REF 65-9502-0
20 Test Kit

DPP® HIV-Syphilis System

For *in vitro* diagnostic use only

For professional use only

Single-Use Rapid Test for the Detection of Antibodies to HIV-1/2 and/or *Treponema Pallidum*

Read this Product Insert completely before using the product. Conformance with the test procedure is necessary to ensure accurate results. Users of this test should follow the CDC Universal Precautions for prevention of transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other bloodborne pathogens.[1]

STORAGE: Store at 2 to 30°C (36 to 86°F)

COMPLEXITY: Moderate

NAME AND INTENDED USE

The DPP® HIV-Syphilis System is a single-use rapid, qualitative, multiplex, immunoassay for the detection of antibodies to Human Immunodeficiency Virus Types 1 and 2 (HIV-1/2), and/or *Treponema pallidum* bacteria (the causative agent of syphilis) in fingerstick whole blood, potassium-EDTA venous whole blood or potassium-EDTA plasma specimens. The test is intended to be used with the DPP Micro Reader. The test is intended for use by trained professionals in point of care and laboratory settings to aid in the diagnosis of HIV and syphilis infection.

This test is suitable for use in multi-test algorithms designed for the statistical validation of rapid HIV test results and when multiple rapid HIV tests are available.

The test is intended to be used as the first-tier assay in the reverse sequence syphilis screening algorithm to aid in the detection of infection with *T. pallidum*. A diagnosis of syphilis must be made in the context of treponemal and non-treponemal test results and in conjunction with clinical findings. This test is not intended for use as a confirmatory test in the reverse sequence syphilis screening algorithm.

The results pf DPP HIV-Syphilis test are read and interpreted only by DPP Micro Reader with dedicated software.

The test is not intended for use in screening blood, blood products, or human cells or tissue or cellular and tissue-based products (HCT/Ps) for HIV and Syphilis.

RESTRICTIONS

- **Sale of the DPP HIV-Syphilis System is restricted to clinical laboratories that have an adequate quality assurance program including planned activities to provide adequate confidence that requirements for quality will be met; and**
- **Where there is assurance that operators will receive and use instructional materials;**
- **The DPP HIV-Syphilis System is approved for use only by an agent of a clinical laboratory;**
- **Test subjects must receive the "Subject Information" brochure, prior to specimen collection and appropriate counseling when test results are provided.**
- **The DPP HIV-Syphilis System is not approved for use to screen donors of blood, plasma, cells, or tissue.**

SUMMARY AND EXPLANATION

Discovered in 1983, the Human Immunodeficiency Virus is a retrovirus and identified as the etiologic agent for the Acquired Immunodeficiency Syndrome (AIDS), and AIDS related complex.[2] AIDS is characterized by changes in the population of T-cell lymphocytes that play a key role in the immune defense system. In the infected individual the virus causes a depletion of a subpopulation of T-cells, called T-helper cells, which leaves these patients susceptible to opportunistic infections and certain malignancies. The major routes of transmission are sexual contact, exposure to contaminated blood or blood products (including sharing of contaminated syringes and needles) and mother-to-newborn transmission.[3-5] The HIV virus consists of a genomic RNA

molecule protected by a capsid and an envelope. The HIV envelope is the major target for a humoral antibody response. The presence of the virus in patients causes the immune system to elicit the production of antibodies, which will develop between 23 to 90 days following exposure.[6,7] The detection of these antibodies can be used as a diagnostic tool. In a nonclinical or point of care setting for HIV testing, individuals are commonly screened with a rapid HIV and if are reactive, are linked to care or laboratory follow-up. As per CDC Guidelines, laboratory testing consists of an initial antibody/antigen assay which if reactive would be followed by a supplemental antibody assay that differentiates between HIV-1 and HIV-2 antibodies. A nonreactive or indeterminate result for both HIV-1 and HIV-2 antibodies on the supplemental assay would be followed by an HIV-1 Nucleic Acid Test (NAT) to rule out an acute HIV-1 infection.[8,9]

Syphilis is a sexually transmitted disease (STD) caused by the spirochete organism *Treponema pallidum,* and depending on the stage of the disease, manifestation of symptoms includes ulcers or chancres at the infection site (primary syphilis); skin rash, mucocutaneous lesions, and lymphadenopathy (secondary syphilis); and/or cardiac, gummatous lesions, tabes dorsalis, and general paresis (tertiary syphilis). Latent syphilis, which lacks the clinical manifestations of symptoms described is detected by serologic testing. At any stage, *T. pallidum* can infect the central nervous system and result in neurosyphilis which may manifest as cranial nerve dysfunction, meningitis, stroke, acute altered mental status and auditory or ophthalmic abnormalities.[10] As *T. pallidum* cannot be cultured on artificial media, the diagnosis of syphilis depends on the correlation of clinical data with antibodies demonstrated by serological tests. Two types of antibody responses normally result: non-specific (non-treponemal/anti-cardiolipin)[11,12] and specific (anti-treponemal). Non-treponemal antibodies are typically produced 3 to 6 weeks after exposure while anti-treponemal antibodies are typically produced 2 to 4 weeks after exposure.[13] Treponemal antibodies typically remain detectable for life, even following successful treatment.[14] Syphilis is diagnosed via serology testing using one of two algorithms, a traditional algorithm consisting of initial screening with a non-treponemal test followed by retesting a reactive specimen with a treponemal test, or a reverse sequence screening algorithm where a screening is initiated using a treponemal test and confirmed with a non-treponemal test. In the reverse sequence screening algorithm, if the non-treponemal test is nonreactive, then a different treponemal test is performed to confirm the results of the initial test. If the second treponemal test is positive, treatment should be dependent on the individual's history of treatment for syphilis.[10,15]

HIV and syphilis represent serious public health concerns not only in isolation from another but also due to the potential for coinfection. Syphilis facilitates both HIV transmission and HIV acquisition, reflecting the complex interplay between the two diseases. Chancres cause epithelial and mucosal breaches, facilitating the transmission of HIV virions.[16]

BIOLOGICAL PRINCIPLES OF THE TEST

The DPP HIV-Syphilis System employs Chembio's patented DPP (Dual Path Platform) technology and consists of a sample path and a reagent path, which intersect in the antibody detection TEST (1) (2) and CONTROL (C) areas in the readout window of the test cassette. To initiate the test, a specimen is mixed with pre-measured buffer in a DPP SampleTainer® Bottle for 10 seconds, and is applied to the SAMPLE+BUFFER Well #1 of the DPP test device. The sample migrates along the sample path membrane and is delivered to the TEST (1) (2) area of the reagent strip, where specific HIV antigens, a syphilis recombinant antigen and Protein A are immobilized. Antibodies to HIV and/or *Treponema pallidum* (i.e. treponemal antibodies), if present in the sample, bind instantly to the immobilized HIV and/or syphilis antigens in the TEST (1) (2) area, while non-specific IgG binds to the Protein A in the CONTROL (C) area. Successful sample application is indicated by the dissolution of soluble dye lines in the TEST and CONTROL areas. Five minutes after adding the sample, buffer is added to the BUFFER Well #2. The buffer hydrates the dried antibody-binding colored conjugate, which migrates to the TEST area. The test results are interpreted using the DPP Micro Reader between 10 and 25 minutes after Running Buffer is added to BUFFER Well #2. The DPP Micro Reader is a reflectance reader for use with the DPP HIV-Syphilis System. The DPP Micro Reader is a portable, battery-powered instrument that uses assay-specific algorithms to analyze the test and control line reflectance to determine the presence or absence of the antibodies to HIV and/or *Treponema pallidum* in the sample. The reader verifies the presence of the control line and measures color intensity at each of the test line positions; it interprets the results using an algorithm including assay-specific cut-off values, and reports a positive, negative, or invalid result. The results are displayed through a 14-segment liquid crystal display (LCD) on the top of the instrument. The DPP Micro Reader has been developed to minimize human interpretation errors, therefore the results cannot be visually interpreted by the operator. The DPP Micro Reader is maintenance-free, not configurable by the user and is operated by a single, multi-function button.

MATERIALS PROVIDED

Each kit contains the items to perform 20 tests:
20 Individually Pouched DPP HIV-Syphilis Test Devices, each containing:

- 1 DPP HIV-Syphilis Test Device
- 1 Desiccant Pouch

20 Disposable 10µL Sample Loops with Break Point – BLUE
20 DPP SampleTainer® Bottle – BLACK Cap
- 1mL, a phosphate buffer containing sodium chloride, EDTA, Tween 20, Avidin, and chicken serum, antimicrobials and sodium azide as preservative.

1 DPP Running Buffer – GREEN Cap
- 6mL, a phosphate buffer containing sodium chloride, EDTA, Tween 20, Avidin, and chicken serum, urea, antimicrobials and sodium azide as preservative.

