliquot tubes or additional assay volume requirements, refer to the ABBOTT PRISM Operations Manual, Section 5.

PROCEDURE

Materials Provided

- No. 7K35-68 ABBOTT PRISM Chagas Assay Kit

Materials Required but not Provided

- No. 7K35-58 ABBOTT PRISM Chagas Wash Kit
- No. 1A75-02 or 3L27-02 ABBOTT PRISM **ACTIVATOR CONCENTRATE**
- No. 1A75-01 or 3L27-01 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. 6L86-10 ABBOTT PRISM Chagas Run Control Kit
- No. 6A36-31 ABBOTT PRISM **RUN CONTROL ADAPTERS**
- Protective Disposable Gloves
- Disinfectant
- Purified Water-rinsed or Clean Disposable Measuring Equipment

For Cadaveric Specimens Only

- No. 2P41-01 Millipore GV Filters
- 10 cc Sterile Syringes

Additional Materials Available

- No. 7B36-01 ABBOTT PRISM **SAMPLE CUPS**

ABBOTT PRISM Chagas Assay Procedure

Key procedures that require operator interaction for testing samples are listed below. 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 homogeneous solution. Additional gentle inversion may be required to thoroughly resuspend microparticles. Avoid foaming. Each component of the ABBOTT PRISM Chagas 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 onto the ABBOTT PRISM System.
- Verify that an adequate number of ABBOTT PRISM Reaction Trays are in the Tray Loader.
- Verify that an 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, Controls**, Control Handling Procedure, in this package insert.
- After the calibrators have been automatically pipetted, remove the calibrator rack. Close the calibrator 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/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 Chagas assay is a two-step ChLIA procedure.

QUALITY CONTROL PROCEDURES

Calibration

The ABBOTT PRISM Chagas Negative and Positive Calibrators are automatically tested in triplicate at the beginning of each batch. The ABBOTT PRISM System will not generate results when calibrator values do not meet specifications. This may indicate either deterioration or contamination of reagents or instrument failure.

Controls

1. The ABBOTT PRISM Chagas 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 Chagas Positive Control is automatically tested as a single replicate. This control must meet specifications defined in the ABBOTT PRISM Chagas Run Control package insert in order to validate the system functionality and release sample results. If this control does not meet specifications, 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 Chagas 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 Chagas 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 Chagas 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 Chagas 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 Chagas assay cutoff value using the following formula:

$$\text{Cutoff Value} = (0.16 \times \text{Mean Positive Calibrator [PC] Net Counts}) + \text{Mean Negative Calibrator [NC] Net Counts}$$

Example: Mean PC Net Counts = 5,000
Mean NC Net Counts = 200
(0.16 x 5,000) + 200 = 1,000
Cutoff Value = 1,000

The ABBOTT PRISM System calculates the ABBOTT PRISM Chagas assay S/CO for each sample and control using the following formula:

$$\text{S/CO} = \text{Sample Net Counts} \div \text{Cutoff Value}$$

Example: Sample Net Counts = 4,750
Cutoff Value = 1,000
4,750 ÷ 1,000 = 4.75
S/CO = 4.75

Interpretation of Results

- In the ABBOTT PRISM Chagas assay, specimens with net counts less than the cutoff value are nonreactive and need not be tested further. Nonreactive specimens are considered negative for antibody to *T. cruzi* by the criteria of the ABBOTT PRISM Chagas assay.
- Specimens with net counts greater than or equal to the cutoff value are considered initially reactive by the criteria of the ABBOTT PRISM Chagas assay. All initial reactive specimens retested within 24 hours of initial centrifugation do not require recentrifugation. All initial reactive specimens stored greater than 24 hours after initial centrifugation must be recentrifuged prior to retesting according to the **Preparation for Analysis** section of this package insert. Initially reactive specimens must be retested in duplicate using the ABBOTT PRISM Chagas Assay Kit.
- If the sample net counts for both retests are less than the cutoff value, the specimen is nonreactive. Nonreactive specimens are considered negative for antibody to *T. cruzi* by the criteria of the ABBOTT PRISM Chagas 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 antibodies to *T. cruzi* by the criteria of the ABBOTT PRISM Chagas assay.
- US customers must follow the appropriate FDA recommendations and regulations for specimens found to be repeatedly reactive. Customers outside the US must follow their country's government recommendations and regulations for specimens found to be repeatedly reactive.
- Although the association of infectivity of donated blood or plasma and the presence of antibodies to *T. cruzi* is strong, it is recognized that presently available methods for detection of antibodies to *T. cruzi* are not sensitive enough to detect all potentially infectious units of blood, plasma, or possible cases of *T. cruzi* infection. A nonreactive test result does not exclude infection.

