Evaluation of the DPP HIV-Syphilis test performance characteristics at the point-of-care clinical setting (FDOH-Miami-Dade STD clinical lab)

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Conflict of Interest

- 60 out of 140 DPP HIV-Syphilis test kits used in the study were donated by the Manufacturer (Chembio Diagnostics Inc.), but the manufacturer was not involved in study design, data collection, analysis and interpretation or writing of the report.
- I have no other conflicts to declare

Objectives of Study

1) To evaluate performance characteristics (accuracy, sensitivity and specificity) of the FDA approved, CLIA moderate complexity point-of-care (POC) DPP HIV-Syphilis Test (DPP) for HIV-1/2 and Treponemal antibodies detection.
2) To determine the benefits of DPP HIV-Syphilis test as initial screening test in reverse syphilis testing algorithm at the Health Department STD clinic.

Florida Department of Health in Miami-Dade County Laboratory is CLIA-certified for moderate complex and waived testing, performing about 4500 Non-Treponemal (RPR) Antibodies tests and similar volume of rapid HIV antibodies tests annually in its high syphilis and HIV seroprevalence public health population.

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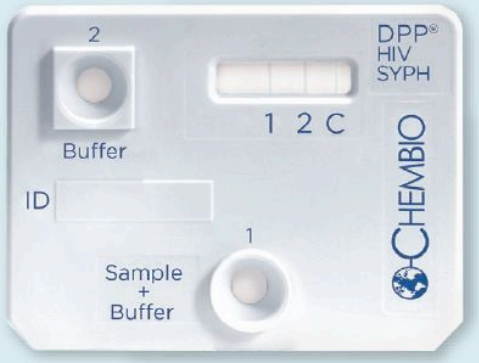
DPP® HIV-Syphilis

The Chembio DPP HIV-Syphilis Assay is a single-use rapid, qualitative, multiplex immunoassay for the simultaneous detection of antibodies to HIV virus (types 1/2) and Treponema Pallidum bacteria in fingerstick whole blood, venous whole blood or plasma specimens.



The STD Epidemic in Miami-Dade County

- In a recent sexually transmitted disease surveillance report from the CDC, Miami-Dade County had the nation's fourth highest rate of infectious syphilis.
- In 2019, the rate per 100,000 of Infectious Syphilis Cases in Miami-Dade County was 20.8 compared to Florida 15.1 and the U.S. 11.88.
- New HIV infection rate is nearly four times the national average: 54 new diagnoses of HIV for every 100,000 people—making it the highest new HIV rate in the country.

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Design of Study

Study testing algorithm included:

- Initial HIV screening by Chembio HIV-1/2 Ab SureCheck Rapid Test followed by DPP HIV-Syphilis assay and qualitative and quantitative RPR testing (Arlington Scientific, Inc) performed at the STD clinical lab.
- Subsequent confirmatory testing for both HIV and Syphilis infection performed at the State public health lab (BPHL-Miami).

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Design of Study

- Confirmation of the HIV results were done per CDC recommended diagnostic algorithm (2014):
  - Abbott Architect HIV Ag/Ab Combo IA,
  - Bio-Rad Geenius HIV-1/HIV-2 Supplemental differentiation assay
  - Hologic Aptima HIV-1 RNA Assay for discordant results.
- Confirmation of syphilis infection was done by traditional syphilis diagnostic algorithm:
  - non-treponemal antibody testing (BD Macro-Vue RPR)
  - total treponemal antibody testing for reactive results using Syphilis TP IA (Abbott ARCHITECT)
  - TPPA as secondary treponemal antibody test for discordant results (Fujirebio SERODIA®-TP-PA).

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Implementation

- 140 DPP HIV-Syphilis kits and control materials with 2 microreaders were provided by Chembio (60) and the FDOH (80).
- The performance of DPP test:
  - From May to July 2021
  - Plasma and WB samples collected from 121 individuals self-referred to the DOH-MD STD clinic.
  - plasma samples from patients
    - ✓ known to be infected with HIV only,
    - ✓ being positive for syphilis only,
    - ✓ being positive for both syphilis and HIV,
    - ✓ known to be negative for both syphilis and HIV;
  - whole blood samples collected from patients visiting STD clinic for routine syphilis and HIV testing.

Implementation

- All testing procedures and required QC have been performed according to manufacturers' Instructions for Use (IFUs) and laboratory Standard Operating Procedures (SOPs).
- All testing personnel participated in the verification study are licensed laboratory technicians/technologists and have been properly trained.
- Sensitivity, specificity and accuracy were calculated for each test.