1 Product Insert for the DPP HIV-Syphilis System

ACCESSORIES AVAILABLE AND REQUIRED

DPP HIV-Syphilis Rapid Test Control Pack (Catalog # 60-9555-0)
Each package contains:
- 1 HIV-1 Reactive Control (0.5mL)
  Heat inactivated human plasma positive for antibodies to HIV-1, diluted in normal human plasma; negative for Hepatitis B surface antigen, Hepatitis C antibody and HTLV I/II antibodies.
- 1 HIV-2 Reactive Control (0.5mL)
  Heat inactivated human plasma positive for antibodies to HIV-2, diluted in normal human plasma; negative for Hepatitis B surface antigen, Hepatitis C antibody and HTLV I/II antibodies.
- 1 Treponemal antibody Reactive Control (0.5mL)
  Human plasma positive for antibodies to *T. pallidum,* diluted in stabilizing matrix containing normal human plasma; negative for Hepatitis B surface antigen, Hepatitis C antibody and HTLV I/II antibodies.
- 1 Nonreactive Control (0.5mL)
  Normal human plasma; negative for antibodies to HIV-1, HIV-2 and *T. pallidum*; negative for Hepatitis B surface antigen, Hepatitis C antibody and HTLV I/II antibodies.
- 1 Product Insert for the DPP HIV-Syphilis Rapid Test Control Pack

DPP Micro Reader (Catalog # 70-1056-0)
Each kit contains:
- 1 DPP Micro Reader configured for use in the DPP HIV-Syphilis System
  - 3 Lithium-ion, type CR2032 (3 V/230 mAh), coin cell batteries (installed)
- 1 DPP Test Device Holder
- 1 USB Wall Power Adapter (5v / 1000 mA) with cable
- 1 Microfiber cloth
- 1 User Manual

MATERIALS REQUIRED BUT NOT PROVIDED
- Clock, watch, or other timing device
- Pipettor capable of delivering 10µL of specimen may be used in lieu of the disposable 10µL sample loop supplied with the Kit (for venous whole blood or plasma specimens)
- Disposable gloves
- Sterile gauze (for fingerstick whole blood specimens)
- Antiseptic wipes
- Biohazard disposal container
- Sterile Safety Lancet (for fingerstick whole blood specimens)
- Collection devices (for venous whole blood or plasma specimens)

WARNINGS

For *in-vitro* diagnostic use

1. Read the Product Insert completely before using this assay. Conformance with the test procedure is necessary to ensure accurate results.
2. Users of this test should follow the CDC Universal Precautions for prevention of transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other bloodborne pathogens.[1]

3. Use of this test kit with sample types other than those specifically approved for use with this device may result in inaccurate test results.
4. Ensure that the test components are at room temperature before performing the test. This test should be performed at 18 to 30°C (64 to 86°F).
5. The results of DPP HIV-Syphilis test are read and interpreted only by DPP Micro Reader with dedicated software. Results should not be read manually.
6. This test has not been evaluated for newborn screening, cord blood specimens, or individuals less than 2 years of age.
7. Individuals infected with HIV-1 and/or HIV-2 who are receiving highly active antiretroviral therapy (HAART), PrEP (Pre-exposure prophylaxis) or PEP (Post-exposure prophylaxis) may produce false negative results.

PRECAUTIONS

SAFETY PRECAUTIONS

1. Handle the samples, materials contacting samples, and kit controls as if capable of transmitting infection.
2. Do not eat, drink or smoke in the area where samples and kit reagents are handled. Avoid any contact between hands, eyes or mouth during sample collection and testing.
3. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when handling patient samples.
4. Dispose of all samples and materials used in the test procedure in a biohazard waste container. Lancets should be placed in a puncture-resistant container prior to disposal. The recommended method of disposal of biohazard waste is autoclaving for a minimum of 1 hour at 121°C. Disposable materials may be incinerated. Liquid wastes may be mixed with appropriate chemical disinfectants. A freshly prepared solution of 10% bleach (0.5% solution of sodium hypochlorite) is recommended. Allow 60 minutes for effective decontamination. **NOTE: Do not autoclave solutions that contain bleach.**
5. Use 10% bleach or other appropriate disinfectants to wipe all spills. The bleach solution should be made fresh each day.
6. For additional information on biosafety, refer to "Universal Precautions for prevention of transmission of Human Immunodeficiency Virus, Hepatitis B Virus, and other bloodborne pathogens"[1] and "Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposure to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis."[17] and "Update U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HIV and Recommendations for Postexposure Prophylaxis". [18]

HANDLING PRECAUTIONS

1. If Desiccant Packet is missing, DO NOT USE. Discard test device and use a new test device.
2. Do not use any test device if the pouch has been perforated.
3. Each test device is for single use only.
4. Do not use the test beyond the expiration date printed on the pouch. Always check expiration date prior to testing.
5. Do not mix reagents from different lot numbers of kits.
6. Adequate lighting is required to read the test results with the DPP Micro Reader.
7. Do not open the sealed foil pouch until just prior to use.

8. Ensure finger is completely dry before performing fingerstick.

STORAGE AND STABILITY

The DPP HIV-Syphilis Test Devices should be stored in unopened pouches at 2 to 30°C (36 to 86°F). Do not freeze. Do not open pouch until you are ready to perform a test. When stored as indicated, test devices are stable until the expiration date marked on the pouch. Both Running Buffer and DPP SampleTainer Bottles should be stored at 2 to 30°C (36 to 86°F) in their original containers.

SPECIMEN COLLECTION

Prior to specimen collection, provide test subjects with Subject Information Notice and pre-test counseling according to CDC Guidelines for Rapid HIV Testing.[19]

The DPP HIV-Syphilis System can be performed on fingerstick whole blood, potassium-EDTA venous whole blood or potassium-EDTA plasma samples.

FINGERSTICK WHOLE BLOOD

Before collecting the sample, write the patient sample ID on the DPP SampleTainer Bottle with the BLACK CAP. Remove (unscrew) the WHITE CAP keeping the BLACK CAP screwed onto the white part of the cap (Figure 1).

Figure 1

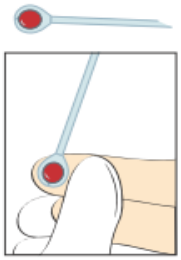
DPP SampleTainer Bottle with BLACK CAP

Prepare to perform the fingerstick collection procedure. Clean the finger of the person being tested with an antiseptic wipe. Allow the finger to dry thoroughly or wipe dry with a sterile gauze pad.

Using a sterile lancet, puncture the skin just off the center of the finger and wipe away the first drop of blood with sterile gauze. Avoid squeezing the fingertip to accelerate bleeding as this may dilute the blood with excess tissue fluid.

Figure 2

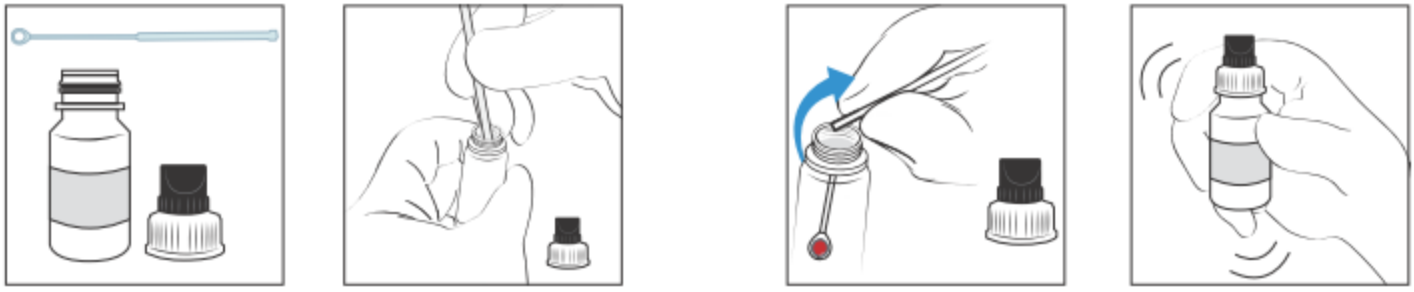
Properly filled Sample Loop



Collect the sample from the second drop, touching the disposable Sample Loop provided to the drop of blood until the Sample Loop is full as shown in Figure 2.

Insert the filled Sample Loop into the DPP SampleTainer Bottle with the BLACK CAP, such that the loop is touching the bottom. Snap and twist the shaft at the BREAK-NOTCH to dislodge the Sample Loop into the DPP SampleTainer Bottle, as shown in Figure 3. Replace the BLACK/WHITE CAP assembly onto the DPP SampleTainer Bottle and gently shake for 10 seconds. Test immediately, following Test Procedure instructions.

Figure 3



DPP SampleTainer BOTTLE AND SAMPLE LOOP

SAMPLE LOOP INSERTED INTO DPP SampleTainer BOTTLE

SNAP AND TWIST THE SHAFT AT THE BREAK-NOTCH TO DISLODGE LOOP INTO THE DPP SampleTainer BOTTLE

REPLACE CAP ON DPP SampleTainer BOTTLE AND SHAKE

POTASSIUM-EDTA VENOUS WHOLE BLOOD

Draw blood following laboratory procedure for obtaining potassium-EDTA venous blood. Collect sample in a tube containing potassium-EDTA. Be sure the tube of blood is well mixed before sampling.

If using a laboratory pipette, withdraw 10µL of the blood from the tube. Pipette the sample into the DPP SampleTainer Bottle with the BLACK CAP.

If using the Sample Loop, dip the Sample Loop into the blood tube and allow it to fill. Insert the filled Sample Loop into the DPP SampleTainer Bottle with the BLACK CAP, such that the loop is touching the bottom. Snap and twist the shaft at the BREAK-NOTCH to dislodge the loop into the DPP SampleTainer Bottle, as shown in Figure 3.

