

SUMMARY OF SAFETY AND EFFECTIVENESS

Product: Chembio DPP® HIV 1/2 Assay

I. General Information

Device Generic Name: Rapid HIV 1/2 Antibody Test

Device Trade Name: Chembio DPP® HIV 1/2 Assay

Applicant's Name and Address:

Chembio Diagnostic Systems, Inc.
3661 Horseblock Road
Medford, NY 11763
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Premarket Approval Application (PMA) Number: BP 120032

Office's Signatory Authority: Jay S. Epstein, M.D.
Director, OBRR/CBER

- I concur with the summary review.**
- I concur with the summary review and include a separate review to add further analysis.**
- I do not concur with the summary review and include a separate review.**

Date of Notice of Approval to the Applicant:

Material Reviewed/ Consulted: The PMA, amendments to the PMA, and other specific documentation used in developing the Summary of Safety and Effectiveness (SSE)

Review memos from the following reviewers were used in developing the SSE:

Discipline reviewed	Reviewer names
Clinical and Non-clinical/Analytical	Pawan K. Jain Krishnakumar Devadas Xue Wang
Product Design	Pawan K. Jain Krishnakumar Devadas
CMC	Pawan K. Jain Krishnakumar Devadas Xue Wang
Statistical	Paul Hshieh
Facility	Nicole Trudel Satheesh Thomas Sarah Wangseng
Bioresearch Monitoring	Janet White
Labeling and Promotional Advertising	Joseph Manik
Policy	Pradip Akolkar Elliot Cowan Indira Hewlett

II. Intended Use

The Chembio DPP® HIV 1/2 Assay is a single-use immunochromatographic test for the detection of antibodies to Human Immunodeficiency Virus Types 1 and 2 (HIV-1/2) in oral fluid, fingerstick whole blood, venous whole blood, serum, or plasma samples. The Chembio DPP HIV 1/2 Assay is intended for use as a point-of-care test to aid in the diagnosis of infection with HIV-1 and HIV-2. This test is suitable for use in multi-test algorithms designed for the statistical validation of rapid HIV test results. When multiple rapid HIV tests are available, this test should be used in appropriate multi-test algorithms.

CLIA Complexity: Moderate

III. Device Description

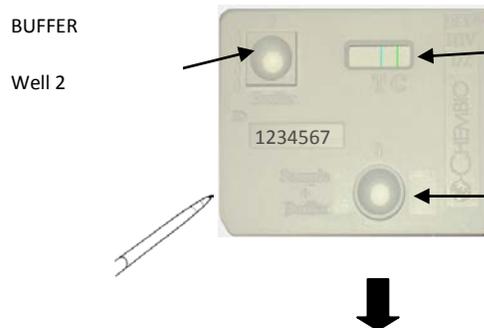
The Chembio DPP HIV 1/2 Assay employs Chembio's patented DPP (Dual Path Platform) technology and consists of a sample path and a reagent path, which intersect in the antibody detection (TEST and CONTROL) areas in the readout window of the test cassette. To initiate the test, a specimen is added to Sample Buffer vial and the mixture is applied to the SAMPLE+BUFFER Well of the DPP test cassette. The sample flows along the sample path membrane and is delivered to the test area of the reagent strip, where specific HIV antigens and Protein A are immobilized. HIV antibodies, if present in the sample, bind instantly to the immobilized HIV antigens in the TEST area, while non-specific IgG binds to the Protein A in the CONTROL 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. The buffer hydrates the dried antibody-binding colored conjugate, which migrates to the TEST area. The colored conjugate binds to HIV-1/HIV-2 antibodies that are complexed with immobilized viral antigen in the Test area and IgG-protein A complex in the Control area, forming a pink/purple line. In the absence of HIV-1 and HIV-2 antibodies, there is no pink/purple line in the TEST area. The procedural control serves to demonstrate that specimen and reagents have been properly applied and have migrated through the device.

Test Procedure and Interpretation of the Results

a) TEST PROCEDURE

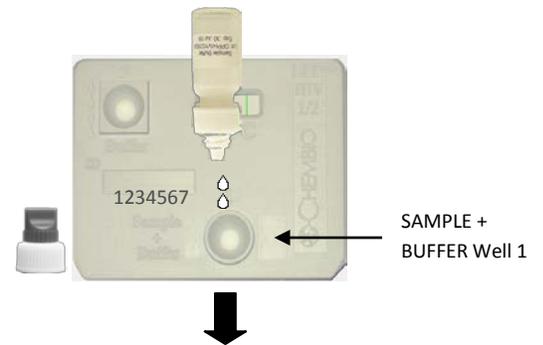
All components for the Chembio DPP HIV 1/2 Assay are ready to use as supplied. Follow directions as indicated. If the sample and/or kit components have been refrigerated, remove them from the refrigerator and allow them to come to a temperature of 18 to 30° C (64 to 86°F) prior to testing. Specimen collection procedures are described in the package insert.

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1. Chembio DPP HIV 1/2 Test Device is taken out from its pouch and placed on a flat surface (not necessary to remove the Desiccant Packet from the pouch). Note: If Desiccant Packet is missing, it is NOT USED; the Test Device is discarded and a new Test Device is used.



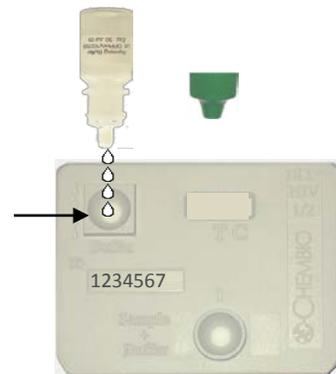
The Test Device is labeled with patient ID or identification number. The DPP Test Device has 2 colored lines in the Test Window; one is blue and the other is green. If the 2 colored lines are absent, the device is NOT USED; it is discarded and a new Test Device is used.

