COVER PAGE

Abbott Laboratories

Official Title of the Study: Abbott Laboratories Alinity s Blood Screening Assays – Clinical Evaluation Protocol

NCT Number: NCT03285295

Type of Document: Study Protocol

Protocol Number: 9DY-02-14U01-03

Version: 5

Date of Document: April 18, 2018

Date of Document Approval: April 24, 2018

Abbott Laboratories
Alinity s Blood Screening Assays - Clinical Evaluation Protocol

WARNING:

FOR PERFORMANCE EVALUATION, ONLY

FOR INVESTIGATIONAL USE, ONLY. The performance characteristics of this product have not been established. No clinical decision or patient notification should be made based on the results obtained with this product.

Protocol No.: 9DY-02-14U01-03
Version: 5
Date: April 18, 2018
Incorporating Amendment 4
Rationale for amendment: Incorporates Scientific Changes

Abbott Monitors:

Tuan L. Bui
Clinical Research Manager
Phone: 224.668.4702
e-mail: tuan.l.bui@abbott.com

Nira Joshi
Sr. Clinical Research Assoc.
Phone: 224.667.9672
e-mail: nira.joshi@abbott.com

Susan Sullivan
Sr. Clinical Research Assoc.
Phone: 224.668.7949
e-mail: susan.sullivan@abbott.com

John Birdsall
Specialist Medical Affairs.
Phone: 224.668.2276
e-mail: john.birdsall@abbott.com

Address/Fax: Abbott Laboratories
for all monitors
09TM, CP1
100 Abbott Park Road
Abbott Park, Illinois 60064-6070
Fax: (224) 667-7836

Table of Contents

I. Introduction

This protocol is for the evaluation of the Alinity s investigational assays using the Alinity s System. The Alinity s System is a high-volume, automated, blood-screening analyzer that is designed to determine the presence of specific antigens and antibodies by using chemiluminescent microparticle immunoassay (CMIA) detection technology. The system performs high-throughput routine and stat processing that features continuous access and automated retesting. The Alinity s System may also be referred to as BSQ. Some materials (e.g., calibrators, assay controls, reagents, bulk solutions) received may be labeled as BSQ instead of Alinity s. This material is considered equivalent and operates the same as Alinity s labeled material.

The Alinity s System is used for infectious disease marker testing in blood-screening and plasma laboratories for the following assays:

- The Anti-HBc assay is used for the qualitative detection of antibody to hepatitis B core antigen (anti-HBc) in human serum and plasma.
- The Anti-HCV assay is used for the qualitative detection of antibodies to hepatitis C virus (anti-HCV) in human serum and plasma.
- The HTLV I/II assay is used for the qualitative detection of antibodies to human T-lymphotropic virus type I and/or human T-lymphotropic virus type II (anti-HTLV-I/anti-HTLV-II) in human serum and plasma.
- The Chagas assay is used for the qualitative detection of antibodies to *Trypanosoma cruzi* (the causative agent of Chagas disease) in human serum and plasma.
- The HBsAg assay is used for the qualitative detection of hepatitis B surface antigen (HBsAg) in human serum and plasma.
- The HBsAg Confirmatory assay is used to confirm the presence of hepatitis B surface antigen (HBsAg) in human serum and plasma by means of specific antibody neutralization.
- The HIV Ag/Ab Combo assay is used for the simultaneous qualitative detection of human immunodeficiency virus (HIV) p24 antigen and antibodies to HIV type 1 (HIV-1 group M and group O) and/or type 2 (HIV-2) in human serum and plasma.

The performance of the Alinity s blood screening assays will be evaluated by performing system reproducibility and specimen testing as described in the Testing Procedure section of this protocol.

The Abbott monitor will provide assay clinical brochures for each of the assays which contain relevant referenced literature, applicable technology, and summary of any known and potential risks and benefits to humans. Alinity s clinical brochures will be

provided for the Alinity s calibrators, the Alinity s assay controls, and the Alinity s release controls.

This study will be conducted in compliance with this protocol, Good Clinical Practice (GCP) and the applicable regulatory requirements.

II. Objectives

The objective of this study is to demonstrate the performance and intended use of each of the Alinity s investigational assays in a donor screening environment using clinical samples to evaluate assay performance characteristics. A comparison of assay performance will be done versus the Food and Drug Administration (FDA) licensed assays. The data will be used to support regulatory submissions and/or publications.

III. Study Design

A. Overview

Protocol directed testing will be performed at a minimum of 3 testing sites, to evaluate system reproducibility, specificity and sensitivity. For specificity, one of the sites that test specimens from whole blood donor collections will also test specimens from plasmapheresis collections. Specimens will be provided by clinical sites or by Abbott. In addition, panels will be provided by Abbott. A minimum of 3 lots of each of the Alinity s investigational assay reagents, calibrators and controls will be used throughout the study.

The testing or collection sites will provide random donor specimens that are collected as part of the routine blood or plasma donation process to evaluate specificity of each assay. A minimum of 15,000 random donor specimens are needed for the Anti-HCV, HBsAg and HIV Ag/Ab Combo assays collected across a minimum of three whole blood donor centers and one plasmapheresis center. A minimum of 15,000 random donor specimens are needed for the Anti-HBc, HTLV I/II and Chagas assays collected across a minimum of three whole blood donor centers. Each donor specimen may be tested on one or more assays, therefore specimens may be obtained from approximately 23,000 to 90,000 blood donors depending on the number of assays tested on each donor sample. At the time of the blood donation, the donor will be informed that the donor center may use their donation for research studies. Donors will be provided an information sheet explaining this process. The donor may also be asked to return and participate in a follow-up blood collection based on results obtained. The donor will sign a

separate research consent form for the follow-up blood collection and have approximately 20 to 60 mLs of blood drawn for testing.

Abbott will provide frozen samples characterized as positive or at risk for infectious disease to evaluate sensitivity of each assay. The specimens will be designated by the Abbott monitor for each specific assay study. All specimens will be identified using a sample identification number (SID).

1. System Reproducibility

Abbott will provide reproducibility panel members for each assay that will be randomized during testing. System reproducibility will be performed in two runs per day on each of 5 (nonconsecutive) days with a minimum of one break of 1 day with a minimum of 3 lots of each Alinity s blood screening assay reagents, calibrators, and controls at a minimum of 3 sites.

