

HIV Testing Update

Estelle Piwowar-Manning MT (ASCP) SI HPTN LC Deputy Director, JHU Baltimore MD USA



Disclosure

- I have no financial disclosures and no financial interest in any of the companies mentioned
- The assays discussed are cleared by the US FDA
- Some slides were provided by Bio-Rad



General schema for HIV testing

Screening assay

High sensitivity

Lower cost

Confirmatory assay

High specificity May discriminate between HIV-1 and HIV-2 Higher cost



Introduction

- Current US CDC testing algorithm
- Evolution of HIV screening assays
- 4th generation screening assays (CMIA/EIA)
- 5th generation screening assays
- Confirmatory and discriminatory assays
- HIV testing at the HPTN LC



Evolution of HIV Screening Assays



1st Gen:

Viral lysate, IgG Ab detection **2nd Gen:**

Recombinant / synthetic peptides, HIV-1/-2 IgG Ab detection

3rd Gen:

Recombinant / synthetic peptides, HIV-1 Ab (groups M and O), IgG and IgM Ab detection

4th Gen:

3rd Gen assay design with HIV-1 p24 Ag detection

Increasing sensitivity



Current US CDC Testing Algorithm





4th Generation HIV Screening Assays US FDA Cleared





Architect HIV Ag/Ab Combo Test Abbott Diagnostics



Sample volume	150 uL initial, 350 uL with repeats
Time to result	<30 minutes
Throughput	100 samples / hour for the i1000 200 samples / hour for the i2000





GS HIV Combo Ag/Ag EIA Bio-Rad Laboratories



	Evolis	Manual
Sample volume	150 uL initial, 350 uL with repeats	75 uL initial, 225 uL with repeats
Time to result	180 minutes or 210 minutes	180 minutes
Throughput	87 samples or 174 samples / run	87 samples / run





ADVIA Centaur HIV Combo (CHIV) Assay Siemens Healthineers USA



Sample volume	100 uL initial, 300 uL with repeats
Time to result	<15 minutes
Throughput	180 samples / hour



5th Generation HIV Screening Assay US FDA Cleared





Bio-Rad 2200 HIV Ag-Ab Assay (Bio-Rad Laboratories)



Sample volume	350 uL initial, 700 uL with repeats
Time to result	<64 minutes
Throughput	84 samples / hour

BioPlex 2200 HIV Ag-Ab: Why"5th Generation Screening Assay

"5th Generation" BioPlex 2200 HIV Ag-Ab assay design

Simultaneously detects and reports a <u>screen</u> and <u>three individua</u>l HIV results:

HIV Ag-Ab Screen with HIV-1 p24 Ag HIV-1 Ab (Groups M & O) HIV-2 Ab

Includes HIV-1 and HIV-2 Ab Differentiation



HIV Ag-Ab Dyed Bead Mix

Assay Principle

- The BioPlex 2200 assay design allows for the simultaneous detection and identification of multiple HIV analytes for each sample processed.
- The bead reagent consists of a mixture of four distinct populations of dyed microparticle beads
- In addition to three internal quality beads (SVB, ISB and SNB) that assure quality results



Beads are combined into single "Bead Reagent" for multiplex analysis



Simultaneous Detection of Multiple HIV Analytes







Confirmatory / Discriminatory Assays US FDA Cleared



Discriminatory

Geenius HIV-1/HIV-2 Supplemental Assay (BioRad Laboratories)





Sample volume	5 uL serum or plasma, 15 uL whole blood
Time to result	20 minutes
Throughput	21 samples / hour

The Bio-Rad Multispot assay will be taken off of the market July – Dec 2016



Confirmatory

APTIMA HIV-1 RNA Qualitative Assay Hologic



Sample volume	500 uL
Time to result	6 hours
Throughput	90 tests / run
Sensitivity	30 copies/mL



Confirmatory – Off label

HIV-1 viral load assays Not FDA-cleared for HIV diagnosis



Sample volume	600-1000 uL
Time to result	8 hours
Throughput	92 tests / run
Sensitivity	20 to 40 copies/mL



HIV Testing in HPTN Trials

HIV testing algorithms for HPTN protocols are presented in the Study Specific Procedures (SSP) Manual. The algorithm for each protocol is determined by many factors, including:

- Target population (HIV+, HIV-, or both)
- Type of visit (e.g., screening, enrollment, follow-up, confirmation of seroconversion)
- Nature of the study intervention
- Study design (e.g., "real-world" vs. gold-standard)
- Site location / availability of specific assays