2. SampleTainer (BLACK CAP), containing the collected sample is inverted and held vertically (not at an angle) over the SAMPLE + BUFFER Well 1. Two drops (~65 μ L) are added slowly, dropwise, into the SAMPLE + BUFFER Well 1.



3. After Waiting for 5 minutes, the blue and green colored lines should have disappeared from the rectangular TEST and CONTROL window. If not, the device is not USED; it is discarded and a new Test Device is used.

Running Buffer bottle (Green CAP) is inverted, and held vertically (not at an angle) over BUFFER Well 2, and 4 drops (~135 μ L) of Buffer (GREEN CAP) are added slowly, dropwise, into BUFFER Well 2.



4. **Fingerstick, Venous Whole Blood, Serum or Plasma**

Test Results are read **between 10 and 25 minutes after the addition of the Running Buffer** to BUFFER Well 2.

NOTE: Used Sample Loop, Test Device, and any other test materials are discarded into a biohazard waste container.

5. Oral Fluid

Test Results are read **between 25 and 40 minutes after the addition of the Running Buffer** to BUFFER Well 2.

NOTE: Used Test Device, Oral Fluid Swab and any other test materials are discarded into a biohazard waste container.

b) INTERPRETATION OF TEST RESULTS

NONREACTIVE

One pink/purple line in the CONTROL (C) area, with no line in the TEST (T) area, indicates a NONREACTIVE Test Result. 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. However, this does not exclude possible infection with HIV. CDC guidelines are followed to inform the test subject of the Test Result and its interpretation.

NONREACTIVE



REACTIVE

Two pink/purple lines, one in the TEST (T) area and one in the CONTROL (C) area, indicate a REACTIVE Test Result. The line in the TEST (T) area may look different from the line in the CONTROL (C) area. Intensities of the Test and Control Lines may vary. A Test Result with visible lines in both TEST (T) and CONTROL (C) areas, regardless of intensity, is considered REACTIVE. 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. CDC guidelines are followed to inform the test subject of the Test Result and its interpretation.

REACTIVE



INVALID

If there is no distinct pink/purple line visible in the CONTROL (C) area, whether or not a line appears in the TEST (T) area, the test is considered INVALID and the test should be repeated with a new device.

INVALID



Components of the Chembio DPP HIV 1/2 Assay

The individual components along with the product insert are assembled into a kit box. Each kit contains the following:

- 20 DPP HIV 1/2 Individually Pouched Test Devices
- 20 Disposable 10 microliter Sample Loops
- 20 DPP HIV Sample Buffer Vials (1 ml) - Black Cap
- 20 Oral Fluid Swabs
- 1 DPP HIV Running Buffer Vial (6 ml) - Green Cap
- 20 copies of Subject Information Notice
- 1 Product Insert

DPP HIV Sample Buffer contains sodium phosphate, sodium chloride, EDTA, Tween 20, chicken serum, and gentamycin, streptomycin and sodium azide as preservatives.

DPP HIV Running Buffer contains sodium phosphate, sodium chloride, Tween 20, urea, hydrochloric acid, sodium hydroxide, chicken serum, avidin, and gentamycin, streptomycin and sodium azide as preservatives.

DPP HIV 1/2 Individually Pouched Test Devices: Plastic housing containing nitrocellulose membrane on which two HIV-1 synthetic peptides and one HIV-2 synthetic peptide are painted as Test line, and Protein A as Control line, along with pad containing conjugate reagents.

Accessories Available and Required

HIV Kit Controls:

1 DPP Nonreactive Control (0.5mL): Human serum/plasma; negative for antibodies to HIV and HCV; negative for HBsAg and HIV-1 Ag. Preservative: Sodium azide.

1 DPP HIV-1 Reactive Control (0.5mL): Human HIV-1 antibody in human serum/plasma; negative for HIV-1 Ag, HBsAg, and anti-HCV antibodies. Preservative: Sodium azide.

1 DPP HIV-2 Reactive Control (0.5mL): Human HIV-2 antibody in human serum/plasma; negative for HIV-1 Ag, HBsAg, and anti-HCV antibodies. Preservative: sodium azide.

IV. Restrictions

1. Sale of the Chembio DPP HIV 1/2 Assay is restricted to clinical laboratories that have an adequate quality assurance program, including planned systematic activities that provide adequate confidence that requirements for quality will be met and where there is assurance that operators will receive and use the instructional materials.
2. The Chembio DPP HIV 1/2 Assay is approved for use only by an agent of a clinical laboratory.
3. Test subjects must receive the “Subject Information Notice” prior to specimen collection, and appropriate information when test results are provided.
4. The Chembio DPP HIV 1/2 Assay is not approved for use to screen blood, plasma, cell or tissue donors.

V. Warnings

For *IN VITRO* diagnostic use

1. Read the Product Insert completely before using this assay. Follow the instructions carefully as not doing so may result in inaccurate test results.
2. Use of this test kit with sample types other than those specifically approved for use with this device may result in inaccurate test results.
3. This test should be performed at 18 to 30°C (64 to 86°F). If stored refrigerated, ensure that the pouch is brought to operating temperature before performing testing.
4. This assay has not been evaluated for newborn screening, cord blood specimens, or individuals less than 2 years of age.
5. An individual infected with HIV-1 and/or HIV-2 who is receiving highly active antiretroviral therapy (HAART) may produce a false negative result.

