

INTRODUCTION

In the US, 16% of all syphilis patients and 28% of men infected with syphilis have coinfection with HIV. It is estimated that syphilis infection increases the chance of getting a HIV infection by 2-4 fold and transmission by 2-9 fold. Detection of both HIV and syphilis can play a critical role in reducing the incidences of transmission.

A rapid multiplex test will not only reduce workflow and sample volume problems but also increases access to test especially in low-resource and rural settings.

Designing a new Point-of-Care test for test operators with limited or no handson training is a challenge and comparing it with existing tests provides valuable feedback.

OBJECTIVE

Errors in rapid diagnostics tests can be reduced by designing tests where chances of operational missteps and data misinterpretation are low.

DPP® HIV-Syphilis Assay System (DPP® HIV-SYP) (not FDA approved), a multiplex assay designed to detect both HIV and Syphilis infection includes two tools for reducing errors: Quick Reference Instruction (QRI) and a hand-held digital reader for data interpretation.

We surveyed naïve user reaction to the Trinity Biotech Syphilis Health Check assay (SHC), a 510 (K) cleared syphilis rapid test (RT) and to the Chembio DPP[®] HIV Syphilis Assay System (DPP[®] HIV-SYP), a multiplexed RT utilizing a microreader that simultaneously measures both HIV and Treponema (TP) antibodies. Our intent was to gauge user response to the QRI, assess reaction to a microreader and to a multiplexed rapid test.

METHOD

22 experienced RT users, naïve to both products, read the QRI and completed assessments of both RTs using a random sequence of a blinded panel of primarily weakly reactive specimens (9). After product assessment, the testers rated these products on its usability and ease of use on a 5 point Likert scale. In addition, operators were encouraged to provide unrestricted comments based upon their experience with both products.

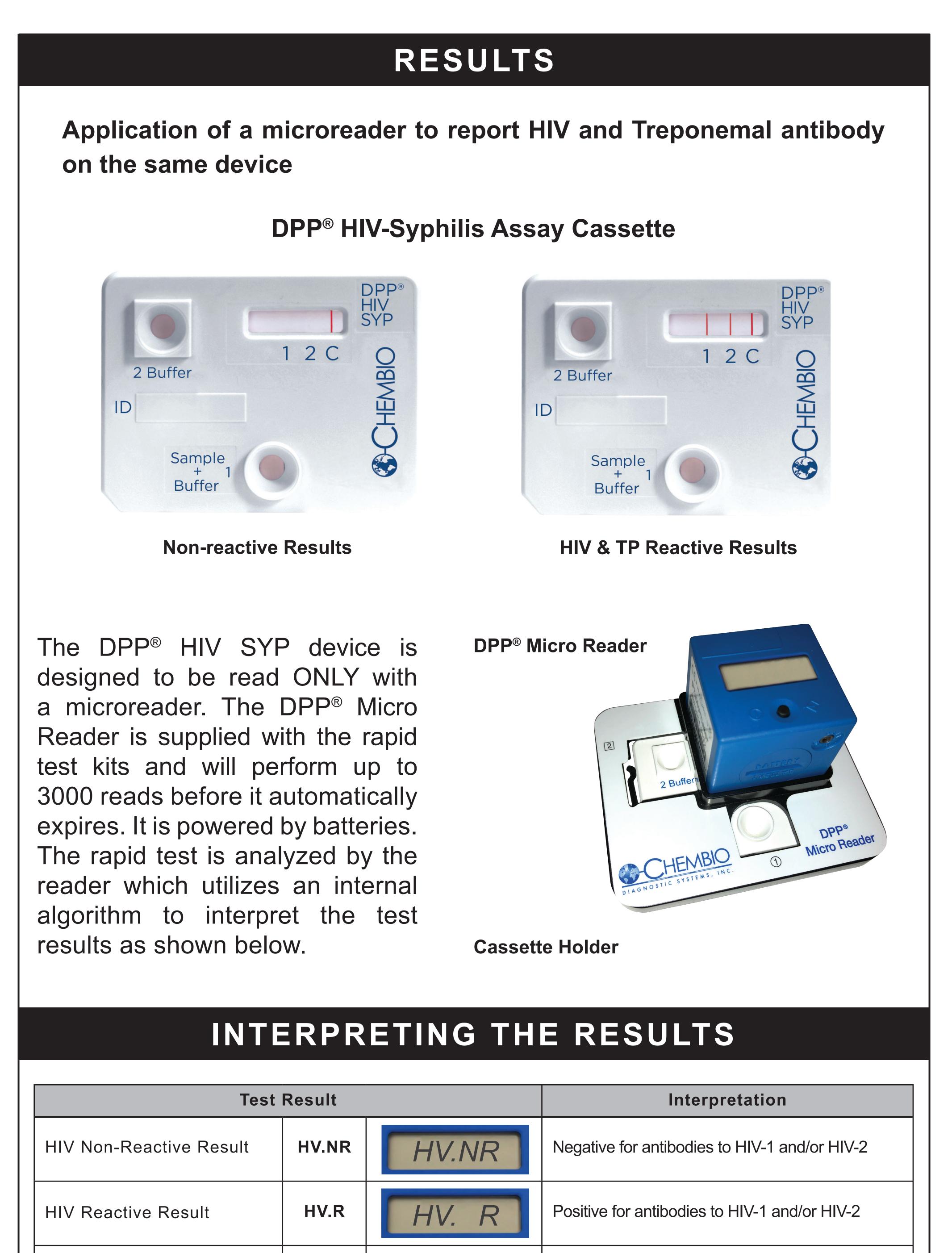
• The testers also evaluate the utility of the DPP[®] Micro Reader to reduce subjectivity of operators in interpreting Treponemal test line reactivity