Quality Assurance / Quality Control Testing

The HPTN LC performs additional testing for Quality Control. The QAQC plan for HIV testing varies by protocol and includes:

- Confirmation of site test results
- Evaluation of discrepant / discordant / inconsistent results
- Confirmation of study endpoints (e.g., seroconversion events)
- Characterization of host responses to HIV infection in different settings (e.g., antibody maturation, viral load)



HPTN LC Research on HIV Testing

The HPTN LC also performs research related to HIV testing that includes:

- Evaluation of new diagnostic assays
- Evaluation of special testing protocols (e.g., for low volume samples)
- Evaluation of assay performance for samples from different clinical settings and regions with different prevalent subtypes
- Identification of factors that impact the host response to HIV infection and assay performance



ACKNOWLEDGEMENTS

The HIV Prevention Trials Network is sponsored by the National Institute of Allergy and Infectious Diseases, the National Institute of Mental Health, and the National Institute on Drug Abuse, all components of the U.S. National Institutes of Health.

The HPTN Laboratory Center is funded through UM1-AI068613.





Screening Visit





Follow-up Visits



4th Generation Assay: Adds detection of HIV-1 p24 antigen to the 3rd Generation design

- They detect HIV-1, Group O, and HIV-2 IgG and IgM antibodies
- They detect HIV-1 p24 antigen to improve HIV infection 'window' of detection about seven days earlier than third-generation tests

Limitations of 4th Gen:

- Their results are only 'Reactive' or 'Non-reactive' and <u>do not differentiate the analytes</u>
- Primary infection samples are detected but they <u>cannot distinguish from a late</u> <u>infection</u>
- HIV-2 reactive samples can <u>only be identified during confirmation (supplemental)</u> <u>testing</u>



- Due to the unique attributes (i.e., enhanced sensitivity for p24 and analyte differentiation) of the BioPlex 2200 HIV Ag-Ab test, Bio-Rad believe we should not diminish the assay by to referring to the test as simply a 4th generation HIV screening test.
- □ HIV 4th generation diagnostic screening tests on the market normally state in their intended use statement that their Ag-Ab test <u>does not</u> distinguish/differentiate between HIV-1 p24 Ag, HIV-1 Ab and HIV-2 Ab.
- □ The BioPlex 2200 HIV Ag-Ab test has this unique [first and only] (*i.e.*, screen with individual analyte reporting capability).



Excellent Overall Performance:

- Best Analytical Sensitivity for: HIV-1 p24 Ag LOD = 0.33 IU/mL, the best sensitivity for serological HIV screening on the market
- High Reproducibility: Total CV's of 4.5- 11.7%
- High Specificity: Low Risk Population- 99.86%

Differentiates Between HIV-1 and HIV-2 Ab:

 Capability to effectively differentiate HIV-1 from HIV-2 antibody reactive results from initial Ag-Ab Screen- 100% capability rate for <u>HIV-1</u> and 93.5% for <u>HIV-2</u>

Potentially Directs Supplemental (Confirmation) Testing:

 Knowing which analytes are detected (through differentiation) helps identify which supplemental tests to perform

Approved for Organ Donor Specimen Testing

Long specimen stability:

Up to four days at room temperature and seven days at 2-8°C



Customer Communication Requirement to Run HIV Ag-Ab Assay

Mandatory discussion with Customer/Operator:

Customer Notification PN 12000544RevA: "BioPlex 2200 Minimum Volumes For HIV Ag-Ab"



The document is LB000823A and can be ordered separately as <u>PN 12000544</u>

350 to 450 ul needed

- Minimum sample volume required for a single HIV Ag-Ab BioPlex test.
- Decreases likelihood of short samples as operator still should ensure that samples do not have foam/bubbles and are aligned in green (sample) rack properly.
- The HIV Ag-Ab kit uses 40uL per test (per RV), thus a 'Minimum Sample Volume Guide' has been created for the assay



HIV Ag-Ab Specimen Types

Specimen Type	Anticoagulant	Glass	Plastic
Serum	None	Х	Х
Serum-SST*	None	Х	Х
Plasma	Dipotassium (K_2) and Tripotassium (K_3) EDTA		Х
Plasma	Sodium Citrate (Do not use frozen Sodium Citrate samples)		Х
Plasma	Sodium Heparin		Х
Plasma	Lithium Heparin		Х
Plasma-PST**	Lithium Heparin		Х

*Serum Separator Tube; ** Plasma Separator Tube

Specimen preparation: Ensure specimens are thoroughly mixed and homogenous. Centrifuge specimens to remove gross particulate matter.