VI. Precautions

1. Safety Precautions
 - a. Handle the samples and materials contacting samples, and kit controls as if capable of transmitting infection.
 - b. 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.
 - c. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when handling patient samples.
 - d. 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.**
 - e. Use 10% bleach or other appropriate disinfectants to wipe all spills. The bleach solution should be made fresh each day.
 - f. For additional information refer to: Centers for Disease Control and Prevention (CDC): Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Post-exposure Prophylaxis.

2. Handling Precautions
 - a. If Desiccant Packet is missing or damaged, DO NOT USE. Discard test device and use a new test device.
 - b. Do not use any test device if the pouch has been perforated.
 - c. Each test device is for single use only.
 - d. Do not use the test beyond the expiration date printed on the pouch. Always check expiration date prior to testing.
 - e. Do not mix reagents from different lot numbers of kits.
 - f. Adequate lighting is required to read the test results.

VII. Limitations of the Test

1. The Chembio DPP HIV 1/2 Assay must ONLY be used with oral fluid, capillary (fingerstick) or venous whole blood, serum or plasma. Using other types of samples or testing of venipuncture whole blood and plasma samples collected using a tube containing an anticoagulant other than citrate, heparin or EDTA may not yield accurate results. For serum samples, collect blood without anticoagulant.
2. The Chembio DPP HIV 1/2 Assay must be used in accordance with the instructions in this Product Insert to obtain accurate results.
3. Reading test results for capillary (fingerstick), venous whole blood, serum or plasma specimens earlier than 10 minutes or later than 25 minutes after the addition of Running Buffer to BUFFER Well 2 may yield erroneous results.
4. Reading test results for oral fluid specimens earlier than 25 minutes or later than 40 minutes after the addition of Running Buffer to BUFFER Well 2 may yield erroneous results.
5. Do not open the sealed foil pouch until just prior to use.
6. Do not use kit contents beyond labeled expiration date.
7. Ensure finger is completely dry before performing fingerstick.
8. Read results in a well-lit area.
9. A Reactive result using the Chembio DPP HIV 1/2 Assay 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 Chembio DPP HIV 1/2 Assay 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 clinically.
10. Reactive test results are confirmed by additional testing using other tests.
11. 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.
12. For a Reactive result, the intensity of the test line does not necessarily correlate with the titer of antibody in the sample.
13. A Nonreactive 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.
14. This assay has not been evaluated for newborn screening, cord blood specimens, or individuals less than 2 years of age.
15. An individual infected with HIV-1 and/or HIV-2 who is receiving highly active antiretroviral therapy (HAART) may produce a false negative result.

VIII. Alternative Practices and Procedures

Detection of antibodies against HIV epitopes can be done in a variety of ways, including enzyme or chemiluminescent immunoassays, Western blot, and immunochromatographic assays.

Immunochromatographic assays may be either lateral or transverse flow. Tests may be intended for laboratory use by laboratory professionals, at the point of care by health care professionals, or for home use by lay persons.

Most rapid HIV assays are based on lateral flow technology. The signal mechanism for immunochromatographic tests may utilize enzymatic or chemiluminescent reactions or entail visualization of a metal colloid (primarily gold, although selenium has also been used). Capture antigens may be peptides, proteins, fusion peptides or viral lysate. Samples for these tests are serum, plasma, whole blood, or oral fluid. Usually a qualitative or semi-quantitative result is reported. Most tests are utilized as screening assays and require confirmation. Rapid tests may also be used as part of a diagnostic testing algorithm. The Chembio DPP HIV 1/2 Assay is a qualitative, immunochromatographic assay which utilizes colloidal gold to determine the presence of HIV-1/2 antibodies in oral fluid, serum, plasma, or whole blood.

IX. Marketing History

This device has not been marketed previously.

X. Potential Adverse Effects of the Device on Health

Potential adverse effects of the Chembio DPP HIV 1/2 Assay relate to the risk of false positive and false negative results. While performance studies indicate that this risk is likely to be very small, the potential for inaccurate results exists. The risk of incorrect results is minimized by following the procedures and instructions outlined in the Package Insert.

XI. Summary of Preclinical Studies

The Chembio DPP HIV 1/2 Assay was evaluated in non-clinical studies using a number of well-defined panels of specimens.

Seroconversion Panels (Comparison to EIA)

Twenty-one commercial seroconversion panels (serum/plasma) were tested. Each panel consisted of sequential collections from a single individual who seroconverted. The table below presents the days elapsed from the date of the initial bleed to the last Nonreactive sample and first Reactive sample (Table 1). Data are presented for two FDA licensed EIA tests and the Chembio DPP HIV 1/2 Assay. In comparing test performance, positive numbers indicate earlier detection of HIV antibodies by the Chembio DPP HIV 1/2 Assay and negative numbers indicate earlier detection of HIV antibodies by EIA. The Chembio DPP HIV 1/2 assay detected HIV antibodies as early as EIA 1 in 15 out of 21 seroconversion panels and later than EIA 1 in the remaining six panels. The Chembio DPP HIV 1/2 assay detected HIV antibodies earlier than EIA 2 in 11 out of 21 seroconversion panels, as early as EIA 2 in 8 out of the remaining 10, and later than EIA 2 in two panels.

Seroconversion panels were not available for oral fluid specimens; therefore, a dilutional endpoint study compared to blood-based specimens was not conducted. However, it would be expected that the

analytical sensitivity of the Chembio DPP HIV 1/2 Assay using oral fluid specimens would be less than that for blood-based specimens.