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Results (HIV line)

- The sensitivity and specificity of DPP HIV-Syphilis assay to detect HIV antibodies were evaluated using a panel of 38 previously tested plasma samples where 14 individuals have been known to be infected with HIV.
- All 14 samples were tested HIV reactive by DPP.
- Of the 81 WB samples from high-risk patients 17 were reactive by both SureCheck and by DPP but only 16 have been confirmed as HIV positive by CDC algorithm at the BPHL.
- Overall sensitivity and specificity for DPP HIV line were 100% and 98.89% respectively.

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Results (TP line)

- DPP treponemal line performance was evaluated by calculating the Positive (PPA) and Negative Percent Agreement (NPA) with the final comparator result based on an algorithm of results from STD clinical lab and public health lab using traditional syphilis testing algorithm.
- Florida STD surveillance records were checked for previous syphilis infection on DPP Reactive RPR Non-Reactive samples.
- DPP demonstrated 100% (63/63) PPA for treponemal antibodies detection in WB and plasma samples. The NPA was 94.74% (18/19) for plasma and 100% (39/39) for WB.

Results

DPP HIV-Syphilis Performance Data

Matrix	DPP HIV-Syphilis (HIV line)				DPP HIV-Syphilis (Treponemal line)				SureCheck HIV-1/2			
	Sensitivity		Specificity		Positive Percent Agreement (PPA)		Negative Percent Agreement (NPA)		Sensitivity		Specificity	
	%	Ratio	%	Ratio	%	Ratio	%	Ratio	%	Ratio	%	Ratio
Plasma	100	14/14	100	24/24	100	17/17	94.74	18/19	100	13/13	100	24/24
Whole blood	100	16/16	98.46	64/65	100	46/46	100	39/39	82	12/15	98.46	64/65
All	**100**	**30/30**	**98.89**	**88/89**	**100**	**63/63**	**98.28**	**57/58**	**89.2**	**25/28**	**98.88**	**88/89**

Results (TP line)

- Out of **36** plasma samples previously tested by traditional syphilis algorithm, 18 individuals were tested Reactive by DPP but only 17 had been known as positive
  - (14 were positive by both RPR and Treponemal IA, and 3 had history of syphilis in records).
- 1 DPP reactive result was determined to be false positive as RPRs from two labs were non-reactive and there were no records of past syphilis infection in the state database.

Results (TP line)

- Of the 85 blood samples, 46 were DPP reactive:
  - 33 were reactive by RPR and Treponemal IA,
  - 7 were RPR reactive from patients returning for treatment monitoring,
  - 5 with non-reactive RPR had records of past syphilis infection in the state surveillance database,
  - **and one sample was RPR negative but IA and TPPA positive.**
- This one newly identified syphilis case would have been missed by using traditional algorithm.

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Results

- Performance characteristics of DPP HIV-Syphilis and HIV-1/2 Ab SureCheck were compared as part of the study.
- 25 HIV positive samples have been correctly identified as reactive by SureCheck but 3 samples from patients with established HIV infection produced false negative results.
- DPP test didn’t produce false negative HIV results during the study.

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Results

- At the same time both DPP and SureCheck showed false reactive result on one HIV-negative sample (confirmed by NAAT).
- DPP HIV test line sensitivity was 100% (30/30) that exceeded manufacturer' test characteristics for both venous blood (99.5%) and plasma (99.3%) samples, although more data is recommended to identify acute/early infection.
- DPP HIV test line specificity exceeded manufacturer's characteristic for plasma (100% vs 99.6%) but was slightly below for venous blood (98.46% vs 99.5%).

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Results

- DPP test demonstrated better performance as screening POC test for HIV antibodies detection compared to SureCheck HIV test (100% vs 89.2% sensitivity) with similar specificity (98.89%-98.88%).
- DPP test demonstrated 100% PPA for detection of treponemal antibodies in blood and plasma samples that exceeded manufacturer's specifications (96.5% and 96.8% respectively).
- NPA (97.74% for plasma and 100% for blood) also exceeded manufacturer's characteristics (94.3% and 93.9% respectively).

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Lessons Learned

- DPP test was easy to perform and interpret using microreader that minimizes errors related to subjective reading and interpretation.
- DPP demonstrated high degree of accuracy and provided a reliable way to perform rapid HIV and syphilis screening at the POC settings.
- DPP demonstrated better performance for HIV antibodies detection compared to SureCheck test.
- The DPP test can be used as first-tier assay in reverse syphilis testing algorithm followed by non-treponemal test during patients visits. Only discordant results may require second Treponemal test as “tie-breaker”.

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Lessons Learned

- Such algorithm may increase disease detection especially in late latent and early primary syphilis and enhance turn-around time and timely partner notification.
- During the study one newly identified syphilis case would have been missed by traditional algorithm.
- More data is needed to determine cost-effectiveness of the reverse algorithm.
- Additional resources would be needed to enhance laboratory module of the statewide Health Management System to report syphilis diagnostic results into the state STD surveillance database in HL7 format.

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Thank you