2. Specimen Testing

To evaluate sensitivity for each of the Alinity s blood screening assays, Abbott will provide specimens that were prospectively collected under separate protocols or are not individually identifiable. These specimens include the following populations:

- Preselected positives (all assays)
- U.S. individuals at increased risk of disease (all assays, except Chagas)
- Individuals from endemic areas (Chagas, HIV Ag/Ab Combo, and HTLV-I/II)

To evaluate specificity for the Alinity s blood screening assays, the sites will provide residual serum or plasma from routine donations from the following;

- Whole blood donors (EDTA plasma or serum for each of the Alinity s blood screening assays)
- Plasmapheresis donors (Source Plasma for HIV Ag/Ab Combo, HBsAg & Anti-HCV assays)

3. Additional System Testing

In addition, testing on the Alinity s System may be performed to align with the clinical site's specific procedure(s) for the validation of a new system. Any associated analyses for this testing will be reviewed/ performed by Abbott and a data package will be provided to the clinical sites and maintained in the site study file.

B. Ethics

The protocol will be reviewed by the Institutional Review Board (IRB) as part of study oversight.

The blood or plasma donor specimens will be collected as part of the routine blood donation process. The blood donor will review an IRB-approved information sheet as part of the consent process. The information sheet indicates that by consenting to donate blood or plasma their sample may be used in research studies.

For the blood donor testing, if results of the investigational assay do not agree with the final specimen status based on supplemental testing, the donor may be asked to provide a follow-up sample. For these individuals providing follow-up samples, their consent to participate must be documented on an IRB-approved consent form prior to the collection of the follow-up specimen.

The specimens provided by Abbott were either obtained prospectively and are considered linked or are not individually identifiable. The specimens will be identified by sample identification number, and the testing sites will have no access to subject data. Refer to the Section VI.A.1 Study Population/Sample Size for the specimen categories for each group.

The specimens obtained prospectively were collected using IRB/IEC approved specimen collection protocols and consent forms that comprehend the testing of these specimens as outlined in this testing protocol. These specimen collection studies were either sponsored by Abbott or by specimen collection vendors. Specimens that are leftover, not individually identifiable were obtained according to the FDA Guidance on Informed Consent for *In Vitro* Diagnostic Device Studies using Leftover Human Specimens that are not Individually Identifiable, April 25, 2006 or specimens were obtained according to applicable laws and guidance regarding informed consent and the use of leftover human specimens. The unidentified specimens are being used when the scientific value is based on characterization of the sample rather than the subject's medical history.

These specimens will be identified by sample identification number, and the testing sites will have no access to subject data. The clinical testing sites will be blinded from knowledge of the specimen categories for specimens provided by Abbott.

Donor specimens may be used to assess system performance. Specimens used for this assessment will be leftover residual samples that have been de-identified and cannot be linked to a subject. These specimens will be re-labeled with a new study identification number (SID).

All reports transferred to and communications with Abbott which pertain to specimens in the study must identify each specimen by a sample identification number to ensure subject confidentiality.

C. General Schedule of Events

Each site will configure and calibrate the Alinity s blood screening assays on the Alinity s System.

Prior to the start of protocol directed testing, the study staff will be trained in the operation of the Alinity s System. This training may occur at an Abbott facility or at the clinical site. The training will involve an overview of the system operation including system configuration, system maintenance, system calibration, control and specimen testing procedures. If needed, the clinical sites may supply leftover de-identified residual samples for the purpose of training or to confirm Alinity s System readiness. Documentation of study staff training will be maintained in the clinical study files.

Testing personnel will be required to demonstrate acceptable performance with each investigational assay prior to beginning system reproducibility or specimen testing for that assay. The Abbott monitor will provide the samples for this testing. This testing is used for training and to confirm the site's ability to perform the assay.

After successful completion of training, testing personnel will perform reproducibility and specimen testing using the Alinity s blood screening assay, calibrator and assay control clinical brochures and the procedures as described in this protocol.

Case report forms (CRF) will be utilized to document completion of the test procedures. The Abbott monitor will review the data and CRF to assure compliance to the study-directed procedures and to monitor the progress of the study.

The study will take approximately 5-10 months to complete.

D. Comparator Method

Each donor specimen and each specimen provided by Abbott will be tested with a designated FDA-licensed assay using the ABBOTT PRISM system, with the exception of specimens that are well characterized or have limited sample volume. This includes the following:

- HIV-1 Antigen positive - characterized by HIV-1 p24 testing.
- HIV-1 viral isolate - characterized by PCR amplification, DNA sequence, and phylogenetic analysis.
- Preselected *T cruzi* Parasite Positive - characterized parasite positive by

xenodiagnosis, hemoculture, or blood smear.

- Subset of preselected *T cruzi* serology positive and Chagas endemic specimens with limited sample volume that have comparator and supplemental testing data from a previous clinical study. If any discrepant ABBOTT PRISM Chagas results occurs between new results and the previous clinical study results, all of the archived specimens in these 2 categories will be tested with the ABBOTT PRISM Chagas assay.

The Abbott monitor will provide specific details of which specimens do not require comparator testing. All comparator testing will be performed according to the manufacturer's instructions and will include retesting, where required.

The comparator assay results will be compared to the corresponding results of the investigational assay.

E. Supplemental Testing

HIV, HBV and HCV nucleic acid testing (NAT) results for each of the donor specimens will be provided to Abbott to further characterize the donor specimens.

Specimens from donors, individuals at increased risk, individuals from endemic areas, Recovered HBV Individuals (for HBsAg assay) and individuals with HTLV-I/II associated diseases that are repeatedly reactive by either the Alinity s investigational assay or the comparator method or repeatedly gray zone negative (≥ 0.80 S/CO to < 1.00 S/CO) by the Alinity s investigational assay will be further tested using FDA licensed assays or research use only methods. This supplemental testing will be performed at the clinical sites or at external reference laboratories. Results obtained from this testing will be used to better characterize the specimen and assess final status.

The detailed algorithms for supplemental testing will be provided in a separate document for use with the clinical study protocol. Supplemental testing will be performed per each assay algorithm and if a specific assay is no longer commercially available or changes occur in the donor center's routine procedure, a revised version of the algorithm will be provided by the clinical monitor. Additional testing may be performed based on the clinical site's internal supplemental testing procedures. Data generated will be provided to Abbott and will be used for informational purposes.

Preselected positive specimens for each assay will have documented positive results prior to testing at the clinical sites. Supplemental testing is not required, but may be requested by the monitor for troubleshooting purposes.

F. Follow-up Specimens

For all donor specimens with investigational Alinity s results that are discordant with final statuafter supplemental testing, an attempt will be made to obtain a follow-up whole blood specimen approximately 4 to 6 weeks after initial donation for further analysis. The subject will sign a study specific consent form for collection of the additional specimen. The follow-up specimen will be tested by the applicable investigational Alinity s blood screening assay, the comparator method, and supplemental testing as required.