Replace the BLACK/WHITE CAP assembly onto the DPP SampleTainer Bottle and shake for 10 seconds. Test immediately, following Test Procedure instructions.

If tested the same day, potassium-EDTA venous whole blood may be kept at room temperature. Potassium-EDTA venous whole blood may be stored for up to 3 days between 2 and 8°C (36 to 46°F) before testing.

DO NOT FREEZE WHOLE BLOOD! Allow refrigerated sample to reach room temperature and mix gently before testing.

POTASSIUM-EDTA PLASMA

Draw blood following laboratory procedure for obtaining potassium-EDTA plasma specimens. Collect plasma specimens in tubes containing potassium-EDTA. Collect specimen in a clean container following standard laboratory procedures. Samples collected into potassium-EDTA tubes should be processed according to the manufacturer's direction for centrifugation and removal of the plasma from red blood cells.

If using a laboratory pipette, withdraw 10µL of potassium-EDTA plasma. Pipette the sample into the DPP SampleTainer Bottle with the BLACK CAP.

If using the Sample Loop, dip the Sample Loop into the tube and allow it to fill. Insert the filled Sample Loop into the DPP SampleTainer Bottle with the BLACK CAP, such that the loop is touching the bottom. Snap and twist the shaft at the BREAK-NOTCH to dislodge the loop into the DPP SampleTainer Bottle, as shown in Figure 3.

Replace the BLACK/WHITE CAP assembly onto the DPP SampleTainer Bottle and shake for 10 seconds. Test immediately, following Test Procedure instructions.

Potassium-EDTA plasma specimens may be tested immediately after collection. If specimens are not tested immediately, refrigerate them at 2 to 8°C (36 to 46°F) following collection. These specimens should be tested within 3 days of collection. If specimens are not tested within 3 days of collection, potassium-EDTA plasma specimens should be frozen at -20°C (-4°F) or colder.

SPECIMEN SHIPPING

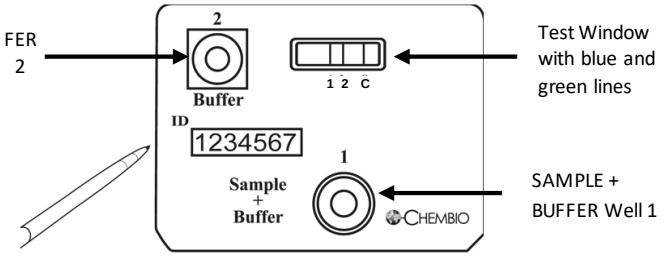
If specimens are to be shipped, they should be packed in compliance with regulations covering the transportation of etiologic agents. Potassium-EDTA venous whole blood and potassium-EDTA plasma specimens should be shipped refrigerated with cold packs or wet ice.

TEST PROCEDURE

All components for the DPP HIV-Syphilis System are ready to use as supplied. Follow directions as indicated. If the sample and / or kit components have been refrigerated, remove them from the refrigerator and allow them to come to a temperature of 18 to 30° C (64 to 86°F) prior to testing.

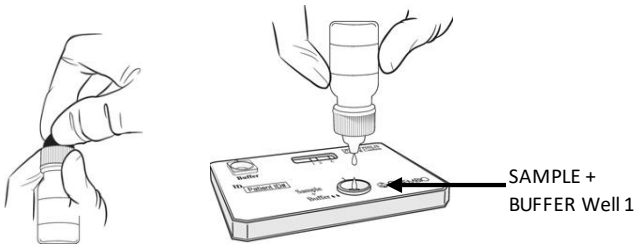
1. Remove the DPP HIV-Syphilis Test Device from its pouch and place it on a flat surface (it is not necessary to remove the Desiccant Packet from the pouch). Note: If Desiccant Packet is missing, DO NOT USE, discard Test Device and start a new test.

Label the Test Device with patient ID or identification number. Note that the DPP HIV-Syphilis Test Device has 3 colored lines in the Test Window; the 2 test lines are blue and the control line is green. If the 3 colored lines are absent, DO NOT USE, discard Test Device and a new Test Device should be used.



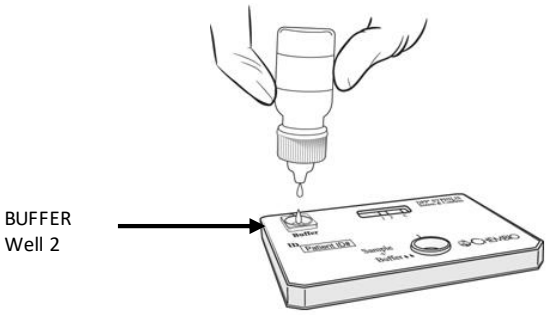
2. Remove (unscrew) the DPP SampleTainer Bottle BLACK CAP keeping the WHITE CAP with the dropper tip screwed onto the bottle.

Invert the DPP SampleTainer Bottle (BLACK CAP), containing the collected sample, and hold it vertically (not at an angle) over the SAMPLE + BUFFER Well 1. Add 2 drops (~65µL) slowly, dropwise, into the SAMPLE + BUFFER Well 1.



3. **Wait 5 minutes.** The blue and green colored lines should have disappeared from the rectangular Results window. If not, DO NOT USE, discard test device and repeat the procedure with a new DPP test device.

Invert the Running Buffer bottle (GREEN CAP) and hold it vertically (not at an angle) over BUFFER Well 2. Add 4 drops (~135µL) of Buffer (GREEN cap) slowly, dropwise, into BUFFER Well 2.



4. **Fingerstick, Potassium-EDTA Venous Whole Blood, or Potassium-EDTA Plasma**
Test Results can be read using the DPP Micro Reader between 10 and 25 minutes after the addition of the Running Buffer to BUFFER Well 2 using the DPP Micro Reader. DO NOT ATTEMPT TO INTERPRET THE RESULTS VISUALLY. ALWAYS USE THE DPP Micro Reader TO OBTAIN THE RESULTS.

NOTE: Discard the used Sample Loop, Test Device, and any other test materials into a biohazard waste container

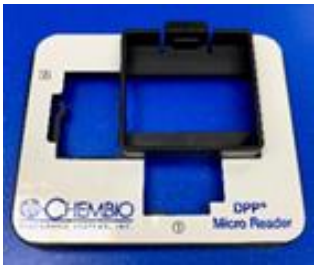
5. Using the DPP Micro Reader

Check to make sure that the window at the bottom of the reader is clean of finger marks and dust or lint before using the reader.

The Reader and Test Device Holder assembly must be on top of the Test Device when reading the device for results to be valid. Place the DPP Test Device Holder on a flat surface. Match the Reader with the DPP Test Device Holder by inserting the base of the Reader so that the "slanted edge" meets the corresponding "slanted corner" in the Test Device Holder socket.

A. Connect the DPP Micro Reader to the supplied Test Device Holder as shown below. The DPP Micro Reader is secure in the DPP Test Device Holder once a "clicking" sound is heard.

DPP Micro Reader



Test Device Holder

DPP Micro Reader with Test Device Holder and Test Device

B. At the time indicated for reading the test results, place the DPP Micro Reader and Test Device Holder on top of the Test Device and press the button. The DPP Micro Reader will go through the start-up process:

- Self-check shows all display segments

- Number of remaining tests available

- Display "RDY": Ready to read

C. Press the button again and the DPP Micro Reader will show "RUN".

After a few seconds, results for HIV and for treponemal antibodies will be displayed one after the other. (Please see section on the next page: Interpretation of Test Results).

NOTE: Results will be displayed for approximately 50 seconds before the DPP Micro Reader shuts-off.

NEXT TEST

To read another test while the previous results are still scrolling, press the button. The DPP Micro Reader goes to the "RDY" mode. Insert the next Test Device into the Test Device Holder. At the time indicated to read the result, follow instructions starting with Step C.

INTERPRETATION OF TEST RESULTS
NOTE: DO NOT ATTEMPT TO INTERPRET RESULTS VISUALLY

Result	Display
Nonreactive for HIV-1 or HIV-2 antibodies Nonreactive for treponemal antibodies	 
Reactive for HIV-1 and/or HIV-2 antibodies Nonreactive for treponemal antibodies	 
Nonreactive for HIV-1 or HIV-2 antibodies Reactive for treponemal antibodies	 
Reactive for HIV-1 and/or HIV-2 antibodies Reactive for treponemal antibodies	 
Invalid result. An invalid result cannot be interpreted. It is recommended that the invalid test be repeated with a new device. Call Customer Support if repeat run result is invalid.	

HIV Results Interpretation:
A nonreactive test result means that HIV-1 and HIV-2 antibodies were not detected in the specimen. The test result is interpreted as NEGATIVE for HIV-1 and HIV-2 antibodies.

A reactive test result means that HIV-1 and/or HIV-2 antibodies have been detected in the specimen. The test result is interpreted as Preliminary POSITIVE for HIV-1 and/or HIV-2 antibodies. Follow CDC guidelines to inform the test subject of the Test Result and its interpretation.[19]

Syphilis Results Interpretation:
Test results are intended to aid in diagnosis only. As with all serological tests for syphilis, results should always be interpreted in conjunction with additional treponemal or non-treponemal serologic test results (as appropriate), the patient's clinical symptoms, medical history, and other clinical and/or laboratory findings. Diagnostic considerations should be based on treponemal and non-treponemal testing according to the CDC guidelines.[10]

Reactive test result for treponemal antibodies may indicate recent, past, or successfully treated syphilis. A reactive treponemal test result on the DPP HIV-Syphilis System is not diagnostic of syphilis without additional non-treponemal serologic testing and a full clinical evaluation.