For frozen samples:

- Thaw samples completely,
- Mix thoroughly by inverting 10 times, or by vortexing,
- Continue to mix until samples are visibly homogenous,
- Centrifuge at > 10,000 RCF for 10 minutes,
- Avoid multiple freeze/thaw cycles (up to 4 cycles is acceptable).

HIV Ag-Ab Reagent Pack Specifications

Features	BioPlex 2200 HIV Ag-Ab Reagent Pack
Catalog Number	665-3455 (US/Can)
IFU Catalog Number	665-3465X (where X denotes latest version)
Number of Tests	200
Intended Use	Qualitative detection and differentiation of HIV-1 p24 antigen, antibodies to HIV-1 (Groups M and O) and HIV-2
Beads	Monoclonal antibody against HIV-1 p24 Ag, purified HIV-1/ HIV-2 antigen (recombinant protein or peptides), SVB, ISB and SNB
Sample Type	Serum or Plasma (K_2 or K_3 EDTA, Sodium or Lithium Heparin fresh Sodium Citrate)
Sample Volume*	40 μL (25 μL for testing + 15 μL for waste)
Sample (Specimen) Storage at 2-8°C	7 Days (4 Days @ Room Temperature)
Time to First Results	64 Minutes
Throughput	Up to 84 Samples per hour or 336 results per hour
Result Type	Qualitative with Index (IDX)
Reportable Range	0.00 – 200 IDX
Interpretation Composite Screen and Individual Analytes	Non-Reactive: < 1.00 IDX (for all analytes) REACTIVE: \geq 1.00 IDX (for at least one analyte)
Reactive Repeat	Run in duplicate: 2 out of 3 rule
Shelf Life	15 months at 2-8°C at launch 24 months at 2-8°C target
Open Pack Stability at 2-8°C	60 Days

* See " BioPlex 2200 Minimum Volume Guide For HIV Ag-Ab Assay" for more information

A BioPlex 2200 HIV Ag-Ab reagent pack reagents necessary to perform the HIV assays for 200 tests.

Three Internal Quality Beads:

NEW Quality Bead! <u>Signal</u> <u>Normalization Bead</u> (SNB). The SNB is designed to help normalize overall assay signals.

Serum Verification Bead (SVB) The SVB confirms presence of serum/plasma.

Internal Standard Bead (ISB) The ISB standardizes detector performance.

Note: The HIV Ag-Ab assay has very low nonspecific binding (NSB) which obviates the need for an RBB. The streptavidin PE binds only to the Biotin of Conjugate 1; and does not bind directly to any lgG.

>



Index (IDX)	Retest	Retest Result	Final Interpretation
< 1.00 IDX for all analytes	No	Not Applicable	Non-Reactive
≥ 1.00 IDX for at least one analyte	Yes (Must Retest In Duplicate)	Both retest results have an Index (IDX) < 1.00 for all analytes	Non-Reactive
		Index (IDX) of at least one retest result is ≥1.00 for the analyte(s) that was initially reactive	REACTIVE for HIV Ag-Ab <u>with</u> REACTIVE for HIV-1 Ag and/or REACTIVE for HIV-1 Ab and/or REACTIVE for HIV-2 Ab or REACTIVE, Undifferentiated

<u>REQUIREMENT (US Only)</u>: When testing with the BioPlex 2200 HIV Ag-Ab assay, all of the

individual HIV analytes (HIV-1 Ab, HIV-2 Ab, and HIV-1 p24 Ag) must be reported.

Note: The BCM/software <u>will not</u> automatically re-order (add to the Worklist) the retest of the 'reactive' result. It is up to the operator, LIS or middleware to do so.



Special Results Interpretation:

- If the Index for HIV-1 and/or HIV-2 Ab is ≥ 100 and the HIV-1 p24 Ag Index is ≥ 1.00, the HIV-1 p24 Ag results will state "Not reportable due to high HIV Ab level".
- If both HIV-1 Ab and HIV-2 are ≥ 1.00 and the Index ratio of HIV-1 Ab and HIV-2 Ab is < 5-fold, the result for HIV-1 and/or HIV-2 Ab is reported as "REACTIVE, Undifferentiated".
- If there is ≥ 5-fold difference in the Indices, the higher Ab is reported as REACTIVE and lower Ab is reported as Non-Reactive.