Table 1: Testing Seroconversion Panels Using the Chembio DPP HIV-1/2 Assay

Panel	EIA 1 and Chembio DPP HIV 1/2 Assay			EIA 2 and Chembio DPP HIV 1/2 Assay		
	EIA 1 Repeatedly Reactive Test Result on Day:	Chembio DPP HIV 1/2 Reactive Test Result on Day:	Difference in Days to Anti-HIV Reactive Result: EIA Minus DPP HIV 1/2	EIA 2 Repeatedly Reactive Test Result On Day:	Chembio DPP HIV-1/2 Reactive Test Result on Day:	Difference in Days to Anti-HIV Reactive Result: EIA Minus DPP HIV 1/2
PRB904	92	92	0	92	92	0
PRB910	26	26	0	26	26	0
PRB914	0	0	0	4	0	4
PRB916	30	30	0	30	30	0
PRB917	65	65	0	72	65	7
PRB919	9	9	0	11	9	2
PRB922	0	4	-4	>11	4	>7
PRB924	35	35	0	>40	35	>5
PRB926	27	27	0	27	27	0
PRB927	33	33	0	40	33	7
PRB928	111	111	0	120	111	9
PRB929	25	28	-3	28	28	0
PRB930	10	10	0	>10	10	>0
PRB933	21	27	-6	27	27	0
PRB934	7	7	0	11	7	4
PRB939	103	103	0	103	103	0
PRB944	14	14	0	16	14	2
PRB952	17	17	0	>21	17	>4
PRB953	10	>10	<0	10	>10	<0

PRB958	15	>17	<-2	15	>17	<-2
PRB959	9	14	-5	14	14	0

Reactivity with an HIV-1 Low Titer Panel

A 15-member HIV-1 commercially available low titer panel of serum and plasma specimens was used to evaluate the Chembio DPP HIV 1/2 Assay and the results were compared to FDA licensed HIV-1 EIAs and Western blot (WB). The Chembio DPP HIV 1/2 Assay detected the presence of antibodies to HIV-1 low-titer specimens similarly to licensed HIV EIAs and WB. In no case was the Chembio DPP HIV 1/2 Assay Nonreactive when both licensed EIAs were repeatedly reactive or WB was positive (Table 2).

Table 2: Testing an HIV-1 Low Titer Panel Using the Chembio DPP HIV 1/2 Assay

Panel Member ID	Chembio DPP HIV 1/2 Assay	EIA 1	EIA 2	WB
PRB108-1	R	RR	RR	P
PRB108-2	NR	NR	NR	N
PRB108-3	R	RR	RR	IND
PRB108-4	R	RR	RR	P
PRB108-5	R	RR	RR	P
PRB108-6	R	RR	RR	IND
PRB108-7	R	RR	RR	P
PRB108-8	R	RR	RR	P
PRB108-9	R	RR	RR	P
PRB108-10	R	RR	NR	IND
PRB108-11	R	RR	RR	P
PRB108-12	NR	RR	NR	N
PRB108-13	R	RR	NR	IND
PRB108-14	NR	RR	NR	N
PRB108-15	R	RR	RR	IND

R=Reactive, NR=Nonreactive, P= Positive, N=Negative, IND=Indeterminate

Reactivity with HIV-1 Specimens of Different Virus Subtype

To assess the ability of the Chembio DPP HIV 1/2 Assay to detect HIV-1 antibodies directed to different HIV-1 group M subtypes and HIV-1 Group “O”, specimens (serum/plasma) from different worldwide geographical regions such as Africa (Ghana, Cote d’Ivoire, Mozambique, Uganda, and Zimbabwe), Asia (Thailand, China, and India), Europe (England, France, Spain, and Belgium) and Latin America (Brazil and Argentina) were tested. Of these 204 specimens, 203 tested Reactive with the Chembio DPP HIV 1/2 Assay. One subtype D tested false Nonreactive. The results are presented in Table 3.

Table 3: Testing HIV-1 Specimens from Various Geographic Regions using the Chembio DPP HIV 1/2 Assay

HIV Subtype	Number of Specimens	Chembio DPP HIV 1/2 Assay Reactive
A	7	7
AD	3	3
AE	13	13
AG	21	21
B	64	64
B/D	2	2
C	22	22
D	16	15
F	9	9
G	18	18
H	5	5
J	4	4
K	11	11
O	9	9
TOTAL	204	203

Effect of Unrelated Medical Conditions on Analytical Sensitivity and Specificity

To evaluate the effect of unrelated medical conditions on the performance of the Chembio DPP HIV 1/2 Assay, 370 specimens representing unrelated medical conditions were tested. The specimens were spiked with saline (nonreactive) or an HIV-1 reactive serum specimen or an HIV-2 reactive serum specimen to a low level of reactivity. All HIV-1 and HIV-2 specimens gave Reactive results, while all unspiked samples, with the exception of one Syphilis specimen gave Nonreactive results (Table 4).

Table 4: Effect of Unrelated Medical Conditions on Analytical Sensitivity and Specificity of the Chembio DPP HIV 1/2 Assay

Description	Chembio DPP HIV 1/2 Assay (# Reactive / Total # Tested)		
	Saline	HIV-1 (Weak Reactive)	HIV-2 (Weak Reactive)
Cirrhosis	0/10	10/10	10/10
CMV IgM	0/10	10/10	10/10
EBV IgG	0/10	10/10	10/10
Influenza Vaccination	0/10	10/10	10/10
HBV	0/10	10/10	10/10
HCV	0/10	10/10	10/10
HTLV-I/II	0/10	10/10	10/10
Dialysis	0/10	10/10	10/10
Multiparous	0/10	10/10	10/10
Rheumatoid Factor	0/10	10/10	10/10
Syphilis	1/20 ¹	10/10	10/10
Tuberculosis	0/10	10/10	10/10

¹ One specimen gave a weak Reactive test result on the Chembio DPP HIV 1/2 Assay. This specimen was nonreactive by EIA. An additional 50 specimens from individuals known to be infected with Syphilis gave Nonreactive test results for Chembio DPP HIV 1/2 Assay. All 70 specimens were tested by an RPR test for Syphilis infection.