When a follow-up specimen is not obtained or to obtain additional information when an investigational Alinity s result is discordant with final status, an independent sample from the index donation (e.g., plasma unit) may be tested. Testing on the independent sample may include the investigational Alinity s blood screening assay, the comparator method, and supplemental testing as required.

The follow-up result will be used to better characterize the initial donation and may be used to indicate seroconversion (or rule out seroconversion). If seroconversion occurs and the follow-up results are repeatedly reactive for PRISM and positive on supplemental testing, the status for that donor will be considered positive and the index sample results will be removed from the specificity calculation.

IV. Operating Conditions

A. Material and Equipment

1. Product Description

All investigational products, supplies, and materials will be supplied by Abbott Laboratories.

The investigational products include reagents, calibrators, assay controls, and release controls for each assay, and the consumables and commodities as follows:

Alinity s HIV Ag/Ab Combo		8100/6P01
Alinity s HBsAg		8100/6P02
Alinity s HBsAg Confirmatory		8100/6P03
Alinity s Anti-HCV		8100/6P04
Alinity s Anti-HBc		8100/6P06
Alinity s HTLV-I/II		8100/6P07
Alinity s Chagas		8100/6P08
Alinity s Consumables/Commodities		
*	Alinity Trigger	8100/6P11-60
*	Alinity Pre-Trigger	8100/6P12-65

*	Alinity s Concentrated Wash Buffer	8100/6P13-88
*	Alinity Reaction Vessels	8100/ 6P14-01
*	Alinity s Sample Cups	8100/ 3R01-01

Additional materials provided by Abbott:
- Training panel
- Reproducibility panel

A description of the reagents, controls, accessories, consumables, and disposables required to operate the Alinity s System is presented in each of the assay specific clinical brochures. A further description of calibration and control procedures is presented in the Calibrator Clinical Brochure and Assay Control Clinical Brochure.

Expired material(s) must not be used.

All materials for the operation of the comparator device must be used within the expiration dates defined by the manufacturer's instructions.

2. Product Storage and Handling Requirements

Storage instructions for the investigational reagents, calibrators, and controls are provided in the clinical brochure. Secured storage of these supplies with appropriately restricted access is required.

The Alinity s accessories, consumables, and disposables must be stored as indicated on the product label or packaging.

Abbott Laboratories will provide the sites with training panels and reproducibility panels. The panels will be shipped frozen and must remain frozen at -20°C or below upon receipt. Refer to the "Specimen Collection and Preparation for Analysis" section of the clinical brochure for storage and handling requirements.

All commercially available products will be handled according to the manufacturer's package insert instructions.

3. Instructions for Use

Testing on the Alinity s System for this study will utilize current version of system software. The site will operate the Alinity s System following investigational labelling instructions in the investigational Alinity s System Operations Manual and the clinical protocol.
Instructions for use can also be found in the Alinity s blood screening assay, Calibrator, and Assay Control Clinical Brochures.

All versions of the clinical brochures used and a copy of the comparator method package inserts used in this study will be retained in the clinical study files.

B. Environment

Testing of the Alinity s blood screening assays will be performed at a minimum of 3 external donor testing facilities that will test whole blood donor collections. One of the sites that test specimens from whole blood donor collections will also test specimens from plasmapheresis collections.

C. Testing Personnel Requirements

Personnel involved in executing the study must be trained on operating and maintaining the Alinity s System. Each individual will also be trained on the protocol and clinical brochures and will be required to demonstrate acceptable performance with the investigational assay prior to beginning Testing Procedures described in this protocol.

V. Product Accountability

The testing site must maintain records and accountability documentation of the receipt dates, lot numbers, quantities, and the use, destruction and/or return of all investigational products. The Abbott monitor will periodically verify the accuracy of these inventories.

All investigational products must be returned to Abbott or disposed of on-site. An investigator will not supply investigational products to any individual who is not named as a study investigator.

VI. Study Methods and Procedures

A. Specimen Selection

1. Study Population/Sample Size

Approximately 7,600 specimens provided by Abbott will be distributed across a minimum of 3 clinical sites for the testing with the designated Alinity s blood screening assay. Each site will test approximately 2,500 specimens representing similar distribution across assay and specimen categories on the designated Alinity s blood screening assay. Comparator testing will be performed at a minimum of one clinical site.

Assay		Number	Prospectively Collected Linked	Not Individually Identifiable
Alinity s HIV Ag/Ab Combo				
*	Individuals at Increased Risk of HIV-1/2 Infection	600	X	X
*	Individuals at Increased Risk of HIV Infection from an HIV-2 Endemic Area	500	X	
*	Preselected HIV-1 Positive	1000	X	
*	Preselected HIV-2 Positive	200		X
*	Preselected HIV-1 Antigen Positive/ viral isolates	50		X
Alinity s HTLV I/II				
*	Individuals at Increased Risk of HTLV I/II Infection	500	X	X
*	Individuals from an HTLV I/II Endemic Areas	500	X	
*	Preselected HTLV I/II Positive	600	X	X
*	Individuals with HTLV I/II Associated Diseases	100	X	
Alinity s HBsAg/HBsAg Confirmatory				
*	Individuals at Increased Risk of HBV Infection	400	X	X
*	Preselected HBsAg Positive	400	X	X
*	Recovered HBV	50	X	X
Alinity s Anti-HBc				
*	Individuals at Increased Risk of HBV Infection	400	X	X
*	Preselected Total Anti-HBc Positive	400	X	X
Alinity s Anti-HCV				
*	Individuals at Increased Risk of HCV Infection	400	X	X
*	Preselected Anti-HCV Positive	400	X	X
Alinity s Chagas				
*	Individuals from Chagas Endemic Areas	600	X	
*	Preselected *T cruzi* Parasite Positive	100	X	
*	Preselected *T cruzi* Serology Positive	200	X	X

Demographic information including age, gender, and race are documented, where available. Risk factors, medical history, and supplemental results are documented, as applicable.

2. Whole Blood Donor and Plasmapheresis Specimens

Plasma or serum specimens from unique blood donors and plasma specimens from unique plasmapheresis donors will be obtained.

Leftover specimens with sufficient residual volume of either plasma or serum specimen will be tested on each Alinity s blood screening assays as shown in the following table.

Assay	**Whole Blood Donor (serum or EDTA plasma)***	**Plasmapheresis Donor (source plasma)**
HIV Ag/Ab Combo HBsAg/Confirmatory Anti-HCV	12,000	3,000
HTLV I/II Anti-HBc Chagas	15,000	NA

*At least one third of total whole blood donors will be EDTA plasma specimens and at least one third will be serum specimens.