A nonreactive syphilis result on the DPP HIV-Syphilis System does not exclude incubating or early primary syphilis.

For problems or questions, please read the DPP Micro Reader User Manual, or contact Chembio Diagnostic Systems Customer Service at 844-243-6246.

LIMITATIONS OF THE PROCEDURE

1. The DPP HIV-Syphilis System must ONLY be used with capillary (fingerstick) or potassium-EDTA venous whole blood, or potassium-EDTA plasma. Using other types of samples or testing of venipuncture whole blood or plasma samples collected using a tube containing an anticoagulant other than potassium-EDTA may not yield accurate results.
2. The DPP HIV-Syphilis System must be used in accordance with the instructions in this product insert to obtain accurate results.
3. Reading test results using the DPP Micro Reader earlier than 10 minutes or later than 25 minutes after the addition of DPP Running Buffer to BUFFER Well 2 may yield erroneous results.
4. An HIV REACTIVE result using the DPP HIV-Syphilis System suggests the presence of antibodies to HIV-1 and/or HIV-2 in the sample and the REACTIVE test result is interpreted as Preliminary Positive for HIV-1 and/or HIV-2 antibodies. The DPP HIV-Syphilis System is intended as an aid in the diagnosis of infection with HIV-1/2. AIDS-related conditions are clinical syndromes, and their diagnosis can only be established using clinical and/or serological methods.
5. A NONREACTIVE HIV result does not preclude the possibility of exposure to HIV or infection with HIV. An antibody response to a recent exposure may take several months to reach detectable levels.
6. A person who has antibodies to HIV-1 or HIV-2 is presumed to be infected with the virus, except that a person who has participated in an HIV vaccine study may develop antibodies to the vaccine and may or may not be infected with HIV.
7. An individual infected with HIV-1 and/or HIV-2 who is receiving highly active antiretroviral therapy (HAART) may produce a false negative result.
8. This assay has not been evaluated for newborn screening, cord blood specimens, or for screening blood, blood products, tissue or organ donors for HIV and syphilis.
9. Specimens from individuals with Systematic Lupus Erythematosus (SLE), anti-Cytomegalovirus (CMV) IgM antibodies, or anti-Double Stranded DNA (dsDNA) antibodies may cross-react with the treponemal test line, generating false reactive results for treponemal antibodies.

QUALITY CONTROL

Built-in Control Feature

The control line serves as a built-in internal control and gives confirmation of sample addition and proper test performance. The DPP Micro Reader verifies the presence of the control line and measures color intensity at each of the test line positions; it interprets the results using an algorithm including assay-specific cut-off values, and reports a reactive, nonreactive or invalid result after approximately 3 seconds. (Please see: Interpretation of Test Results).

External Quality Control

Chembio DPP HIV-Syphilis Reactive/Nonreactive Controls (Catalog #: 60-9555-0) are available separately for use with the Chembio DPP HIV Syphilis System. The Controls are used to verify the operator's ability to properly perform the test and to interpret the results. The HIV-1/Syphilis Reactive Control will produce an HIV and syphilis reactive test result when read using the DPP Micro Reader. The HIV-2 Reactive Control will produce an HIV reactive and syphilis nonreactive test result when read using the DPP Micro Reader. The Nonreactive Control will produce a nonreactive test result for HIV and Syphilis when read using the DPP Micro Reader. Run the controls as described in the Test Procedure section for a plasma sample and follow the directions in the Interpretation of Test Results section of this product insert. It is the responsibility of each facility using the Chembio DPP HIV-Syphilis System to establish an adequate quality assurance program to ensure the performance of the device under specific locations and conditions of use.

RUN THE KIT CONTROLS UNDER THE FOLLOWING CIRCUMSTANCES:

- **Each new operator prior to performing tests on patient samples**
- **When opening a new test kit lot**
- **Whenever a new shipment of test kits is received**
- **If the temperature of the test storage area falls outside of 2 to 30°C (36 to 86°F)**
- **If the temperature of the testing area falls outside of 18 to 30°C (64 to 86°F)**
- **At periodic intervals as indicated by the user facility**

PERFORMANCE CHARACTERISTICS

Overall Summary

The performance of the DPP HIV-Syphilis System was evaluated from May 2016 to November 2019 with samples prospectively collected and tested from 2,762 individuals at ten (10) geographically distinct study sites within the United States. The study sites included HIV/STD Testing Clinics/Outreach Centers, Primary Care Clinics, Obstetrics and Gynecology (OB/GYN) Centers and an Outpatient Addiction Treatment Center.

The HIV performance of the DPP HIV-Syphilis System was evaluated using samples collected from five groups of individuals: known infected with HIV-1 only, known positive for syphilis only, known positive for both HIV-1 and syphilis, at high risk for infection with HIV-1 and syphilis, and at low risk for infection with HIV-1 and syphilis.

The performance of the DPP HIV-Syphilis System for detecting treponemal antibodies was evaluated using samples collected from four groups of individuals: those presenting for routine syphilis testing, those known positive for HIV-1 at enrollment, pregnant women, and those previously diagnosed with syphilis.

The clinical performance from the intended use population is summarized below for the DPP HIV-Syphilis System.

HIV Performance

Matrix	Sensitivity % (Ratio) (95% CI)	Specificity % (Ratio) (95% CI)
Capillary (Fingerstick) Whole Blood	99.4% (635/639) (98.4-99.8%)	99.6% (1352/1357) (99.1-99.8%)
Venous Whole Blood	99.5% (635/638) (98.6-99.8%)	99.5% (1352/1359) (98.9-99.8%)
Plasma	99.3% (405/408) (97.9-99.7%)	99.6% (902/906) (98.9-99.8%)

Treponemal Test Line Performance

Matrix	Positive Percent Agreement % (Ratio) (95% CI)	Negative Percent Agreement % (Ratio) (95% CI)
Capillary (fingerstick) Whole Blood	94.7% (108/114) (89.0-97.6%)	95.5% (1116/1168) (94.2-96.6%)
Venous Whole Blood	96.5% (110/114) (91.3-98.6%)	94.3% (1100/1166) (92.9-95.5%)
Plasma	96.8% (60/62) (89.0-99.1%)	93.9% (1034/1101) (92.3-95.2%)

HIV-1 Sensitivity

Capillary (Fingerstick) Whole Blood

The sensitivity of the DPP HIV-Syphilis System to detect HIV-1 infection in fingerstick whole blood was evaluated using 619 samples from individuals known to be infected with HIV-1, 151 of which were known positive for both HIV-1 and syphilis, and 468 were known positive for HIV-1 only. All 619 samples were confirmed HIV-1 positive via HIV 1/2 Ag/Ab EIA. Six hundred fifteen (615) samples out of 619 tested HIV reactive using the DPP HIV-Syphilis System.

In addition, samples from 91 individuals known positive for syphilis only, from 728 individuals at high risk for HIV and syphilis, and from 558 individuals at low risk for HIV and syphilis were tested. Samples from these groups were tested for HIV via an HIV 1/2 Ag/Ab EIA and if reactive were confirmed using an HIV-1/HIV-2 differentiation assay. Of the 91 known positive syphilis only individuals, 6 were confirmed HIV positive, of the 728 high risk individuals, 13 were confirmed HIV positive, and of the 558 low risk individuals, 1 was confirmed HIV positive. All 20 of these samples were HIV reactive on the DPP HIV-Syphilis System.

The sensitivity of the DPP HIV-Syphilis System was evaluated using 639 (619 known HIV-1 positives and 19 true positives identified from the high-risk population and 1 true positive identified from the low-risk population) (see Table 1). Of these, 635 specimens tested reactive using the DPP HIV-Syphilis System (615 known positive, 19 high risk and 1 low risk) when fingerstick whole blood was tested in this study. In these studies, the DPP HIV-Syphilis System gave false nonreactive results for four confirmed positive specimens from known positive individuals when fingerstick whole blood specimens were tested. The calculated HIV sensitivity of the DPP HIV-Syphilis System for fingerstick whole blood was 635/639 = 99.4% (95% Confidence Interval = 98.4% - 99.8%).

Table 1: Detection of antibody to HIV-1 in capillary whole blood (fingerstick) specimens from individuals known to be infected with HIV-1, and at high risk for infection with HIV-1

Patient Infected Status	DPP HIV-Syphilis System – HIV Result		Total
	Reactive	Nonreactive	
Positive	635	4[1]	639
Negative	5	1352	1357
Total	640	1356	1996

[1]All 4 false nonreactive results were from individuals on ART or HAART.

Venous Whole Blood

The sensitivity of the DPP HIV-Syphilis System to detect HIV-1 infection in venous whole blood was evaluated using 618 samples from individuals known to be infected with HIV-1, 151 of which were known positive for both HIV-1 and Syphilis, and 467 were known positive for HIV-1 only. All 618 samples were confirmed HIV-1 positive via HIV 1/2 Ag/Ab EIA. Six hundred fifteen (615) samples out of 618 tested were HIV reactive using the DPP HIV-Syphilis System.