Effect of Potentially Interfering Substances on Analytical Sensitivity and Specificity

To evaluate the effect of potentially interfering substances on the performance of Chembio DPP HIV 1/2 Assay, 300 specimens containing potentially interfering substances were tested. The specimens were spiked with saline (nonreactive), or an HIV-1 reactive serum specimen or an HIV-2 reactive serum specimen to a low level of reactivity. All HIV-1 and HIV-2 specimens gave Reactive results, while all unspiked samples gave Nonreactive results.

Table 5: Effect of Potentially Interfering Substances on Analytical Sensitivity and Specificity of Chembio DPP HIV 1/2 Assay

Description	Chembio DPP HIV 1/2 Assay (# Reactive / Total # Tested)		
	Saline	HIV-1 (Weak Reactive)	HIV-2 (Weak Reactive)
Hemoglobin Samples, 0.98 – 500 mg/dL	0/10	10/10	10/10
Triglyceride/Triolin, 5.86 – 3,000 mg/dL	0/10	10/10	10/10
Bilirubin Mixed Isomer, 0.04 – 20 mg/dL	0/10	10/10	10/10
Total Protein (HAS), 6.0 – 11.0 g/dL	0/10	10/10	10/10
<i>E. coli</i> , 98 – 50,000 CFU/mL	0/10	10/10	10/10
EDTA, 1.56 – 800 mg/dL	0/10	10/10	10/10
Sodium Citrate, 1.95 – 1,000 mg/dL	0/10	10/10	10/10
Lithium Heparin, 15.63 - 8,000 mg/dL	0/10	10/10	10/10
Sodium Heparin, 15.63 – 8,000 mg/dL	0/10	10/10	10/10
<i>Candida albicans</i> , 44 – 22,500 cells/mL	0/10	10/10	10/10

In a separate study, oral fluid specimens collected from 85 individuals known to be infected with HIV-1 and 85 individuals presumed to be negative for HIV-1 infection were prospectively collected and tested on the Chembio DPP HIV 1/2 Assay. Information was collected from the participants regarding concurrent diseases or medical conditions, oral pathologies, and other factors. In this study, consumption of alcoholic and non-alcoholic beverages, use of mouthwash, brushing teeth, chewing gum, or smoking tobacco 5 minutes to 24 hours prior to testing did not affect the sensitivity or specificity of the Chembio DPP HIV 1/2 Assay.

Reproducibility

Reproducibility was tested at three laboratories using three lots of the Chembio DPP HIV 1/2 Assay. A panel of five blinded (four plasma and one serum) samples representing nonreactive, low reactive HIV-1, low reactive HIV-2, high reactive HIV-1, and high reactive HIV-2 were run on three separate days by three separate technicians at each laboratory. Testing was performed according to the Product Insert of the Chembio DPP HIV 1/2 Assay. Results were read at 10 minutes. Results were read semi-quantitatively using a common strip evaluation scale. A total of 405 data points was taken. The reproducibility of the Chembio DPP HIV 1/2 Assay was calculated to be $405/405 = 100\%$ (95% confidence interval 99.1 to 100%).

XII. Summary of Clinical Studies

HIV-1 Sensitivity

ORAL FLUID

The sensitivity of the Chembio DPP HIV 1/2 Assay to detect infection with HIV-1 in oral fluid was evaluated using 868 specimens from individuals known to be infected with HIV-1. All 868 specimens tested repeatedly reactive using an FDA licensed EIA. Of these, 867 specimens tested positive using HIV-1 WB and one tested positive using HIV-1 NAT. Eight hundred sixty (860) out of 868 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay.

In addition, specimens from 976 individuals at high risk for infection with HIV-1 were tested. Of these, 96 specimens tested repeatedly reactive using an FDA licensed EIA, and positive using HIV-1 WB (true positive). On testing these 976 specimens using the Chembio DPP HIV 1/2 Assay, 94 specimens tested Reactive and 882 specimens tested Nonreactive. One specimen tested false Reactive and three specimens tested false Nonreactive using the Chembio DPP HIV 1/2 Assay.

The sensitivity of the Chembio DPP HIV 1/2 Assay was evaluated using 964 (868 known positives and 96 true positives identified from the high risk population) (see Table 6). Of these, 953 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay (860 known positive and 93 high risk). The Chembio DPP HIV 1/2 Assay gave false Nonreactive results for 11 specimens (8 known positives and 3 high risk) and one false positive result (high risk) when oral fluid specimens were tested in this study. Of the 11 false Nonreactives, seven were from individuals on HAART. The calculated sensitivity of the Chembio DPP HIV 1/2 Assay for oral fluid specimens in these studies was $953/964 = 98.9\%$ (95% confidence interval 98.0 to 99.4%).

Table 6: Detection of Antibody to HIV-1 in Oral Fluid Specimens from Individuals Known to be Infected with HIV-1 and at High Risk for Infection with HIV-1

True Status	Chembio DPP HIV 1/2		Total
	Reactive	Nonreactive	
Positive ¹	953	11 ²	964
Negative	1	879	880
Total	954	890	1844

1. Based on repeatedly reactive test results using an EIA and positive using an FDA licensed WB or NAT.

2. Of these 11 false Nonreactive individuals, seven were on HAART.

CAPILLARY (FINGERSTICK) WHOLE BLOOD

The sensitivity of the Chembio DPP HIV 1/2 Assay to detect infection with HIV-1 in capillary (fingerstick) whole blood was evaluated using 868 specimens from individuals known to be infected with HIV-1. All 868 specimens tested repeatedly reactive using an FDA licensed EIA. Of these, 867 specimens tested positive using HIV-1 WB and one tested positive using HIV-1 NAT. Eight hundred sixty seven (867) specimens out of 868 tested Reactive using the Chembio DPP HIV 1/2 Assay.