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 Chagas assay, specimens with S/CO values of less than 1.00 are reported as nonreactive. Specimens with an S/CO value of greater than or equal to 1.00 are reported as 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.

- 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.
- For living donors and cadaveric (non-heart-beating) donors, serum from heparinized patients may be incompletely coagulated, resulting in potential instrument errors such as drain time errors due to the presence of fibrin. To prevent this phenomenon, draw specimen prior to heparin therapy or after heparin therapy is discontinued and activated partial thromboplastin time (aPTT) levels return within normal range.
- 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.
- 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.
- An increased occurrence of drain time errors may be observed for cadaveric specimens.
- Do not use cadaveric plasma specimens.
- All specimens must be centrifuged according to the **Preparation for Analysis** section of this package insert prior to running the assay.
- Performance has not been established using plasmapheresis 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 Chagas assay.
- Do not use heat-inactivated specimens.
- Do not use specimens with obvious microbial contamination or gross lipemia.
- Do not use specimens with obvious gross hemolysis. No qualitative performance differences were observed when living donor specimens were spiked with 500 mg/dL of hemoglobin. No qualitative performance differences were observed for living donor specimens with up to 1730 mg/dL endogenous levels of hemoglobin. No qualitative performance differences were observed for cadaveric donor specimens with up to 821 mg/dL of hemoglobin.
- Avoid microbial contamination of reagents or wash kit components by carefully following handling precautions within this package insert.
- A test result that is negative does not exclude the possibility of exposure to or infection with *T. cruzi*.

SPECIFIC PERFORMANCE CHARACTERISTICS

Reproducibility

Reproducibility was determined with the ABBOTT PRISM Chagas assay by testing a 6-member panel consisting of 1 strongly reactive specimen (panel member 4), 1 moderately reactive specimen (panel member 3), 2 reactive specimens near the assay cutoff (panel members 2 and 6), and 2 nonreactive specimens (panel members 1 and 5). Panel member 4 was prepared using pooled *T. cruzi* positive human plasma. The other panel members were prepared in recalcified human plasma. Each panel member was tested in replicates of 4 in 5 runs over 5 days with each of 3 reagent lots on a total of 3 instruments across 2 sites. The Negative and Positive Controls were tested once at the beginning and end of each run on each subchannel. The Negative and Positive Calibrators were tested in replicates of 3 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 analysis¹⁵ for a random effects model¹⁶ (Table III).

Table III
ABBOTT PRISM Chagas Assay Reproducibility

Panel Member or Control	Number of Replicates	Mean S/CO	Intra-assay SD	%CV	Inter-assay ^a SD	%CV
1	180	0.21	0.072	NA ^b	0.082	NA
2	180	1.84	0.189	10.3	0.223	12.1
3	180	9.27	0.695	7.5	0.961	10.4
4	180	18.73	1.391	7.4	2.311	12.3
5	180	0.18	0.028	NA	0.033	NA
6	180	2.15	0.179	8.3	0.286	13.3
Negative Control	180	0.20	0.026	NA	0.030	NA
Positive Control	180	2.83	0.275	9.7	0.378	13.4

Cutoff Value = (0.16 x Mean Positive Calibrator [PC] Net Counts) + Mean Negative Calibrator [NC] Net Counts

Calibrator	Number of Replicates	Mean Net Counts	Intra-assay SD	Intra-assay %CV	Inter-assay SD	Inter-assay %CV
Negative Calibrator	270	292	32.3	11.1	41.2	14.1
Positive Calibrator	270	8,427	557.1	6.6	905.9	10.8

^a Inter-assay variability includes intra-assay variability.

^b NA = Not applicable: %CVs are not meaningful when S/CO approaches zero.

Specificity

A total of 16,249 fresh serum and plasma specimens from volunteer blood donors were collected and tested with the ABBOTT PRISM Chagas assay at 3 geographically distinct blood centers in the United States (Table IV). The initial reactive and repeat reactive rates were 0.20% (32/16,249) and 0.16% (26/16,249), respectively. Repeatedly reactive specimens were tested further with a supplemental assay (radioimmuno precipitation assay [RIPA]). Based on these RIPA test results, 3 of the 26 specimens were positive and 23 were negative.

Specificity based on assumed zero prevalence of antibody to *T. cruzi* in blood donors was estimated in this study to be 99.86% (16,223/16,246) with a 95% confidence interval of 99.79% to 99.91%.