In addition, samples from 91 individuals known positive for syphilis only, from 729 individuals at high risk for HIV and Syphilis, and from 559 individuals at low risk for HIV and Syphilis were tested. Samples from these groups were tested for HIV via an HIV 1/2 Ag/Ab EIA and, if reactive, were confirmed using an HIV-1/HIV-2 Differentiation Assay. Of the 91 known positive syphilis only individuals, 6 were confirmed HIV positive, of the 728 high risk individuals, 13 were confirmed HIV positive, and of the 559 low risk individuals, 1 was confirmed HIV positive. All 20 of these samples were HIV reactive on the DPP HIV-Syphilis System.

The sensitivity of the DPP HIV-Syphilis System was evaluated using 638 (618 known HIV-1 positives and 19 true positives identified from the high-risk population and 1 true positive identified from the low risk population) (see Table 2). Of these, 635 specimens tested reactive using the DPP HIV-Syphilis System (615 known positive, 19 high risk and 1 low risk) when venous whole blood was tested in this study. In these studies, the DPP HIV-Syphilis System gave false nonreactive results for three confirmed positive specimens from known positive individuals when fingerstick whole blood specimens were tested. The calculated HIV sensitivity of the DPP HIV-Syphilis System for venous whole blood was 635/638 = 99.5% (95% Confidence Interval = 98.6% - 99.8%).

Table 2: Detection of antibody to HIV-1 in venous whole blood specimens from individuals known to be infected with HIV-1, and at high risk for infection with HIV-1

Patient Infected Status	DPP HIV-Syphilis System – HIV Result		Total
	Reactive	Nonreactive	
Positive	635	3[1]	638
Negative	7	1352	1359
Total	642	1355	1997

[1]Of these 3 false nonreactive individuals, 2 were on HAART

Potassium-EDTA Plasma

The sensitivity of the DPP HIV-Syphilis System to detect HIV-1 infection in plasma was evaluated using 398 samples from individuals known to be infected with HIV-1, 101 of which were known positive for both HIV-1 and syphilis, and 297 were known positive for HIV-1 only. All 398 samples were confirmed HIV-1 positive via HIV 1/2 Ag/Ab EIA. Three hundred ninety-five (395) samples out of 398 tested HIV reactive using the DPP HIV-Syphilis System.

In addition, samples from 75 individuals known positive for syphilis only, from 422 individuals at high risk for HIV and syphilis, and from 419 individuals at low risk for HIV and syphilis were tested. Samples from these groups were tested for HIV via an HIV 1/2 Ag/Ab EIA and if reactive were confirmed using an HIV-1/HIV-2 Differentiation Assay. Of the 75 known positive for syphilis only individuals, 5 were confirmed HIV positive, of the 422 High risk individuals, 4 were confirmed HIV positive, and of the 419 Low risk individuals, 1 was confirmed HIV positive. All 10 of these samples were HIV reactive on the DPP HIV-Syphilis System.

The sensitivity of the DPP HIV-Syphilis System was evaluated using 408 (398 known HIV-1 positives and 9 true positives identified from the high-risk population and 1 true positive identified from the low risk population) (see Table 3). Of these, 405 specimens tested reactive using the DPP HIV-Syphilis System (395 known positive, 9 high risk and 1 low risk) when plasma was tested in this study. In these studies, the DPP HIV-Syphilis System gave false nonreactive results for three confirmed positive specimens from known positive individuals when plasma specimens were tested. The calculated HIV sensitivity of the DPP HIV-Syphilis System for plasma was 405/408 = 99.3% (95% Confidence Interval = 97.9% - 99.7%).

Table 3: Detection of antibody to HIV-1 in plasma specimens from individuals known to be infected with HIV-1, and at high risk for infection with HIV-1

Patient Infected Status	DPP HIV-Syphilis System – HIV Result		Total
	Reactive	Nonreactive	
Positive	405	3[1]	408
Negative	4	902	906
Total	409	905	1314

[1]All 3 false nonreactive results were from individuals on HAART.

Reactivity with HIV-1 Specimens of Different Virus Subtypes

To assess the ability of the DPP HIV-Syphilis System to detect HIV-1 antibodies directed to different HIV-1 group M subtypes and HIV-1 Group "O", a total of 213 specimens (serum/plasma) from different worldwide geographical regions were tested. All 213 specimens were reactive with the DPP HIV-Syphilis System for an overall sensitivity of 100% (95% CI = 98.3% to 100%). The results are presented in Table 4.

Table 4: Reactivity with HIV-1 Specimens from Various World Wide Geographic Regions

HIV Subtype	Number of Specimens	DPP HIV-Syphilis System Reactive
A	30	30
AE	15	15
AG	30	30
B	5	5
B/D	1	1
C	39	39
D	**19**	**19**
F	9	9
G	20	20
H	7	7
J	2	2
K	3	3
CRF01/CRF15	1	1
CRF01_AE	2	2
CRF02_AG	3	3

CRF03_AB	2	2
G/CRF02	1	1
H/A1	1	1
K/CRF09	1	1
URF_01A1G	1	1
URF_A1C	2	2
URF_A1CD	2	2
URF_A1D	8	8
URF_CD	1	1
Recomb. Of F1, K	2	2
Recomb. Of G, K	1	1
Recomb. Of K, A1	1	1
O	4	4
TOTAL	**213**	**213**

Seroconversion Panels (Comparison to EIA)

Twenty-five commercial HIV-1 seroconversion panels were tested. Each panel consisted of sequential collections from a single individual who seroconverted. The table, summarized below, presents the days elapsed from the date of the initial bleed to the last negative sample and first reactive sample. Data are presented for two FDA licensed EIA tests and the DPP HIV-Syphilis System.

Table 5: Testing Seroconversion Panels Using the DPP HIV-Syphilis System

	EIA 1 and DPP HIV-Syphilis System			EIA 2 and DPP HIV-Syphilis System		
	EIA 1 Repeatedly Reactive Test Result on Day:	DPP HIV-Syphilis System Repeatedly Reactive Test Result on Day:	Difference in Days to Anti-HIV Reactive Result: EIA1 Minus DPP HIV-Syphilis System	EIA 2 R Repeatedly Reactive Test Result on Day:	DPP HIV-Syphilis System Repeatedly Reactive Test Result on Day:	Difference in Days to Anti-HIV Reactive Result: EIA2 Minus DPP HIV-Syphilis System
PRB917	60	65	-5	72	65	7
PRB924	33	35	-2	ND	35	-
PRB927	28	33	-12	40	33	7
PRB929	25	28	-3	28	28	0
PRB930	7	10	-3	10	10	0
PRB939	103	103	0	103	103	0
PRB970	10	14	-4	10	14	-4
PRB944	14	14	0	ND	14	-
PRB945	13	20	-7	ND	20	-
PRB947	11	20	-9	20	20	0
PRB955	12	14	-2	14	14	0
PRB967	17	19	-2	17	19	-2
PRB968	28	33	0	28	33	-5
PRB969	70	72	0	70	72	-2
9014	10	10	-14	24	10	0
9031	146	153	-7	157	153	-4
9032	24	49	-25	29	49	-20
9075	30	30	0	30	30	0
9077	57	52	-5	52	52	0
12007	117	126	-9	126	126	0
9079	47	57	-10	47	57	0
HIV-002	31	33	-2	NT	33	N/A
HIV-003	69	76	-8	NT	76	N/A
HIV-007	47	47	0	NT	47	N/A

ND = Not Detected, NT = Not Tested, N/A = Not Applicable

HIV-2 Sensitivity

The sensitivity of the DPP HIV-Syphilis System to detect HIV-2 antibody was determined by testing 210 serum/plasma specimens that were positive for HIV-2 antibodies only. These specimens were obtained from repository sources. A total of 546 specimens from an area endemic for HIV-2 infection were also tested. All specimens reactive with the DPP HIV-Syphilis System were also reactive by FDA approved/licensed HIV 1/2 Assays. The sensitivity of DPP HIV-Syphilis System for detection of antibodies to HIV-2 in these studies were calculated to be 210/210 = 100% with the 95% confidence interval extending from 98.3 to 100%.

Table 6: Detection of antibody to HIV-2 in known HIV-2 reactive specimens and endemic samples

Study Population	Samples	DPP HIV-Syphilis System Reactive	True HIV-2 Positive Only[1]
Known HIV-2 Positive	210	210	210
Endemic Samples	546	196[2]	0
Total	756	406	210

[1] Confirmation based on results using a research use HIV-2 Western Blot.
[2] Of these 196 reactive specimens, 91 were reactive on HIV-1 WB only, 105 were reactive on HIV-1 and HIV-2 WB.

HIV Specificity

Capillary (Fingerstick) Whole Blood

The HIV specificity of the DPP HIV-Syphilis System was evaluated by testing fingerstick blood specimens from 91 syphilis known positive only, 728 High risk and 558 individuals Low risk for HIV and syphilis at 7 clinical study sites. Specimens were tested with an HIV 1/2 Ag / Ab EIA and if nonreactive were determined Negative for HIV.