LIMITATIONS

- . Fixed volume pipettes were used to apply specimens
- 2. TP specimens were chosen to provide a challenging range of reactivity

Introduction of Experienced Rapid Testers to a New Multiplex Rapid Test Allampallam K^{1,4}, Klugewicz SW¹, Cabbler A², Logo M², and Martin EG³

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Treponema pallidum TP.NR TP.NR Negative for antibodies to Treponema pallidum Non-Reactive Result Treponema pallidum TP Positive for antibodies to Treponema pallidum TP.R Reactive Result Invalid result. Repeat test with a new device INV Invalid INV Call customer support if repeat run result is invalid

Note: The reader will turn off after approximately 50 seconds of inactivity. There is no active function to shut off the DPP[®] Micro Reader.

SYPHILIS HEALTH CHECK VS DPP® HIV-SYP

Syphilis Health Check			DPP [®] HIV-Syphilis Assay System				
TP Results			TP Re	esults	HIV Results		
Positive	Negative	INTERPRETATION	Positive	Negative	Positive	Negative	
	100.0% (43/43)	Correctly Called Negative		97.7% (43/44)			
13.1% (20/153)		Correctly Called Positive TP	94.1% (143/152)				
	86.9% (133/153)	Missed a Positive TP		5.9% (9/152)			
Not applicable		Correctly Called Positive HIV			95.5% (21/22)		
Not applicable		Missed a Positive HIV				4.5% (1/22)	

SHC RT experienced monitors re-interpreted 28 SHC results (14.1%) as reactive compared to the operator visual read

The microreader used in the DPP assay re-interpreted 3/196 results (1.5%)