No demographic information will be collected from these blood donors.

Inclusion and Exclusion Criteria

Random donor specimens selected for the study must have sufficient volume to complete designated testing. The Abbott monitor will provide the recommended volume requirements for each assay.

The subject/specimen must meet the following inclusion/exclusion criteria to be eligible for participation in this study:

Inclusion Criteria

Serum or EDTA plasma from a whole blood donor for each of the Alinity s assays or a plasmapheresis sample from a plasmapheresis donor (for HIV Ag/Ab Combo, HBsAg & Anti-HCV assays).

Exclusion Criteria

For testing with the Alinity s Chagas assay, exclude donors that have been screened on a previous donation using a licensed test for antibodies to *T cruzi.*

Note: A subject may participate at different times during the study for separate assay studies, but each subject should be represented only once for each assay.

Frozen samples provided by Abbott have no specific inclusion/exclusion criteria that the clinical site needs to verify prior to testing.

3. Specimen Handling, Storage, and Accountability

Donor specimens will be handled according to the facility's policies and procedures for collecting and storing specimen.

Specimens obtained from whole blood donations at the clinical site are residual or left-over collected in either serum or EDTA collection tube. Specimens obtained from plasmapheresis donations are representative of the citrated plasma from the donation. Each specimen is to be tested using the unique blood donation identification number.

Follow-up specimens from donors will be collected via routine venipuncture into EDTA and/or serum tubes according to the site's routine collection procedures. Whole blood volume will be approximately 20 to 60 mLs. Specimen centrifugation will be done following the requirements of the comparator assay package insert and the requirements of the investigational Alinity s clinical brochure. After testing of the investigational assay and comparator assay, the remaining volume should be stored frozen at -20ºC or colder. Your Abbott monitor will provide details of any supplemental testing needed.

Frozen specimens will be shipped to the site and must be stored frozen at -20°C or below, until tested. All frozen aliquots must be handled and stored at the clinical sites as described in the clinical brochure. Testing with the investigational assay will be performed using specimens subjected to the same number of freeze/thaw cycles (one thaw cycle). The comparator method testing should be done on the same freeze/thaw cycle (one thaw cycle). Sample aliquots used for testing on the comparator method should be handled or processed per the comparator method package insert. If a specimen is thawed and refrozen prior to testing or retesting, the occurrence must be documented on an Incident CRF and the Abbott monitor notified.

The clinical testing sites must maintain records (e.g., packing slips) of the delivery and receipt of each shipment, as well as document the condition of the clinical specimens upon arrival and the location where the specimens are being stored. Specimen accountability documentation must be maintained by the testing site to document the use and destruction and/or return of specimens used in the study.

Specimens should be shipped to Abbott Laboratories for additional testing or to a reference laboratory for supplemental testing as directed by the Abbott monitor. Store the specimens at -20 ºC or below and ship overnight on dry ice. When shipped, specimens must be packaged and labeled in compliance with

applicable state, federal, and international regulations governing the transport of clinical specimens and infectious substances.

A specimen may be removed from the study if the sample is found unacceptable for testing (e.g. inappropriate handling prior to testing, inadequate volume), or for other assignable causes. The reason for removal must be documented on an Incident CRF. Specimens removed from the study may need to be replaced, if deemed necessary by the Abbott monitor, to meet requirements for the minimum number of specimens.

B. General Study Procedures

1. Assay and/or System Configuration

The investigational Alinity s software is installed onto the Alinity s System at the time of instrument installation. The monitor will provide instructions on software configurations needed to start the study.

2. Instrument System General Procedures

Maintenance procedures are to be performed as instructed in the Investigational Alinity s System Operations Manual. Reports for maintenance and any documentation for component replacements that occurred during the study should be filed in study records.

The on-board inventory of the Alinity s System supplies and reagents will be checked daily. Load consumables and update inventory as necessary.

Refer to the Investigational Alinity s System Operations Manual.

3. Assay Calibration

Each Alinity s blood screening assay will be calibrated as described in the Alinity s Assay Clinical Brochure and the Alinity s Calibrator Clinical Brochure. The calibrator lot number and expiration date information will be read from barcodes when the material is tested on the instrument system. Refer to Calibration Procedures Section of the Alinity s System Operations Manual.

Calibration is to be performed for each investigational reagent lot. Print or transfer electronic report of the calibration and control results for each reagent lot tested. Refer to the Alinity s Assay Clinical Brochure and Alinity s Calibrator Clinical Brochure for frequency of calibration.

Refer to the Alinity s Assay Control Clinical Brochure to determine acceptability of the quality control results used during calibration. If unexpected results are obtained or problems are encountered, contact the Abbott monitor.

4. Assay Training

The study staff will be trained in the operation of the Alinity s System prior to performing protocol directed activities. This training will involve an overview of the system operation including system configuration, system maintenance, system calibration, control and specimen testing procedures.

Training materials (e.g., training panel) will be used to assess proficiency of the user performing the investigational assays. Assay training is to be performed by each user for each assay. Testing will be performed as described in a separate workflow document. The Abbott monitor will evaluate the results for acceptability.

5. Quality Control Validity Criteria

Daily quality control for each Alinity s blood screening assay will include all Alinity s assay controls tested a minimum of once each day, on each reagent lot tested for that day.

Refer to the Investigational Alinity s System Operations Manual for testing of the quality controls.

Daily quality control for each Alinity s blood screening assay will be assessed for validity using the ranges described in the Alinity s assay control clinical brochure.

6. Troubleshooting Quality Controls

The following steps must be used when troubleshooting and documenting quality control failures.

1) Determine if an assignable cause can be found (e.g., incorrect placement, bubbles). If an assignable cause can be found, correct the identified problem.

2) Retest the quality control from the **original control bottle**. If the quality controls are within the validity criteria, testing may continue.

3) If the quality control value still does not meet the validity criteria, test the quality control substituting a **new control bottle**. If the quality control value is within the established range, continue testing.

4) If the quality control value still does not meet the validity criteria, **repeat assay calibration** on the instrument and **repeat all quality controls**. If the quality control values are within the established range, continue testing.

5) If the quality control value still does not meet the validity criteria, place **new**

reagents on the instrument, **repeat assay calibration**, and **repeat all quality control testing**. If the controls are within the validity criteria, testing may continue.

Do not discard any reagents, calibrators, or controls that may have caused the out of range results.

6) If the quality control value still does not meet the validity criteria, contact the Abbott monitor for further instruction. Any test results generated since the last acceptable control run must be evaluated to determine if test results may have been adversely affected.