Specimens from 6 syphilis known positive, 13 high risk and 1 low risk individuals were reactive on a licensed HIV-1/2 Ag/Ab EIA and were excluded from these calculations. Based on these studies, the HIV specificity of DPP HIV-Syphilis System in capillary (fingerstick) whole blood specimens was calculated to be 1352/1357 = 99.6% with the 95% confidence interval extending from 99.1 to 99.8%.

Table 7: Performance of the DPP HIV-Syphilis System on capillary whole blood (fingerstick) specimens from individuals presumed to be negative for HIV-1 infection

Study Population	Samples	True HIV Negative	DPP HIV-Syphilis System Nonreactive
Syphilis Known Positive	91	85	85
High Risk for HIV	728	715	711
Low Risk for HIV	558	557	556
TOTAL	1377	1357	1352

Venous Whole Blood

The HIV specificity of the DPP HIV-Syphilis System was evaluated by testing venous blood specimens from 91 syphilis known positive only, 729 high risk and 559 individuals low risk for HIV and syphilis at 7 clinical study sites. Specimens were tested with an HIV 1/2 Ag / Ab EIA and if nonreactive were determined Negative for HIV.

Specimens from 6 syphilis known positive, 13 high risk and 2 low risk individuals were reactive on a licensed HIV-1/2 Ag/Ab EIA and were excluded from these calculations. Based on these studies, the HIV specificity of DPP HIV-Syphilis System in capillary (fingerstick) whole blood specimens was calculated to be 1352/1359 = 99.5% with the 95% confidence interval extending from 98.9 to 99.8%.

Table 8: Performance of the DPP HIV-Syphilis System on venous whole blood specimens from individuals presumed to be negative for HIV-1 infection

Study Population	Samples	True HIV Negative	DPP HIV-Syphilis System Nonreactive
Syphilis Known Positive	91	85	84
High Risk for HIV	729	716	711
Low Risk for HIV	559	558	557
TOTAL	1379	1359	1352

Plasma

The HIV specificity of the DPP HIV-Syphilis System was evaluated by testing plasma specimens from 91 syphilis known positive only, 729 at high risk and 559 individuals at low risk for HIV and syphilis at 7 clinical study sites. Specimens were tested with an HIV 1/2 Ag / Ab EIA and if nonreactive were determined Negative for HIV.

Specimens from 5 syphilis known positive, 4 high risk and 1 low risk individuals were reactive on a licensed HIV-1/2 Ag/Ab EIA and were excluded from these calculations. Based on these studies, the HIV specificity of DPP HIV-Syphilis System in capillary (fingerstick) whole blood specimens was calculated to be 902/906 = 99.6% with the 95% confidence interval extending from 98.9 to 99.8%.

Table 9: Performance of the DPP HIV-Syphilis System on plasma from individuals presumed to be negative for HIV-1 infection

Study Population	Samples	True HIV Negative	DPP HIV-Syphilis System Nonreactive
Syphilis Known Positive	75	70	70
High Risk for HIV	422	418	415
Low Risk for HIV	419	418	417
TOTAL	916	906	902

Treponemal Test Line Performance in Intended Use Population

The treponemal test line performance of the DPP HIV-Syphilis System was evaluated in fingerstick, venous whole blood and plasma samples prospectively collected and tested from 1529 individuals in the intended use population. From these 1529 individuals, 1282 fingerstick whole blood samples were available for testing (629 female, 653 male, 16 – 87 years old), 1280 venous whole blood samples were available for testing (627 female, 653 male, 16 – 87 years old), and 1163 plasma samples were available for testing (638 female, 525 male, 16 – 91 years old). The demographics of the intended use population for each study cohort are presented in the following table.

Table 10: Study Cohort Demographics for Treponemal Test Line Performance

Matrix	Cohort	# of Subjects	# Female	# Male	Age Range (yrs.)
Fingerstick	Routine Syphilis	704	200	504	16 - 87
	HIV Positive at Enrollment	171	22	149	18 - 75
	Pregnant Women	407	407	N/A	18 - 43
	Total	**1282**	**629**	**653**	**16 - 87**
Venous Blood	Routine Syphilis	704	200	504	16 - 87
	HIV Positive at Enrollment	171	22	149	18 - 75
	Pregnant Women	405	405	N/A	18 - 43
	Total	**1280**	**627**	**653**	**16 - 87**
Plasma	Routine Syphilis	688	226	462	16 - 91
	HIV Positive at Enrollment	68	5	63	23 - 75
	Pregnant Women	407	407	N/A	18 - 43
	Total	**1163**	**638**	**525**	**16 - 91**

Positive Percent Agreement with Reference Methods

The clinical performance of the treponemal test line of the DPP HIV-Syphilis System was evaluated by calculating the positive percent agreement and negative percent agreement of the assay with the final comparator result based on an algorithm of results from three commercially available FDA-cleared syphilis assays: a treponemal EIA, a non-treponemal assay (RPR) and a second treponemal assay (TPPA). Because the clinical diagnosis of syphilis must be supported by two reactive laboratory tests, consisting of a treponemal assay and a non-treponemal assay, or at least two treponemal assays, employing an algorithm of three syphilis tests to determine the comparator result presents information closest to the serological "truth".

The final comparator result was determined using a two out of three rule. The table below shows how the final comparator result was determined.

Table 11: Serologic Comparator Algorithm for Treponemal Antibodies

1st Treponemal Test (EIA)	Non-Treponemal (RPR)	2nd Treponemal Test (TPPA)	Final Comparator Result
Nonreactive	Nonreactive	Reactive	**Negative**
		Nonreactive	**Negative**
		Inconclusive	**Negative**
Nonreactive	Reactive	Reactive	**Positive**
		Nonreactive	**Negative**
		Inconclusive	**Negative**[1]
Reactive	Reactive	Reactive	**Positive**
		Nonreactive	**Positive**
		Inconclusive	**Positive**
Reactive	Nonreactive	Reactive	**Positive**
		Nonreactive	**Negative**
		Inconclusive	**Positive**[2]
Equivocal	Nonreactive	Reactive	**Positive**
		Nonreactive	**Negative**
		Inconclusive	**Indeterminate**
Equivocal	Reactive	Reactive	**Positive**
		Nonreactive	**Negative**
		Inconclusive	**Indeterminate**

[1]The final comparator result of Negative was assigned based on the nonreactive treponemal test. There were no subjects with this serological profile among the study population.
[2]The final comparator result of Positive was assigned based on the reactive treponemal test. There were 5 subjects with this serological profile among the prospective study population.

A summary of the serological test profile for all prospectively-collected specimens in the intended use population is presented in the following table.

Table 12: Serologic Comparator Algorithm Result Profile for Syphilis in Intended Use Population

Treponemal Screen Assay (EIA)	Non-Treponemal (RPR)	2nd Treponemal (TPPA)	Final Comparator Result	Number of Subjects[1]
NR	NR	N/A	**Negative**	**1395**
NR	R	R	**Positive**	**0**
NR	R	NR	**Negative**	**2**
NR	R	Inconclusive	**Negative**	**0**
R	R	N/A	**Positive**	**58**
R	NR	R	**Positive**	**56**
R	NR	NR	**Negative**	**7**
R	NR	Inconclusive	**Positive**	**5**
Equivocal	NR	R	**Positive**	**0**
Equivocal	NR	NR	**Negative**	**2**
Equivocal	NR	Inconclusive	**Indeterminate**	**0**
Equivocal	R	R	**Positive**	**0**
Equivocal	R	NR	**Negative**	**0**

Equivocal	R	Inconclusive	**Indeterminate**	**0**

WHERE: NR= Nonreactive, R = Reactive, N/A = Test not performed
[1]Four subjects were nonreactive on the Treponemal Screen Assay but did not have enough sample remaining for additional testing required to complete serological comparator algorithm.

The comparison between the DPP HIV-Syphilis System result for treponemal antibodies and the final comparator results for prospectively-collected Fingerstick whole blood specimens in the intended use population is shown in the following tables (Table 13-14).

Table 13: Percent Agreement with Final Comparator Result for Treponemal Antibodies in Prospective Fingerstick Whole Blood Samples

DPP – Treponemal Test Line Result	Reference (Final Comparator Result)		Total
	Positive for Syphilis	Negative for Syphilis	
Reactive	108	52	160
Nonreactive	6	1116	1122
Total	114	1168	1282

Positive percent agreement for the DPP HIV-Syphilis System for treponemal antibodies in the intended use population was 94.7% (108/114) with a 95% confidence interval of 89.0% to 97.6%. Negative percent agreement was 95.5% (1116/1168) with a 95% confidence interval of 94.2% to 96.6%.

Table 14: Percent Agreement with Final Comparator Result for Treponemal Antibodies in Fingerstick Whole Blood Samples, Stratified by Study Cohort

Cohort	Positive Percent Agreement (PPA)			Negative Percent Agreement (NPA)		
	%	Ratio	95% CI	%	Ratio	95% CI
Routine Syphilis	92.5%	49 / 53	82.1 - 97.0%	97.1%	632 / 651	95.5 - 98.1%
HIV Positive at Enrollment	96.6%	57 / 59	88.5 - 99.1%	95.5%	107 / 112	90.0 - 98.1%
Pregnant Women	100.0	2 / 2	N/A	93.1%	377 / 405	90.2 - 95.2%
Total	94.7%	108 / 114	89.0 - 97.6%	95.5%	1116 / 1168	94.2 - 96.6%

The comparison between the DPP HIV-Syphilis System result for treponemal antibodies and the final comparator results for prospectively-collected venous whole blood specimens in the intended use population is shown in the following tables (Table 15-16).