In addition, specimens from 976 individuals at high risk for infection with HIV-1 were tested. Of these, 96 specimens tested repeatedly reactive using an FDA licensed EIA, and positive using HIV-1 WB (true positive). On testing these 976 specimens using the Chembio DPP HIV 1/2 Assay, 95 specimens tested Reactive and 881 tested Nonreactive.

The sensitivity of the Chembio DPP HIV 1/2 Assay was evaluated using 964 specimens (868 known positives and 96 true positive identified from the high risk population). Of these, 962 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay (867 known positive and 95 high risk) (see Table 7). In these studies, the Chembio DPP HIV 1/2 Assay gave false Nonreactive results for one known positive specimen and for one confirmed positive specimen from a high risk individual when capillary whole blood specimens were tested. The calculated sensitivity of the Chembio DPP HIV 1/2 Assay for capillary (fingerstick) whole blood specimens in these studies was $962/964 = 99.8\%$ (95% confidence interval 99.2 to 99.9%).

Table 7: 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

True Status	Chembio DPP HIV 1/2		Total
	Reactive	Nonreactive	
Positive ¹	962	2	964
Negative	0	880	880
Total	962	882	1844

1. Based on repeatedly reactive test results using an EIA and positive using an FDA licensed WB or NAT.

VENOUS WHOLE BLOOD

The sensitivity of the Chembio DPP HIV 1/2 Assay to detect infection with HIV-1 in venous whole blood was evaluated using 868 specimens from individuals known to be infected with HIV-1. All 868 specimens tested repeatedly reactive using an FDA licensed EIA. Of these, 867 specimens tested positive using HIV-1 WB and one tested positive using HIV-1 NAT. All 868 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay.

In addition, specimens from 975 individuals at high risk for infection with HIV-1 were tested. Of these, 96 specimens tested repeatedly reactive using an FDA licensed EIA, and positive using HIV-1 WB (true positive). On testing these 975 specimens using the Chembio DPP HIV 1/2 Assay, 95 specimens tested Reactive and 880 specimens tested Nonreactive.

The sensitivity of the DPP HIV 1/2 Assay was evaluated using 964 (868 known positives and 96 true positives identified from the high risk population). Of these, 963 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay (868 known positive and 95 high risk) (see Table 8). In these studies, the Chembio DPP HIV 1/2 Assay gave false Nonreactive results for one confirmed positive specimen from a high risk individual when venous whole blood specimens were tested. The calculated

sensitivity of the Chembio DPP HIV 1/2 Assay for venous whole blood specimens in these studies was $963/964 = 99.9\%$ (95% confidence interval 99.4 to 99.9%).

Table 8: 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

True Status	Chembio DPP HIV 1/2		Total
	Reactive	Nonreactive	
Positive ¹	963	1	964
Negative	0	879	879
Total	963	880	1843

1. Based on repeatedly reactive test results using an EIA and positive using an FDA licensed WB or NAT.

PLASMA

The sensitivity of the Chembio DPP HIV 1/2 Assay to detect infection with HIV-1 in plasma specimens was evaluated using 868 specimens from individuals known to be infected with HIV-1. All 868 specimens tested repeatedly reactive using an FDA licensed EIA. Of these, 867 specimens tested positive using HIV-1 WB and one tested positive using HIV-1 NAT. All 868 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay.

In addition, specimens from 975 individuals at high risk for infection with HIV-1 were tested. Of these, 96 specimens tested repeatedly reactive using an FDA licensed EIA, and positive using HIV-1 WB (true positive). On testing these 975 specimens using the Chembio DPP HIV 1/2 Assay, 95 specimens tested Reactive and 880 tested Nonreactive.

The sensitivity of the Chembio DPP HIV 1/2 Assay was evaluated using 964 specimens (868 known positives and 96 true positives identified from the high risk population). Of these, 963 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay (868 known positive and 95 high risk) (see Table 9). In these studies, the Chembio DPP HIV 1/2 Assay gave false Nonreactive results for one confirmed positive specimen from a high risk individual when plasma specimens were tested. The calculated sensitivity of the Chembio DPP HIV 1/2 Assay for plasma specimens in these studies was $963/964 = 99.9\%$ (95% confidence interval 99.4 to 99.9%).

Table 9: 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

True Status	Chembio DPP HIV 1/2		Total
	Reactive	Nonreactive	
Positive ¹	963	1	964
Negative	0	879	879
Total	963	880	1843

1. Based on repeatedly reactive test results using an EIA and positive using an FDA licensed WB or NAT.

SERUM

The sensitivity of the Chembio DPP HIV 1/2 Assay to detect infection with HIV-1 in serum specimens was evaluated using 868 specimens from individuals known to be infected with HIV-1. All 868 specimens tested repeatedly reactive using an FDA licensed EIA. Of these, 867 tested positive using HIV-1 WB and one tested positive using HIV-1 NAT. All 868 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay.

In addition, specimens from 976 individuals at high risk for infection with HIV-1 were tested. Of these, 96 specimens tested repeatedly reactive using an FDA licensed EIA, and positive using HIV-1 WB (true positive). On testing these 976 specimens using the Chembio DPP HIV 1/2 Assay, 95 specimens tested Reactive and 881 specimens tested Nonreactive.