An Incident CRF must be completed, documenting the troubleshooting steps performed and any additional action required for resolution (e.g., recalibration, opening a new control bottle). The Abbott monitor must be notified when control failures are observed.

7. Method for Handling Retests and Error Codes

The following conditions may require retesting:

- Specimens with S/CO values ≥ 1.00 are considered initially reactive for all Alinity s and comparator assays. Specimens with S/CO values from 0.80 to < 1.00 are considered initially gray zone negative for all Alinity s assays. Initially reactive and initially gray zone negative specimens must be retested in duplicate.
- Testing of a specimen may be repeated if assignable cause (e.g., operator error, instrument malfunction) can be determined and documented by the site.

- For tests that cannot be completed and result in an **error code**, the test is to be repeated. If unable to retest the specimen or additional troubleshooting steps are required to resolve the error, an Incident CRF should be completed. A copy of the error report or screen display should be printed or electronically transferred, when possible.

The original SID will be used for all repeat testing. Refer to the Specimen Collection and Preparation for Analysis Section of the Alinity s Assay Clinical Brochure. If re-centrifugation is required, document on the appropriate CRF.

8. Additional Troubleshooting

The Abbott monitor may request certain procedures or additional testing to be performed for troubleshooting purposes. The additional testing may require various procedures be repeated.

C. Testing Procedures

All clinical laboratory site testing is to be performed according to the clinical protocol and the appropriate sections of the clinical brochures.

1. System Reproducibility

Alinity s System reproducibility testing will be performed at a minimum of 3 clinical sites using a minimum of 3 lots of each Alinity s blood screening assay reagents, calibrators, and controls.

Testing will include two runs per day on each of 5 (nonconsecutive) days with a minimum of one break of 1 day with a minimum of 3 Alinity s reagent lots at a minimum of 3 sites. Each reproducibility run will include four replicates tested for each reproducibility panel member.

Procedure

1) Test each Alinity s blood screening assay control (Negative and Positive plus any additional controls required for HIV or HTLV testing), if daily quality controls have not been already tested and assessed for validity.

2) Refer to the "Specimen Collection and Preparation for Analysis" section of the assay clinical brochure for detailed procedures on handling of samples prior to placing the reproducibility panel members on the Alinity s System.

3) Place the barcoded sample tubes in a sample rack as directed by the Abbott monitor.

4) Schedule an Alinity s release control for each assay. If release control is not already on the system, place the calibrator and control rack on the Alinity s System in the priority bay to schedule testing.

5) Testing as described in Steps 1 through 4 will be performed on each of five days for each reagent lot for each assay.

Note: If an error occurs during reproducibility testing, contact the Abbott monitor. The reproducibility testing for that day may need to be repeated. Errors which occur during reproducibility testing should be documented on an Incident CRF.

2. Specimen Testing

Testing will be performed to determine the agreement of specimen results obtained from each Alinity s blood screening assay to the comparator method.

Testing of the comparator method will be performed according to each comparator package insert.

Each of the donor collection sites will provide specimens from random donors representing unique individuals for a total of 15,000 donor specimens for each assay. Whole blood donor specimens will be provided by a minimum of three donor collection sites and one site will provide specimens from plasmapheresis donors for HBsAg, anti-HCV, and HIV Ag/Ab Combo assays. Each testing site will test a portion of the whole blood donor specimens with a distribution of testing across a minimum of three Alinity s reagent, calibrator, and control lots as instructed by the monitor. The testing sites for Alinity s and PRISM may be different. The testing of the plasmapheresis specimens will be distributed across three Alinity s reagent, calibrator, and control lots. The results for the corresponding PRISM comparator assay and NAT assay, as applicable will be provided to Abbott for each donor specimen. Testing of any follow-up donor specimens will be done using the procedure below for the investigational Alinity s assay, comparator assay and supplemental testing as needed.

Approximately 7,600 specimens provided by Abbott will be distributed across the clinical testing sites. Specimens will be tested across a minimum of three lots of Alinity s assay reagents, calibrators and controls. Each site may test approximately 2,500 specimens depending on the total number of clinical sites and representing similar distribution across assay and specimen categories. In addition, the specimens will be tested on the corresponding PRISM comparator method at a minimum of one clinical site. The Abbott monitor will provide the details of which specimens to test for each assay, as well as the reagent/calibrator/control lot combination.

Note: After testing of a specimen, any remaining specimen volume must be retained frozen. The Abbott monitor may request certain procedures or additional testing to be performed for troubleshooting purposes. The additional testing may require various procedures to be repeated.

Note: Specimens should be tested on the same freeze thaw cycle for the Alinity s assay and the comparator method. If the sample has been tested or retested on a subsequent freeze thaw cycle, the event should be documented on an Incident Report form.

Procedure

1) Test each Alinity s assay quality control, if daily Alinity s quality controls have not been already tested and assessed for validity.

2) Refer to the “Specimen Collection and Preparation for Analysis” section of the clinical brochure for detailed procedures on handling of samples prior to placing specimens on the Alinity s System.

3) A single replicate of each specimen should be tested with the investigational Alinity s assay. Specimens should be placed in barcoded tubes in a sample rack and placed on the Alinity s System to schedule testing.

4) Schedule a Alinity s release control for each assay. If release control is not already on the system, place the calibrator and control rack on the Alinity s System in the priority bay to schedule testing.

   Note: All testing data generated before the release control will be printed when release control testing is complete.

5) Specimens with an initial S/CO result of ≥ 1.00 are considered initially reactive. Specimens with an initial S/CO result ≥0.80 to <1.00 are considered initially gray zone negative. Both initially reactive and initially gray zone negative specimens should be retested in duplicate with the Alinity s method. Specimens with an initial S/CO results of < 0.80 are considered nonreactive and do not require further testing.

6) Repeat testing should be performed using the same reagent lot and be done on the same day or the following workday. If greater than 48 hours has elapsed from initial centrifugation, re-centrifuge the sample and document on the Incident CRF. Refer to Alinity s assay clinical brochure for further information regarding centrifugation of specimens.

7) If both duplicate retest results are nonreactive (S/CO < 0.80), then the specimen is considered negative and no further testing is required. If either retest result has S/CO ≥0.80, then supplemental testing for the assay will be performed.

8) Each specimen should be tested with the comparator PRISM method. Specimens initially reactive by the comparator method should be retested in duplicate on the same day or on the next work day of testing. If re-centrifugation is required for the comparator method testing, document on the appropriate CRF. Refer to comparator package insert for further information regarding centrifugation of specimens.

9) If the comparator method result is repeatedly reactive, then supplemental testing for the assay will be performed.