Table 15: Percent Agreement with Final Comparator Result for Treponemal Antibodies in Prospective Venous Whole Blood Samples

DPP – *T. pallidum* Result	Reference (Final Comparator Result)		Total
	Positive for Syphilis	Negative for Syphilis	
Reactive	110	66	176
Nonreactive	4	1100	1104
Total	114	1166	1280

Positive percent agreement for the DPP HIV-Syphilis System in the intended use population was 96.5% (110/114) with a 95% confidence interval of 91.3% to 98.6%. Negative percent agreement was 94.3% (1100/1166) with a 95% confidence interval of 92.9% to 95.5%.

Table 16: Percent Agreement with Final Comparator Result for Treponemal Antibodies in Venous Whole Blood Samples, Stratified by Cohort

Cohort	Positive Percent Agreement (PPA)			Negative Percent Agreement (NPA)		
	%	Ratio	95% CI	%	Ratio	95% CI

Routine Syphilis	96.2%	51 / 53	87.2 - 99.0%	96.3%	627 / 651	94.6 - 97.5%
HIV Positive at Enrollment	96.6%	57 / 59	88.5 - 99.1%	95.5%	107 / 112	90.0 - 98.1%
Pregnant Women	100%	2 / 2	N/A	90.8%	366 / 403	87.6 - 93.3%
Total	96.5%	110 / 114	91.3 - 98.6%	94.3%	1100 / 1166	92.9 - 95.5%

The comparison between the DPP HIV-Syphilis System result for treponemal antibodies and the final comparator results for prospectively-collected plasma specimens in the intended use population is shown in the following tables (Table 17-18).

Table 17: Percent Agreement with Final Comparator Result for Treponemal Antibodies in Prospective Plasma Samples

DPP – *T. pallidum* Result	Reference (Final Comparator Result)		Total
	Positive for Syphilis	Negative for Syphilis	
Reactive	60	67	127
Nonreactive	2	1034	1036
Total	62	1101	1163

Positive percent agreement for the DPP HIV-Syphilis System in the intended use population was 96.8% (60/62) with a 95% confidence interval of 89.0% to 99.1%. Negative percent agreement was 93.9% (1034/1101) with a 95% confidence interval of 92.3% to 95.2%.

Table 18: Percent Agreement with Final Comparator Result for Treponemal Antibodies in Plasma Samples, Stratified by Cohort

Cohort	Positive Percent Agreement (PPA)			Negative Percent Agreement (NPA)		
	%	Ratio	95% CI	%	Ratio	95% CI
Routine Syphilis	94.9%	37 / 39[1]	83.1 - 98.6%	95.1%	617 / 649[2]	93.1 - 96.5%
HIV Positive at Enrollment	100.0%	21 / 21	84.5 - 100.0%	97.9%	46 / 47	88.9 - 99.6%
Pregnant Women	100.0%	2 / 2	N/A	91.6%	371 / 405	88.5 - 93.9%
Total	96.8%	60 / 62	89.0 - 99.1%	93.9%	1034 / 1101	92.3 - 95.2%

[1]Includes sample from 1 subject of unknown HIV Status
[2]Includes samples from 106 subjects of unknown HIV Status

Treponemal Test Line Performance in Subjects Previously Diagnosed with Syphilis

The treponemal test line performance of the DPP HIV-Syphilis System in was evaluated in fingerstick, venous whole blood and plasma samples prospectively collected and tested from 162 individuals self-reported as previously diagnosed with syphilis. Fingerstick and venous whole blood samples were available for all subjects (33 female, 129 male, 18 – 77 years old), and plasma samples were available for testing for 129 of 162 subjects (30 female, 99 male, 18 – 77 years old). To determine the Final Comparator Result, all subjects were tested with two FDA cleared syphilis tests at minimum, a treponemal EIA and a non-treponemal assay (RPR). A third syphilis test (TPPA) was used if the if the first two tests disagreed. The comparison between the DPP HIV-Syphilis System result for treponemal antibodies and the Final Comparator Result for prospectively-collected subjects that were previously diagnosed with syphilis is shown in the following table (Table 19).

Table 19: Percent Agreement with Final Comparator Result for Treponemal Antibodies in Subjects Previously Diagnosed with Syphilis

Matrix	Positive Percent Agreement (PPA)			Negative Percent Agreement (NPA)		
	%	Ratio	95% CI	%	Ratio	95% CI
Capillary (Fingerstick) Whole Blood	93.9%	108 / 115	88.0 - 97.0 %	87.2%	41 / 47	74.8 - 94.0%
Venous Whole Blood	96.5%	111 / 115	91.4 - 98.6%	85.1%	40 / 47	72.3 - 92.6%
Plasma	97.8%	91 / 93	92.5 - 99.4%	83.3%	30 / 36	68.1 - 92.1%

Reactivity with Medically Diagnosed Specimens

To assess the performance of the DPP HIV-Syphilis System in detecting *Treponema pallidum* antibodies using various medically staged syphilis specimens, 163 samples representing various clinical stages of syphilis diagnosis (primary, secondary, and latent) and treatment status were tested. The DPP HIV-Syphilis System was reactive in all 163 patients tested (Table 20).

Table 20: Summary of DPP HIV-Syphilis System Results for Treponemal Antibodies in Medically Staged Syphilis Patients

Syphilis Stage	Treatment Status	N	DPP HIV-Syphilis System Reactive
Primary	Treated	18	100%
	Untreated	10	100%
Secondary	Treated	33	100%
	Untreated	30	100%
Latent	Treated	42	100%
	Untreated	30	100%
Total		163	100%

Reactivity for Treponemal Antibodies with Prospectively Collected Pregnant Women Specimens

The treponemal test line performance of the DPP HIV-Syphilis System in was evaluated in fingerstick, venous whole blood and plasma samples prospectively collected and tested from 407 pregnant women. Fingerstick and plasma were available for all subjects (18 – 43 years old), and venous whole blood samples were available for testing for 405 of 407 subjects (18 – 43 years old). To determine the Final Comparator Result, all pregnant women were tested with two FDA cleared syphilis tests at minimum, a treponemal EIA and a non-treponemal assay (RPR). A third syphilis test (TPPA) was used if the if the first two tests disagreed. The performance of the treponemal test line of the DPP HIV-Syphilis system is presented by pregnancy trimester in the table below.

Table 21: Performance of the DPP HIV-Syphilis System for Treponemal Antibodies with Samples Prospectively Collected from Pregnant Women

Trimester	Percent Agreement with the Final Comparator Result					
	Positive Percent Agreement (PPA) % (Ratio) (95% CI)			Negative Percent Agreement (PPA) % (Ratio) (95% CI)		
	Fingerstick	Venous Blood	Plasma	Fingerstick	Venous Blood	Plasma
1st	100 (1/1) (20.7 – 100)	100 (1/1) (20.7 – 100)	100 (1/1) (20.7 – 100)	92.1 (140/152) (86.7 – 95.4)	90.8 (138/152) (85.1 – 94.4)	92.1 (140/152) (86.7 – 95.4)
2nd	100 (1/1) (20.7 – 100)	100 (1/1) (20.7 – 100)	100 (1/1) (20.7 – 100)	96.5 (109/113) (91.3 – 98.6)	93.8 (106/113) (87.8 – 97.0)	91.2 (103/113) (84.5 – 95.1)
3rd	N/A (0/0)	N/A (0/0)	N/A (0/0)	91.4 (128/140) (85.6 – 95.0)	88.4 (122/138) (82.0 – 92.7)	91.4 (128/140) (85.6 – 95.0)

Reactivity for Treponemal Antibodies with Retrospectively Collected Pregnant Women Specimens

To assess the performance of the DPP HIV-Syphilis System in detecting treponemal antibodies, 34 retrospectively collected samples (serum) from pregnant women that were presumed positive for Syphilis infection were tested. These samples included 12 samples that had been tested using an FDA cleared test for non-treponemal antibodies (RPR with titer) and 22 samples that had been tested using FDA cleared tests for treponemal antibodies (IgG) as well as non-treponemal antibodies (RPR with titer).

The DPP HIV-Syphilis System demonstrated a 100% reactivity for treponemal antibodies in all 34 samples from pregnant women that were determined reactive by laboratory testing with FDA cleared tests for syphilis (Table 22).