The sensitivity of the Chembio DPP HIV 1/2 Assay was evaluated using 964 specimens (868 known positives and 96 true positives identified from the high risk population). Of these, 963 specimens tested Reactive using the Chembio DPP HIV 1/2 Assay (868 known positive and 95 high risk) (see Table 10). In these studies, the Chembio DPP HIV 1/2 Assay gave false Nonreactive results for one confirmed positive specimen from a high risk individual when serum specimens were tested. The calculated sensitivity of the Chembio DPP HIV 1/2 Assay for serum specimens in these studies was $963/964 = 99.9\%$ (95% confidence interval 99.4 to 99.9%).

Table 10: Detection of Antibody to HIV-1 in Serum Specimens from Individuals Known to be Infected with HIV-1 and at High Risk for Infection with HIV-1

True Status	Chembio DPP HIV 1/2		Total
	Reactive	Nonreactive	
Positive ¹	963	1	964
Negative	0	880	880
Total	963	881	1844

1. Based on repeatedly reactive test results using an EIA and positive using an FDA licensed WB or NAT.

HIV-2 Sensitivity

The sensitivity of the Chembio DPP HIV 1/2 Assay 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 554 specimens from an area endemic for HIV-2 infection were also tested. All specimens reactive by an FDA approved/licensed HIV 1/2 assay were also Reactive with the Chembio DPP HIV 1/2 Assay (see Table 11). The sensitivity of the Chembio DPP HIV 1/2 Assay for detection of antibodies to HIV-2 in these studies was calculated to be 210/210 = 100% (95% confidence interval 98.3 to 100%).

Table 11: Detection of Antibody to HIV-2 in Known HIV-2 Positive Specimens and Specimens from Endemic Populations

Study Population	Samples	Chembio DPP HIV 1/2 Assay Reactive	True HIV-2 Positive Only ¹
Known HIV-2 Positives	210	210	210
Endemic Samples	554	201 ²	0
Total	764	411	210

¹ Confirmation based on results using a research use HIV-2 WB and not positive on an HIV-1 WB.

² Of these 201 reactive specimens, 93 were Positive on HIV-1 WB only, 108 were Positive on HIV-1 WB and HIV-2 WB.

Detection of Antibody to HIV-2 in Oral Fluid Specimens:

Oral fluid specimens from 11 individuals infected with HIV-2 were collected (one from the United States and 10 from Ivory Coast, Africa). Oral fluid specimens from 11 individuals tested Reactive using the DDP HIV 1/2 Assay. Of these 11, nine specimens were confirmed as infected with only HIV-2 using an HIV-2 specific assay. These specimens were either negative or indeterminate using HIV-1 WB (see Table 12).

Table 12: Detection of Antibody to HIV-2 in Oral Fluid Specimens

Known HIV-2 Individuals from:	Number of Individuals	Chembio DPP HIV 1/2 Reactive	HIV-2 Specific Test ¹	HIV-1 Western Blot ¹		
				Positive	Indeterminate	Negative
Ivory Coast	10	10	10 ²	0	6	4
USA	1	1	1	N/A	N/A	N/A
Total	11	11	11	0	6	4

1. Using serum or plasma specimens.

2. Two out of 10 specimens were dually reactive for HIV-1 and HIV-2 on an HIV-2 assay. These specimens were unconfirmed for HIV-1 by HIV-1 Western Blot.

Specificity

ORAL FLUID

The specificity of the Chembio DPP HIV 1/2 Assay was evaluated by testing oral fluid specimens from 962 individuals at low risk and 976 individuals at high risk for infection with HIV-1 at five clinical study sites. Samples from 96 high risk and 26 low risk individuals were repeatedly reactive on a licensed EIA and positive on Western Blot and were excluded from the study. Of the remaining 1816 specimens one specimen from an individual at high risk for infection with HIV-1 tested Reactive using the Chembio DPP HIV 1/2 Assay that tested negative using WB (see Table 13). Based on these studies, the specificity of the Chembio DPP HIV 1/2 Assay in oral fluid specimens was calculated to be $1815/1816 = 99.9\%$ (95% confidence interval 99.7 to 99.9%).

Table 13: Performance of the Chembio DPP HIV 1/2 Assay on Oral Fluid Specimens from Individuals Presumed to be Negative for HIV-1 Infection

Study Population	Samples	True Negative	Chembio DPP HIV 1/2 Assay Nonreactive
Low Risk	962	936	936
High Risk	976 ^{1,2}	880	879
Total	1938	1816	1815

¹Three specimens from the high risk group tested Nonreactive using the Chembio DPP HIV 1/2 Assay that tested positive using HIV-1 WB.

²One specimen from high risk group tested Reactive using the Chembio DPP HIV 1/2 Assay that tested negative using HIV-1 WB.

CAPILLARY (FINGERSTICK) WHOLE BLOOD

The specificity of the Chembio DPP HIV 1/2 Assay was evaluated by testing capillary (fingerstick) whole blood specimens from 961 low risk and 976 individuals at high risk for infection with HIV-1 at five clinical study sites. Samples from 96 high risk and 26 low risk individuals were repeatedly reactive on a licensed EIA and positive on Western Blot and were excluded from the study. All of the remaining 1815 specimens tested Nonreactive using the Chembio DPP HIV 1/2 Assay (see Table 14). Based on these studies, the specificity of the Chembio DPP HIV 1/2 Assay in capillary (fingerstick) whole blood specimens was calculated to be $1815/1815 = 100\%$ (95% confidence interval 99.8 to 100%).