10) Refer to the Alinity s Supplemental Algorithms and instructions from your Abbott monitor regarding supplemental testing.

11) After supplemental testing is complete for donor specimens, the Abbott monitor will notify you/the collection site of any donors that need to be contacted for follow-up blood collections.

Note: For other situations where retesting may be required (e.g. error codes) refer to the "Method for Handling Retests and Error Codes" section of this protocol.

VII. Methods for Data Collection and Documentation

A. Instrument Data Capture

In addition to the required instrument printouts, Alinity s data will be transmitted electronically using an approved data capture procedure (e.g., Abbott Link) by Abbott personnel on a daily or as needed basis.

For Abbott PRISM comparator data, the data will be transmitted electronically to Abbott using an internet data capture method. Instrument report data (e.g., instrument printout or other approved format) for all PRISM testing related to this study will also need to be provided to Abbott.

If any assay data is not retrieved by the electronic capture system, the data will be manually entered into the database at Abbott using the original instrument printout.

B. Case Report Forms

Case report forms (CRF) will be provided for collection of data including detailed instructions for completion of the CRFs.

CRF data or information related to the study will be recorded electronically using a web based system. Site personnel responsible for entering data will be trained on the use of the electronic system (i.e., access, entry and submission of data). Data entered by the site will be reviewed by an Abbott monitor, and queried if needed. Queries should be resolved in a timely manner.

Data or information recorded on the CRF with no prior written or electronic record, (e.g., specimen processing, storage date and time) will be considered the source document.

The investigator must sign or certify the CRF where indicated. The investigator's signature indicates that the data are accurate and complete. Where signatures are required they must be handwritten or captured electronically per 21 CFR Part 11. Stamps for signatures are not allowed.

At the conclusion of the study, a copy of the completed CRF will be maintained at each investigational site.

C. Supplemental Data Transfer

The HIV, HBV and HCV nucleic acid testing (NAT) results for the donor specimens will be provided to Abbott in a format as agreed upon with the clinical monitor.

The results for supplemental testing will be entered or a copy of the results (e.g., instrument printout, worksheet, report) will be uploaded into the eCRF system by the site.

VIII. Adverse Events

No side effects or adverse events are anticipated. In the unexpected event of a serious adverse event resulting from use of the investigational device, the Abbott monitor must be notified immediately by telephone and subsequently in writing within five (5) days of the occurrence. The event must be described on the adverse event case report form, as applicable. All adverse events are to be followed to satisfactory resolution, and any measures taken, as well as the follow-up, reported on the appropriate CRF.

A. Device Adverse Events

A **Device Adverse Event** is any effect on the health or safety of an individual associated with the use of a product which has or may have caused or contributed to an injury, a system malfunction or user error resulting in personal injury (e.g., electrical shocks, burns), or exposure to potentially hazardous material (e.g., chemical or biohazardous), or a fire or visible smoke that was not self-contained to the system and caused damage outside of the system.

A **Device Serious Adverse Event** is an adverse event that has or may have caused or contributed to a death or serious injury of an individual or an adverse event resulting from malfunction that could cause or contribute to a death or serious injury if the malfunction were to recur. A serious injury includes a life-threatening illness or injury, an illness or injury which results in permanent impairment of a body function or permanent, irreversible damage to body structure, or a condition, an injury or illness necessitating a medical or surgical intervention by a health care professional to prevent permanent, irreversible impairment of a body function, or damage to a body structure.

B. Subject Adverse Event

Donor specimens used in the study are collected as part of the routine blood donation process. Events related to the blood or plasma donation process will be handled according to the donor center procedures and not recorded in the study files.

For donor follow-up specimens collected under this protocol, subject adverse events will be documented if they occur. It is expected that drawing blood or plasma may cause pain, bruising, lightheadedness, and on rare occasion, infection

at the site of the blood draw. These events will not be recorded as adverse events as they are considered to be normal events that may occur during the course of a blood or plasma draw. Other events that may occur such as fainting, that are not routinely associated with a blood or plasma draw, must be recorded on the Subject Adverse Event Case Report Form and be followed to satisfactory resolution.

A **Subject Adverse Event** is any unfavorable or undesirable medical occurrence (e.g., sign, symptom, or disease) temporally associated with the specimen collection procedure performed.

A **Subject Serious Adverse Event** is an untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalization or prolongation of existing hospitalization
- results in persistent or significant disability/incapacity, or
- results in a congenital anomaly/birth defect.

IX. Statistical Procedures

A. General Information

All data analyses will be performed, and tables and listings of data will be provided by ADD Statistics using SAS version 9.2 or higher.

If revised or additional analyses are required, a description of the additional or revised analyses and justifications for the changes will be documented and approved by the same functional areas as the original approvers to the protocol.

The Abbott monitor will review all test results and may request that certain observations be excluded from analysis if there is an assignable cause, i.e., control or validity criteria failure, instrument errors or problems, acknowledged technologist error, and/or noncompliance with the study protocol. All results tested according to the protocol and not excluded will be eligible for analysis.

The statistical analysis output along with a listing containing each observation collected for this study will be completed. The listing will be printed for data included in the analysis and excluded from the analysis. The excluded listing will include the reasons for exclusion. A summary of the usage of every test result will also be completed, together with the final analysis results, to ensure that there is no data point missing or misplaced in the analysis.

There is no plan to perform interim analyses that evaluate interim data against acceptance criteria. However, interim data monitoring will be conducted to ensure data meets validity criteria and minimum sample size requirements.

B. Statistical Analysis Description

1. **Reproducibility**

   a. **Study Design**

   Assay reproducibility will be determined by testing controls and members of a panel at a minimum of three sites with one instrument using a minimum of 3 lots of each Alinity s blood screening assay reagents, calibrators, and controls.

   b. **Analysis Variables**

   The analysis variable is Alinity s assay S/CO values for all panel members and controls.

   c. **Statistical Analysis Method**

   The analysis method is based on CLSI EP15-A2E. The reproducibility panel members and the Negative and Positive controls will be tested twice a day for a minimum of 5 days per reagent lot (minimum 3 lots) and site (minimum 3 sites). Within each run, each panel member/control will be tested in two aliquots and two replicates will be assayed per aliquot, resulting in four results per sample.

   Overall Analysis

   Data from all sites and reagent lots for each reproducibility panel/control member will be used for the reproducibility analysis. The following individual variance components will be estimated: within-run, between-run, between-day, between-lot, between-site, and lot-site interaction. The within-laboratory variance is defined as the summation of within-run, between-run, and between- day variance components. The overall assay variability is defined as the summation of within-run, between-run, between-day, between-lot, between-site, and lot-site interaction variance components. The estimates of the mean S/CO, standard deviation (SD) and %CV will be calculated.