Table 22: Performance of the DPP HIV-Syphilis System for Treponemal Antibodies with Samples from Pregnant Women presumed positive for Syphilis

Syphilis Stage	Treatment Status	Trimester	N	DPP HIV-Syphilis System Reactive
Primary	Treated	Unknown	0	N/A
	Untreated	Unknown	3	100%
Secondary	Treated	Unknown	0	N/A
	Untreated	Unknown	1	100%
Early Latent	Treated	Unknown	0	N/A
	Untreated	Unknown	5	100%
Latent	Treated	Unknown	0	N/A
	Untreated	Unknown	3	100%
Unknown	Unknown	1st	8	100%
		2nd	6	100%
		3rd	8	100%
Total			34	0

Analytical Specificity

Effect of Unrelated Medical Conditions on Analytical Sensitivity and Specificity

To evaluate the effect of unrelated medical conditions on the performance of DPP HIV-Syphilis System, 438 samples containing antibodies against Cirrhosis, CMV (IgM), Dialysis, Syphilis, dsDNA, EBV (IgG), HAV (IgM), HBV Ag, HCV Ab, HIV Ab, HSV-1 (IgG), HSV-2 (IgG), HTLV I/II Ab, Leptospirosis, Rheumatoid Factor, SLE, Tuberculosis, VSV IgG, Cardiolipin (IgG and IgM), specimens containing Human Anti-Mouse Antibodies (HAMA), specimens from individuals who are intravenous drug users (IVDU), multiparous females, pregnant females, those who recently received an influenza vaccine, and individuals with Scleroderma, Hypergammaglobulinemia (IgA, IgE, IgG, and IgM), Antiphospholipid Syndrome, Chlamydia, and Gonorrhea were tested with the DPP HIV-Syphilis System.

Table 23: Unrelated Medical Conditions

Unrelated Medical Condition	Number	# Reactive by DPP (HIV)	# Reactive by DPP (Treponemal)
Cirrhosis	10	0	0
Cytomegalovirus (CMV) IgM	70	0	7[1]
Dialysis	10	0	0
Double Stranded DNA (dsDNA) Ab	72	0	8[2]
Epstein–Barr Virus (EBV) IgG	10	0	0
Hepatitis A Virus (HAV) IgM	10	0	0
Hepatitis B Virus (HBV) Ag	10	0	0
Hepatitis C Virus (HCV) Ab	10	0	0
HIV Ab	10	10	0
Herpes Simplex Virus (HSV)-1 IgG	10	0	0
Herpes Simplex Virus (HSV)-2 IgG	10	0	0
Human T-Lymphotropic Virus (HTLV) I/II	10	0	0
Syphilis	10	0	10
Lipemic	10	0	0
Lyme	10	0	0
Influenza Vaccine	10	0	0
Pregnant Females	12	0	0

Multiparous Females	10	0	0
Rheumatoid Factor	13	0	0
Varicella Zoster Virus (VZV) IgG	11	0	0
Tuberculosis	15	0	0
Drug Users (IVDU)	13	0	0
Leptospirosis	11	0	0
Systemic Lupus Erythematosus (SLE)	44	0	1[3]
Scleroderma	10	0	0
HAMA	10	0	0
Cardiolipin IgG	7	0	0
Cardiolipin IgM	8	0	0
Hypergammaglobulinemia IgA	9	0	0
Hypergammaglobulinemia IgE	10	0	0
Hypergammaglobulinemia IgG	10	0	0
Hypergammaglobulinemia IgM	10	0	0
Antiphospholipid Syndrome	3	0	0
Chlamydia	10	0	0
Gonorrhea	10	0	0
Total	508	10	26

[1]A total 70 CMV IgM specimens were tested on the DPP HIV-Syphilis System, of which 7 samples yielded reactive results on the treponemal test line for an estimated cross-reactivity rate of 10.0% (7/70).
[2]A total of 72 dsDNA specimens were tested on the DPP HIV-Syphilis System, of which 8 yielded reactive results on the treponemal test line for an estimated cross-reactivity rate of 11.1% (8/72).
[3]A total of 44 SLE specimens were tested on the DPP HIV-Syphilis System, of which 1 yielded a reactive result on the treponemal test line for an estimated cross-reactivity rate of 2.3% (1/44).

Effect of Interfering Substances on Analytical Sensitivity and Specificity
The effect of the following potentially interfering substances on assay performance was tested using 100 specimens representing potentially interfering substances. Interferences were tested up to the listed concentrations and no impact on results was observed.

Table 24: Interfering Substances – HIV Test Line, Reported as Number Correct / Expected Results

Interfering Substance	Concentration Tested
Hemoglobin Samples	0.98 – 500 mg/dL
Triglyceride/Triolein	5.86 – 3,000 mg/dL
Bilirubin Mixed Isomer	0.04 – 20 mg/dL
Total Protein (HAS)	6.0 – 11.0 g/dL
E. coli	98 – 50,000 CFU/mL
EDTA	1.56 – 800 mg/dL
Sodium Citrate	1.95 – 1,000 mg/dL
Lithium Heparin	15.63 - 8,000 mg/dL
Sodium Heparin	15.63 – 8,000 mg/dL
Candida albicans	44 – 22,500 cells/mL

Reproducibility in Plasma
Reproducibility studies were performed to demonstrate the inter-day reproducibility of the DPP HIV-Syphilis System in plasma. This study was conducted at three laboratory sites using a panel of eight blinded plasma samples representing the following: nonreactive, HIV-1 low reactive, HIV-2 low reactive, treponemal antibody low reactive, HIV-1 and treponemal antibody low reactive, HIV-1 high reactive, HIV-2 high reactive, and treponemal antibody high reactive. Each panel was run on 3 lots of the DPP HIV-Syphilis System on 3 separate days by 3 separate operators at each site. Results were read at 10 minutes, using the DPP Micro Reader. A total of 648 data points was taken per test line (HIV and treponemal). The results of the reproducibility study in plasma are presented in Tables 25 and 26 below.

Table 25: Reproducibility in Plasma: All Sites, All Operators, All Days

Sample	HIV Test Line % Agreement with Expected Result (No. Reactive/No. Tested)	Treponemal Test Line % Agreement with Expected Result (No. Reactive/No. Tested)
HIV-1 Low Reactive	100% (81/81)	100% (0/81)
HIV-2 Low Reactive	100% (81/81)	100% (0/81)
Treponemal Antibody Low Reactive	100% (0/81)	100% (81/81)
HIV-1 and Treponemal Antibody Low Reactive	100% (81/81)	98.8% (80/81)
HIV-1 High Reactive	100% (81/81)	100% (0/81)
HIV-2 High Reactive	100% (81/81)	100% (0/81)
Treponemal Antibody High Reactive	100% (0/81)	98.8% (80/81)
Nonreactive	100% (0/81)	98.8% (1/81)

Table 26: Reproducibility in Plasma, By Sites

Sample	HIV Test Line (No. Expected / No. Tested)			Treponemal Test Line (No. Expected / No. Tested)		
	Site 1	Site 2	Site 3	Site 1	Site 2	Site 3
HIV-1 Low Reactive	27/27	27/27	27/27	27/27	27/27	27/27
HIV-2 Low Reactive	27/27	27/27	27/27	27/27	27/27	27/27
Treponemal Antibody Low Reactive	27/27	27/27	27/27	27/27	27/27	27/27
HIV-1 and Treponemal Antibody Low Reactive	27/27	27/27	27/27	26/27	27/27	27/27
HIV-1 High Reactive	27/27	27/27	27/27	27/27	27/27	27/27
HIV-2 High Reactive	27/27	27/27	27/27	27/27	27/27	27/27
Treponemal Antibody High Reactive	27/27	27/27	27/27	27/27	26/27	27/27
Nonreactive	27/27	27/27	27/27	27/27	26/27	27/27

Reproducibility in Venous Whole Blood

Reproducibility studies were performed to demonstrate the reproducibility of the DPP HIV-Syphilis System in venous whole blood. This study was conducted at three laboratory sites using a panel of six blinded venous whole blood samples representing the following: nonreactive, HIV-1 low reactive, HIV-2 low reactive, treponemal antibody low reactive, HIV-1 near cut-off (borderline), and treponemal antibody near cut-off (borderline). Each panel was run in duplicate on 5 separate days, twice per day, by 2 separate operators at each site (6 total). Testing was performed according to the Product Insert of the DPP HIV-Syphilis System. Results were read at 10 minutes using the DPP Micro Reader. The results of the study are presented in Tables 27 and 28 below.

Table 27: Reproducibility in Venous Whole Blood: All Sites, All Operators, All Days

Sample	HIV Test Line % Agreement with Expected Result (No. Reactive/No. Tested)	Treponemal Test Line % Agreement with Expected Result (No. Reactive/No. Tested)
Low Reactive HIV-1	100% (120/120)	97.5% (3/120)
Low Reactive HIV-2	100% (120/120)	100% (0/120)
Low Reactive Syphilis	100% (0/120)	100% (120/120)
Nonreactive	100% (0/120)	99.2% (1/120)
Near Cutoff Reactive HIV-1	93.3% (112/120)	99.2% (1/120)
Near Cutoff Reactive Syphilis	100% (0/120)	95.8% (115/120)

Table 28: Reproducibility in Venous Whole Blood, By Sites

Sample	HIV Test Line (No. Reactive/ No. Tested)			Treponemal Test Line (No. Reactive / No. Tested)		
	Site 1	Site 2	Site 3	Site 1	Site 2	Site 3
Low Reactive HIV-1	40/40	40/40	40/40	0/40	0/40	3/40
Low Reactive HIV-2	40/40	40/40	40/40	0/40	0/40	0/40
Low Reactive Syphilis	0/40	0/40	0/40	40/40	40/40	40/40
Nonreactive	0/40	0/40	0/40	1/40	0/40	0/40
Near Cutoff Reactive HIV-1	37/40	40/40	35/40	1/40	0/40	0/40
Near Cutoff Reactive Syphilis	0/40	0/40	0/40	38/40	40/40	37/40

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REF 60-9555-0 DPP HIV-Syphilis Rapid Test Control Pack

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