Table IV
Reactivity of Specimens from Blood Donors with the ABBOTT PRISM Chagas Assay

Volunteer Donors	Number Tested	IR (% of Total) (95% CI)	RR (% of Total) (95% CI)	Number Positive by Supplemental Testing
Serum	12,129	23 (0.19) (0.12 - 0.28)	17 (0.14) (0.08 - 0.22)	1
Plasma	4,120	9 (0.22) (0.10 - 0.41)	9 (0.22) (0.10 - 0.41)	2
Total Donors	16,249	32 (0.20) (0.13 - 0.28)	26 (0.16) (0.10 - 0.23)	3

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

A total of 618 frozen serum and plasma specimens collected from individuals with medical conditions unrelated to *T. cruzi* infection or containing potentially interfering substances were tested with the ABBOTT PRISM Chagas assay (Table V). Of the 618 specimens, 60 (9.71%) were initially reactive and 17 (2.75%) were repeatedly reactive. Of the 17 repeatedly reactive specimens, none were positive by supplemental testing.

Table V
Reactivity of Specimens from Individuals with Medical Conditions Unrelated to *T. cruzi* Infection with the ABBOTT PRISM Chagas Assay

Category	Number Tested	IR (% of Total)	RR (% of Total)	Number Positive by Supplemental Testing
Leishmaniasis ^a	58	5 (8.62)	1 (1.72)	0
Malaria Positive ^b	32	8 (25.00)	4 (12.50)	0
Syphilis Serologic Positive	16	12 (75.00)	3 (18.75)	0
Other Medical Conditions Unrelated to <i>T. cruzi</i> Infection and Specimens Containing Potentially Interfering Substances ^c	512	35 (6.84)	9 ^d (1.76)	0
Total	618	60 (9.71)	17 (2.75)	0

IR = Initially Reactive; RR = Repeatedly Reactive

^a These specimens included the following categories: cutaneous (6) and visceral (52).

^b These specimens included the following categories: *P. falciparum* (16) and *P. vivax* (16).

^c These specimens included the following categories: anti-HBV positive (16), anti-HCV positive (16), HBsAg positive (16), anti-HTLV-I/HTLV-II positive (16), anti-HAV positive (16), anti-HIV-1/HIV-2 positive (16), anti-CMV positive (16), anti-EBV positive (16), anti-HSV positive (16), rubella antibody positive (16), West Nile virus antibody positive (16), varicella-zoster virus antibody positive (16), anti-nuclear antibody positive (16), human anti-mouse antibody positive (16), elevated IgG (16), elevated IgM (16), rheumatoid factor positive (16), toxoplasma antibody positive (16), yeast infection (16), tuberculosis positive (16), multiple myeloma (16), monoclonal gammopathy (16), multiparous females (16), elevated triglycerides (16), elevated bilirubin (16), elevated hemoglobin (16), influenza vaccine recipients (50), Dengue virus antibody positive (16), *E. coli* infection (16), and Lyme disease positive (14).

^d These specimens included the following categories: anti-HCV positive (1), anti-HAV positive (1), anti-CMV positive (1), varicella-zoster virus antibody positive (1), tuberculosis positive (1), *E. coli* infection (1), and influenza vaccine recipients (3).

Sensitivity

A total of 110 serum specimens from individuals known to be positive for the *T. cruzi* parasite were tested with the ABBOTT PRISM Chagas assay (Table VI). Of the 110 specimens, 65 were from individuals that tested positive by identification of the parasite with xenodiagnosis. The remaining 45 specimens were from individuals known to be positive for the *T. cruzi* parasite by historical identification of the parasite with xenodiagnosis or hemoculture. The specimens were obtained from the Chagas-endemic countries of Argentina, Bolivia, Brazil, and Peru. Of the 110 specimens tested, all (100.00%) were repeatedly reactive.

In this study, the sensitivity was estimated to be 100.00% (110/110) for parasite positive specimens with a 95% confidence interval of 96.70% to 100.00%.

Table VI
Reactivity of Specimens (Parasite Positive for *T. cruzi*) with the ABBOTT PRISM Chagas Assay

Category	Number Tested	Number RR (% of Total)
Preselected <i>T. cruzi</i> Parasite Positive	110	110 (100.00)

RR = Repeatedly Reactive

A total of 85 serum specimens from individuals known to be positive for *T. cruzi* antibodies were tested with the ABBOTT PRISM Chagas assay (Table VII). The specimens were obtained from Argentina and presumed positive based on 2 different serologic tests for antibodies to *T. cruzi* (i.e., enzyme-linked immunosorbent assay [ELISA], immunofluorescence assay [IFA], or indirect hemagglutination assay [IHA]). Of the 85 specimens tested, all were RIPA positive and repeatedly reactive on the Abbott PRISM Chagas assay.