Invalid assays were not counted in the denominator

	SHC Results		DPP [®] Results						
	Syphilis Test Line		Syphilis Test Line			HIV Test Line			
Panel - Sample Description	Inv	Pos	Neg	Inv	Pos	Neg	Inv	Pos	Neg
¹ TP & HIV Non-Reactive	0	0	22	0	1	21	0	0	22
² TP Non-Reactive & HIV-1 Reactive	1	0	21	0	0	22	0	21	1
³ TP High Reactive (Syph G - 4.028) and HIV-1 Non-Reactive #1	0	1	21	0	19	3	0	0	22
³ TP Low Reactive (Syph G - 1.67) and HIV-1 Non-Reactive #1	1	9	12	1	21	0	1	0	21
³ TP Low Reactive (Syph G - 1.3418) and HIV-1 Non-Reactive #2	0	2	20	1	18	3	1	0	21
³ TP Low Reactive (Syph G - 0.9185) and HIV-1 Non-Reactive #3	0	0	22	0	22	0	0	0	22
³ TP Low Reactive (Syph G - 1.3023) and HIV-1 Non-Reactive #4	0	3	19	0	21	1	0	0	22
³ TP Low Reactive (Syph G - 0.95) and HIV-1 Non-Reactive #5	0	1	21	0	21	1	0	0	22
³ TP Low Reactive (Syph G - 1.92) and HIV-1 Non-Reactive #6	0	4	18	0	21	1	0	0	22
TOTALS	2	20	176	2	144	52	2	21	175

¹ HIV / TP / RPR non-reactive normal human plasma; ² HIV-1 antibody positive, TP non-reactive plasma ³ All TP specimens: Two sources: Medical Research Networx and Zeptometrix. All specimens TPPA positive and RPR reactive.

Syph G (specimen / cutoff ratio). HIV negative plasma. Inv = Invalid; Pos = Positive; Neg = Negative.

SURVEY RESULTS

Survey: Introduction of Experienced Rapid Testers to a New Multiplex Rapid Test¹

Survey Question	SHC	DPP [®] HIV-SYP	No Preference
Overall Rapid Test Experience	1.9	1.8	
Ease of Use and Ease Reading Test Results	2.4	1.1	
Clarity of Instructions if Test Is Invalid	1.4	2.0	
No Assistance Needed to Operate First Time	2.2	2.9	
Preference/Recommendation to Colleagues	18%	77%	5%

¹ Operators permitted to respond on a 1 (Strongly Agree) to a 5 (Strongly Disagree) basis

- Among respondents, 77% stated a preference for the multiplexed DPP[®] HIV-SYP product. The use of a digital reader to interpret results and the ability to detect both HIV and Treponemal antibodies simultaneously were key influencing factors.
- Read standardization with a microreader reduced the number of true positive results underread by newly trained operators. Rapid screening by both products was considered easy, although experienced monitors observing the test process identified errors ranging from incorrect addition or sequence of reagents. Easy to read instructions was viewed as critical for successful implementation in the field.



DISCUSSION

Multiplex testing has many potential distinct advantages:

- Improve diagnostic efficiency allowing one to test 2 or more biomarkers simultaneously
- Improve diagnostic precision By testing confirmatory biomarkers to generate a meaningful conclusion
- Reduces the diagnostic expense of a rapid screening event
- Reduces manufacturing costs
- Improves Rapid Test Operator productivity (tests/operator)

Why use a digital reader?

- Rapid tests are often used in rural settings under sub-optimal conditions including:
- Varying light conditions: low light to intense light
- Vision of rapid testers can range from Ted Williams sharp (20/5) to blind as a bat! Many testers in CLIA-waived settings are never tested for their visual acuity or potential color blindness
- Not all rapid tests produce sharp, defined lines
- Multiple lines on a rapid test cassette can be confusing
- A digital reader provides an engineered solution minimizing reporting errors and designed to:
 - Produce consistent lighting on every read event
 - Support multiple biomarkers on the same device without confusion
 - Reduce transcription errors by activating data transmission

CONCLUSIONS

Clarity of instruction, simplicity of test design, and the role of a standardized result interpretation were key features appreciated by operators.

Users strongly preferred the DPP[®] HIV-SYP to the SHC because of the ease of test interpretation and ability to simultaneously screen for two diseases.

Given the role of RTs in CLIA-waived settings, micro readers could significantly assist in reducing false interpretations.

REFERENCES

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