   By Site Analysis

   A similar analysis as overall analysis will be performed by site for each reproducibility panel/control member. The within-run, between-run, between- day, and between-lot variance components will be estimated. The within- laboratory variance is defined as the summation of within-run, between-run, and between-day variance components.

   By Lot Analysis

   A similar analysis as overall analysis will be performed by reagent lot for each reproducibility panel/control member. The within-run, between-run, between- day, and between-site variance components will be estimated.

The within- laboratory variance is defined as the summation of within-run, between-run, and between-day variance components.

Percent Agreement

A percent agreement and the 95% confidence interval with the expected results from a sample (reactive or nonreactive) will be performed for each panel/control.

d. Sample Size

The design of the study is based on CLSI EP15-A2E. Each reproducibility panel/control member (sample) will be tested twice a day for 5 days in replicates of 4 at a minimum of 3 sites, using a minimum of three (3) reagent lots to obtain about 360 replicates for each sample (i.e., 2 runs/day x 5 days x 4 replicates x 3 sites x 3 lots = 360 total replicates).

e. Level of Significance/Confidence Statement

A 95% confidence interval will be constructed for agreement analysis.

f. Data Handling Convention

All results from this testing that are performed according to the protocol and not excluded will be eligible for analysis. Reasons for any exclusion will be captured in the database.

g. Outlier Detection

The range of data (difference between the maximum and minimum within a run) will be calculated by sample, site, lot, day, and run. If the range of the data is greater than 9 times the standard deviation (SD) using the applicable imprecision product requirement, investigate and identify the run as an outlier run and the run will be repeated for that panel/control. If the $(5.5 \times SD) < (\text{range of the data}) \leq (9 \times SD)$ from the applicable imprecision product requirement, investigate and identify the run as an outlier run but do not repeat the run for that panel/control.

The reproducibility analyses will be performed with the outlier(s) included and with the outlier(s) excluded.

2. Clinical Specimens

Clinical specimens will be tested with the Alinity s blood screening assay, corresponding comparator method, and supplemental testing assays as needed to determine final status.

a. Study Design

Percent agreement will be calculated between Alinity s blood screening assay results and corresponding comparator method results. Supplemental testing will be performed to determine specimen final status. The sensitivity and specificity will be calculated based on specimen final status. For each Alinity s and comparator assay, the specificity will be calculated using results from donor specimens, a presumed zero prevalence population and the sensitivity will be calculated using results from preselected positive populations and from endemic or increased risk populations.

b. Analysis Variables

- Alinity s blood screening assay interpretation and PRISM comparator assay interpretation
- Specimen Category
- Specimen final status according to Supplemental Testing algorithm.

c. Statistical Analysis Method

Percent Agreement

Percent agreement of Alinity s blood screening assay final results and comparator assay final results will be calculated.

Alinity s Assay	Comparator Assay	
	Repeatedly Reactive	**Nonreactive**
Repeatedly Reactive	A	B
Nonreactive	C	D

Percent Agreement = (A + D) / (A + B + C + D) × 100%

Initial Reactive Rate and Repeat Reactive Rate

The number and percentage of Alinity s blood screening Assay initially reactive donors, the number and percentage of Alinity s blood screening assay repeatedly reactive donors, and the number and percentage of repeatedly reactive donors that are positive by supplemental testing will be summarized.

Two-sided 95% confidence intervals will be calculated for initial and repeat reactive rates using the exact method based on the binomial distributions.

IR Rate not Reactive on Retest and RR Rate not Positive by Supplemental testing

The number and percentage of Alinity s blood screening assay initially reactive donors that are not reactive on retest and the number and percentage of repeatedly reactive donors that are not positive by supplemental testing will be summarized.

Two-sided 95% confidence intervals will be calculated for IR Rate not Reactive on Retest and RR Rate not Positive by supplemental testing using the exact method based on the binomial distributions.

The following table will be used to calculate assay specificity and sensitivity based on the specimen final status.

Alinity s assay	**Final Status**		
	Positive	**Indeterminate (if applicable)**	**Negative**
Repeatedly Reactive	A	B	C
Nonreactive	D	E	F

Specificity

The calculation of specificity will include results from whole blood donors and plasmapheresis donors. Analyses described in this section will be performed for the combined donors, by specimen type, and by site.

The specificity is calculated as the proportion of nonreactive (NR) specimens from specimens with negative status:

$$\text{Specificity} = F / (C + F) \times 100\%$$

Specificity can be also calculated as the proportion of nonreactive (NR) specimens with negative status from specimens with negative status and repeatedly reactive (RR) specimens with indeterminate status:

$$\text{Specificity} = F / (C + B + F) \times 100\%$$

Two-sided 95% confidence intervals will be calculated for specificity using the exact method based on the binomial distributions.

For the combined donors and by specimen type, the specificity will be calculated for the comparator assay.

Histograms

Population distributions for the donor specimens will be presented in histograms and will include mean S/CO values of the nonreactive population, the SD of the population, and the number of SDs from the mean to the cutoff. These histograms will be presented for the combined donor population by site, and by sample type.

Sensitivity

The evaluation of sensitivity will include results of the following specimens: preselected positive, individuals at increased risk of infection, and/or individuals from an endemic area at increased risk of infection.

Sensitivity is calculated as the proportion of repeatedly reactive (RR) specimens from specimens with positive final status:

$$\text{Sensitivity} = A / (A + D) \times 100\%$$

Sensitivity can be also calculated as the proportion of repeatedly reactive (RR) specimens with positive status from specimens with positive status and nonreactive (NR) specimens with indeterminate status:

$$\text{Sensitivity} = A / (A + D + E) \times 100\%$$

A two-sided 95% confidence interval for overall sensitivity will be calculated using the exact method based on the binomial distributions.

All sensitivity calculations described above will also be done for the comparator assay.

d. Sample Size

Sample size for specificity is maximum of 15,000 and calculated based on the minimum power of 80% and $\alpha \leq 0.05$.

Sample size for sensitivity is not determined using statistical power calculations. Sample size is determined by the number of available specimens.

e. Level of Significance/Confidence Statement

Two-sided 95% confidence interval (CI) will be provided.

f. Data Handling Convention

All results from this testing that are performed according to the protocol and not excluded will be eligible for analysis. Reasons for any exclusion will be captured in the database.