A total of 202 plasma specimens that were repeatedly reactive on a previously licensed test for antibodies to *T. cruzi* were tested with the Abbott PRISM Chagas assay. Of the 202 specimens tested, 139 were RIPA positive. All of the 139 RIPA positive specimens were repeatedly reactive on the Abbott PRISM Chagas assay (Table VII).

Table VII
Reactivity of Specimens (Serologic Positive for *T. cruzi*) with the ABBOTT PRISM Chagas Assay

Category	Number Tested	ABBOTT PRISM Chagas Number RR	Number Positive by Supplemental Testing
Preselected <i>T. cruzi</i> Serologic Positive South America	85	85	85
Preselected Samples Reactive with a Licensed <i>T. cruzi</i> ELISA United States	202	163	139
Total	287	248	224

RR = Repeatedly Reactive

Sensitivity and Specificity in a High Risk Population

A total of 524 serum specimens from individuals residing in Chagas-endemic areas were tested with both the ABBOTT PRISM Chagas assay and a *T. cruzi* antibody licensed ELISA. Specimens were obtained from the endemic countries of Argentina, Brazil, Guatemala, Panama, and Peru. Specimens that were repeatedly reactive on either test were tested further with RIPA. Of the 524 specimens tested with both assays, 131 were RIPA positive. Of the 131 RIPA positives, 129 were repeatedly reactive on both the ABBOTT PRISM Chagas assay and the licensed test for antibodies to *T. cruzi*, demonstrating equivalent sensitivity for the two assays.

In this study, the sensitivity of the Abbott PRISM Chagas assay was estimated to be 98.47% (129/131) with a 95% confidence interval of 94.59% to 99.81% (Table VIII). The specificity was estimated to be 98.72% (385/390) with a 95% confidence interval of 97.03% to 99.58%.

Table VIII
ABBOTT PRISM Chagas Assay and Most Probable *T. cruzi* Antibody Status Based on RIPA Results

ABBOTT PRISM Chagas Assay Results	Most Probable <i>T. cruzi</i> Antibody Status			Total
	Positive	Negative	Indeterminate ^a	
Repeatedly Reactive	129	5	3	137
Nonreactive	2	385	0	387
Total	131	390	3	524

^a Indeterminate RIPA results were excluded from calculations.

PERFORMANCE CHARACTERISTICS OF CADAVERIC SERUM TESTING

Reproducibility

Twenty-nine postmortem serum specimens, collected up to 19.9 hours after death, and 20 living donor serum specimens were spiked with human plasma reactive for antibodies to *T. cruzi* to create low-level reactive specimens. Each specimen was tested once per day over 6 days with each of 3 ABBOTT PRISM Chagas reagent lots. Between-day and total %CV values were determined (Table IX).

Table IX
ABBOTT PRISM Chagas Assay Reproducibility

Specimen Category	Number of Replicates	Mean S/CO	Between-day		Total ^a	
			SD	%CV	SD	%CV
Postmortem	522	3.17	0.331	10.4	0.397	12.5
Living Donor	360	3.04	0.299	9.8	0.376	12.4

^a Total variability contains between-day, between-lot, and the specimen-lot interaction variance components.

Specificity

Assay specificity was determined by testing postmortem serum specimens, collected up to 20.4 hours after death, and living donor serum specimens. Each specimen was tested once on each of 3 ABBOTT Chagas reagent lots (Table X).

Table X
ABBOTT PRISM Chagas Assay Reactivity

Specimen Category	Number of Specimens	Mean S/CO	Nonreactive (% of Total)	Initially Reactive (% of Total)
Postmortem	56	0.15	55 (98.21)	1 (1.79)
Living Donor	56	0.16	56 (100.00)	0 (0.00)

Based on this study, the ABBOTT PRISM Chagas assay has an estimated specificity of 98.21% (55/56) (95% binomial confidence interval of 90.45% - 99.95%) for postmortem serum specimens.

Sensitivity

Postmortem specimens, collected up to 23.1 hours after death, and living donor specimens were spiked with human plasma reactive for antibodies to *T. cruzi* to create low-level reactive specimens. Each specimen was tested once, within 24 hours of spiking, on each of 3 ABBOTT PRISM Chagas reagent lots (Table XI).

Table XI
ABBOTT PRISM Chagas Assay Reactivity

Specimen Category	Number of Specimens	Mean S/CO	Nonreactive (% of Total)	Initially Reactive (% of Total)
Postmortem	52	3.01	0 (0.00)	52 (100.00)
Living Donor	60	2.63	0 (0.00)	60 (100.00)

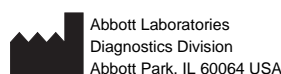
Based on this study, the ABBOTT PRISM Chagas assay has an estimated sensitivity of 100.00% (95% binomial confidence interval of 93.15% - 100.00%) for postmortem serum specimens.

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