Table 14: Performance of the Chembio DPP HIV 1/2 Assay on Capillary Whole Blood (Fingerstick) Specimens from Individuals Presumed to be Negative for HIV-1 Infection

Study Population	Samples	True Negative	Chembio DPP HIV 1/2 Assay Nonreactive ¹
Low Risk	961	935	935
High Risk	976	880	880
Total	1937	1815	1815

¹One specimen tested Nonreactive using the Chembio DPP HIV 1/2 Assay and positive using HIV-1 WB

VENOUS WHOLE BLOOD

The specificity of the Chembio DPP HIV 1/2 Assay was evaluated by testing venous whole blood specimens from 961 low risk and 975 individuals at high risk for infection with HIV-1 at five clinical study sites. Samples from 96 high risk and 26 low risk individuals were repeatedly reactive on a licensed EIA and positive on Western Blot and were excluded from the study. Of the remaining 1814 specimens, one specimen from an individual at low risk for infection with HIV-1 tested Reactive using the Chembio DPP HIV 1/2 Assay that tested negative using HIV-1 WB (see Table 15). Based on these studies, the specificity of the Chembio DPP HIV 1/2 Assay in venous whole blood specimens was calculated to be $1813/1814 = 99.9\%$ (95% confidence interval 99.7 to 99.9%).

Table 15: Performance of the Chembio DPP HIV 1/2 Assay on Venous Whole Blood Specimens from Individuals Presumed to be Negative for HIV-1 Infection

Study Population	Samples	True Negative	Chembio DPP HIV 1/2 Assay Nonreactive
Low Risk	961 ¹	935	934
High Risk	975 ²	879	879
Total	1936	1814	1813

¹One specimen tested Reactive using the Chembio DPP HIV 1/2 Assay and tested negative using HIV-1 WB.

²One specimen tested Nonreactive using the Chembio DPP HIV 1/2 Assay and tested positive using HIV-1 WB.

PLASMA

The specificity of the Chembio DPP HIV 1/2 Assay was evaluated by testing plasma specimens from 961 low risk and 975 individuals at high risk for infection with HIV-1 at five clinical study sites. Samples from 96 high risk and 26 low risk individuals were repeatedly reactive on a licensed EIA and positive on Western Blot and were excluded from the study. Of the remaining 1814 specimens, one specimen from an individual at low risk for infection with HIV-1 tested Reactive using the Chembio DPP HIV 1/2 Assay that tested negative using HIV-1 WB (see Table 16). Based on these studies, the specificity of the Chembio DPP HIV 1/2 Assay in plasma specimens was calculated to be 1813/1814 = 99.9% (95% confidence interval 99.7 to 99.9%).

Table 16: Performance of the Chembio DPP HIV 1/2 Assay on Plasma Specimens from Individuals Presumed to be Negative for HIV-1 Infection

Study Population	Samples	True Negative	Chembio DPP HIV 1/2 Assay Nonreactive
Low Risk	961 ¹	935	934
High Risk	975 ²	879	879
Total	1936	1814	1813

¹One specimen tested Reactive using the Chembio DPP HIV 1/2 Assay that tested negative using HIV-1 WB.

²One specimen tested Nonreactive using the Chembio DPP HIV 1/2 Assay that tested positive using HIV-1 WB.

SERUM

The specificity of the Chembio DPP HIV 1/2 Assay was evaluated by testing serum specimens from 961 low risk and 976 individuals at high risk for infection with HIV-1 at five clinical study sites. Samples from 96 high risk and 26 low risk individuals were repeatedly reactive on a licensed EIA and positive on Western Blot and were excluded from the study. Of the remaining 1815 specimens, one specimen from an individual at low risk for infection with HIV-1 tested Reactive using the Chembio DPP HIV 1/2 Assay that tested negative using HIV-1 WB (see Table 17). Based on these studies, the specificity of the Chembio DPP HIV 1/2 Assay in serum specimens was calculated to be 1814/1815 = 99.9% (95% confidence interval 99.7 to 99.9%).

Table 17: Performance of the Chembio DPP HIV 1/2 Assay on Serum Specimens from Individuals Presumed to be Negative for HIV-1 Infection

Study Population	Samples	True Negative	Chembio DPP HIV 1/2 Assay Nonreactive
Low Risk	961 ¹	935	934
High Risk	976 ²	880	880
Total	1937	1815	1814

1. One specimen tested Reactive using the Chembio DPP HIV 1/2 Assay that tested negative using HIV-1 WB.

2. One specimen tested Nonreactive using the Chembio DPP HIV 1/2 Assay that tested positive using HIV-1 WB.

X. Conclusions Drawn from the Studies

Risk/Benefit Analysis

The Chembio DPP HIV 1/2 Assay provides useful information to the patient and healthcare provider on the HIV status of an individual in the point-of-care setting, and can serve as an aid in the diagnosis of infection with HIV-1 and HIV-2. It has the potential, as a rapid test, to lead to diagnosis in short turnaround time for the test result, counseling and treatment. This is helpful to patients and public health surveillance initiatives in preventing the transmission of HIV infection.

Risks associated with a point-of-care HIV assay relate primarily to its rate of false negative and false positive results. Performance studies have demonstrated that the Chembio DPP HIV 1/2 Assay has a high level of sensitivity and specificity. Consequently, the rate of false Reactive or false Nonreactive results with the Chembio DPP HIV 1/2 Assay is very small.

Overall, the information provided by the sponsor indicates that the benefits of the Chembio DPP HIV 1/2 assay outweigh the risks associated with its use.

Safety and Effectiveness

Performance studies showed that the rate of false positive and false negative results is very small. All operators conducted testing in accordance with instructions for use of the Chembio DPP HIV 1/2 Assay, consistent with the training that was provided. The sensitivity and specificity of the Chembio DPP HIV 1/2 Assay for all specimen types studied (oral fluid, fingerstick whole blood, venous whole blood, serum, and plasma) are greater than or equal to 99% with the lower boundary of the 95% confidence interval greater than or equal to 98% for all sample types.