X. Conduct of the Study

A. Responsibilities for Conduct of the Study

1) The investigator will have written and dated approval/favorable opinion from the [Institutional Review Board (IRB) or Independent Ethics Committee (IEC)] for the protocol and other documents as specified by the [IRB/IEC] before initiating the study. In some cases, the [IRB/IEC] may provide an expedited or exception review.

2) The investigator is responsible for reporting to the [IRB/IEC] and obtaining the necessary approvals from his/her site administration.

3) Abbott Laboratories will not initiate the study until the required pre-study documents are received from the site. Pre-study documents are aligned with GCP requirements and a detailed listing of the required pre-study documents will be provided to the investigator by the Abbott monitor.

4) The investigator will perform the study in accordance with GCP. The Abbott monitor will provide the investigator with the GCP-aligned list of investigator requirements.

5) The Abbott monitor will provide the investigator with the Guidance for Industry Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects (October 2009) for reference.

6) Abbott Laboratories has a responsibility under GCP to monitor this clinical study. The Abbott monitor will provide the investigator with the GCP-aligned list of responsibilities of the Abbott monitor.

7) The investigator will maintain a list of appropriately qualified persons to whom he/she has delegated significant study-related duties. This list must be updated as needed and the Abbott monitor must be notified of the changes.

8) The investigator will assure that all subjects are provided both written and oral informed consents, and that the subject's consent is documented in accordance with local laws. In addition, every subject will be provided a copy of the consent form.

9) The investigator will maintain the subject's original consent form in the subject's permanent medical record or in the investigator's records, depending on site

policy.

10) The investigator agrees to the requirement for guaranteed access to source data and to the investigator himself/herself by the IRB, Abbott monitor(s), auditors, and regulatory inspectors for the purpose of data verification or correction.

B. Withdrawal from the Study

A subject's participation in any clinical study is voluntary and the subject has the right to withdraw from the study anytime without prejudice, however, the request to withdraw agreement does not include information that has already been made known or information gathered as a result of participation in the study. All subjects enrolled must be accounted for and the withdrawal of any subjects from the study will be documented on the appropriate CRF. Individuals withdrawn from the study may be replaced with another individual that meets the subject enrollment criteria.

C. Protocol Amendments

All protocol amendments will be written and approved by Abbott Laboratories prior to its submission for IRB review and approval or exemption.

The investigator will not implement or deviate from the protocol without agreement from Abbott Laboratories and prior review and approval from the IRB. Exceptions to this include instances where it is necessary to eliminate an immediate hazard to study subjects, or when the protocol changes involve only logistical or administrative aspects of the study.

D. Protocol Deviations

A protocol deviation is defined as a planned or unplanned departure from the study protocol. All protocol deviations that occur during this study will be recorded on the protocol deviation CRF.

Planned deviations from this protocol must be reported to the monitor prior to implementation. The implemented deviation and the circumstances regarding the deviation will be documented on the protocol deviation CRF. The monitor will approve in writing the inclusion of any specimen, which does not meet all of the inclusion or exclusion criteria of the study. The monitor may provide verbal approval prior to the written response.

E. Incident Reports

An incident CRF will be used to document any incident(s) that occur during the clinical study. An incident is defined as any unplanned or unexpected event that occurs with or without the input or intervention of the operator. The Incident CRF

should include a description of the incident, possible cause (if known), action taken, and identify any specimens that were affected.

F. Discontinuation of the Study

The study may be terminated prior to the stated time for reasons of safety or efficacy, or for other identified causes. The reason for discontinuation will be documented in the clinical study master file.

G. Site File/Record Storage

The investigator should arrange for the retention of all study documents in the site file. The investigator shall retain the site file records for at least a period of 2 years following the date a marketing application is approved; or if no application is to be filed or if the application is not approved for such an indication, until at least 2 years after the investigation is discontinued and the FDA is notified. These documents should be retained for a longer period, however, if required by the applicable regulatory requirements or by agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution when these documents no longer need to be retained.

H. Site Data

At the completion of the study a listing of the site's data generated during the study will be provided to each site.

I. Correspondence

All correspondence between the Abbott monitor and the testing site must be documented and retained as part of the study records (i.e. any telephone communication with the Abbott monitor should be documented in a telephone log; copies of e-mail messages should be printed).

XI. References

Abbott PRISM Operations Manual

CLSI. *User Verification of Performance for Precision and Trueness; Approved Guideline – Second Edition*, CLSI document EP15-A2E [ISBN 1-56238-574-7]. CLSI, 940 West Valley Road, Suite 1400, Wayne, Pennsylvania, 19087-1898, USA, Apr, 2006.

CDRH guidance document. *Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable,* April 25, 2006.

XII. Investigator's Agreement

By signing this statement, the investigator agrees:

1. I have read and understand the contents of the Alinity s Blood Screening Assays - Clinical Evaluation Protocol (Protocol No. 9DY-02-14U01-03, Version 5, dated April 18, 2018) and appropriate clinical brochure(s) and will adhere to the study requirements as presented, and applicable local regulations.

2. I will protect the rights, safety, and well-being of subjects. Before initiating the study and where required by local regulations, an Institutional Review Board (IRB) will review and approve the study protocol and all other applicable study material. A copy of the approval of the study protocol will be submitted to Abbott Laboratories.

3. I will not use the results from products labeled as "For Investigational Use Only" or "For Performance Evaluation Only" for diagnostic purposes, because the performance characteristics of the product have not been established.

4. I understand that Abbott Laboratories, its designees, and regulatory authorities may require access to source documents for verification of study data.

5. I understand that if any questions arise, now or during the clinical evaluation, I will promptly contact the Abbott monitor or designee at Abbott Laboratories for clarification.

Investigator (Printed Name): _____

Investigator Title: _____

Investigator Signature: _____ Date: _____

Institution Name: _____

Institution Address: _____

_____

_____

Appendix 1: Scientific Amendment

Amendment No: 4

Summary of Changes

The following change incorporated in Protocol No. 09DY-02-14U01-03, Version 5, dated April 18, 2018 is referenced from Version 4, dated October 13, 2017.

1. Change: Section III. C. Study Design, General Schedule of Events, change to "The study will take approximately 5-10 months to complete."

Detailed Description of Changes

Change 1 (Scientific Change)

- Change: Section III. C. Study Design, General Schedule of Events, change "The study will take approximately 5 months to complete." to "The study will take approximately 5-10 months to complete."

- Reason: The change is made to ensure the duration of study reflects the actual duration.

- Justification: Due to the change in strategy for execution of the protocol, the study duration is extended for sites remaining open for Chagas testing. A Protocol Impact Assessment form was completed to assess the impact of clinical study testing. There is no impact to the clinical study.

End of Document