BioPlex 2200 HIV-1 Ag p24 LOD= 0.33 IU/mL or 5.2 pg/mL

Analytical Sensitivity

BioPlex 2200 HIV Ag-Ab: HIV-1 p24 Sensitivity					
Stopdard	Standard Concentration Corresponding to Cut Off				
Standard	Lot 1	Lot 2	Lot 3	Average	
WHO (IU/mL)	0.35	0.29	0.35	0.33	
AFSSAPS (pg/mL)	5.4	5.0	5.2	5.2	



Specificity

• 6395 low risk samples tested

 First time blood donors, normal healthy individual, military recruits – fresh & frozen, pregnant women and healthy pediatric subjects

6367 were non-reactive

- 19 were confirmed positive by supplemental testing
- 9 were falsely reactive

BioPlex [®] 2200 HIV Ag-Ab: Specificity						
Sample Status	HIV Ag-Ab (Composite of All Assays)	HIV-1 Ab	HIV-2 p24 Ag	HIV-2 Ab		
True Negative	6367					
False Positive*	9	7	6	2		
Confirmed Positive	19					
% Specificity	Specificity 99.86 (95% CI 99.73-99.93)					
*False Positive reactivity may occur on more than one assay bead for the same sample. Therefore, FP results among the different assay beads are not additive and counted only once						

In the HIV Ag-Ab composite result.



Sensitivity: Seroconversion Panels

In-house testing of 42 seroconversion panels whose package inserts include results for a reference 4th Generation manufacturer test were tested:

BioPlex 2200 HIV Ag-Ab: Reactivity in HIV-1 Seroconversion Panels BioPlex 2200 Seroconversion FDA-approved HIV-1 Ab Panels HIV Ag-Ab HIV-1 p24 Ag HIV Ag/Ab assay Total Reactive Bleeds 214140 133 205Total Reactive Panels 42 42 39 39 # of Panels More 7 (16.7%) 1 (2.4%) Sensitive



HIV Subtypes: General Information

□ HIV-1 exists as three different groups:

Groups O and P are extremely rare, while Group M is by far the dominant form

The most common form of HIV is the "B" subtype of HIV-1 group M worldwide:

Represents nearly half of all HIV infections worldwide and is the most common form in many areas including North America and Western Europe

However, HIV-1 infections in many areas involve non-B forms

Therefore, more and more non-B HIV-1 infections will be encountered in the US and Western Europe as people continue to travel and to relocate

Failure to detect HIV-1 p24 Ag from non-B forms risks missing early infection samples and failure to detect non-B Ab risks missing early and even late infections



Sensitivity: HIV-1 Subtype Sera

216 antibody positive samples representing 19 subtypes and CRFs* were tested

□ <u>All</u> were 'Reactive' on the BioPlex HIV Ag-Ab assay

BioPlex® 2200 HIV Ag-Ab: HIV-1 group M Antibody Subtypes								
HIV-1 Ab Subtype	# Tested	# Reactive	HIV-1 Ab Subtype	# Tested	# Reactive			
А	29	29	CRF13	7	7			
В	4	4	D	16	16			
с	5	5	F	20	20			
CRF01	11	11	G	16	16			
CRF02	77	77	Н	7	7			
CRF05	1	1	J	2	2			
CRF06	3	3	к	3	3			
CRF07	1	1	U	1	1			
CRF09	2	2	Unknown	1	1			
CRF11	10	10						

The Following Table Describes the Performance of the HIV Ag-Ab kit with HIV-1 Group M Subtypes:

CRF= circulating recombinant forms



Sensitivity: HIV-1 p24 Ag Subtypes

54 cell culture supernatants of various subtypes (52-group M; 2-group O) <u>All</u> were 'Reactive' on the BioPlex HIV Ag-Ab assay

HIV-1 p24 Subtype	# Tested	# Reactive	
A	3	3	
CRF01_AE	10	10	
CRF01 AG	2	2	
В	13	13	
C	8	8	
D	3	3	
F	5	5	
G	4	4	
Н	1	1	
J	2	2	
N	1	1	

The Following Table Describes the Performance of the HIV Ag-Ab kit with HIV-1 p24 Subtypes:



BioPlex 2200 HIV Ag-Ab Assay

HIV-1 Ab: 100% Differentiation Rate (1742/1742)

HIV-2 Ab: 93.5% Differentiation Rate (187/200)

BioPlex 2200 HIV Ag-Ab: HIV-1/HIV-2 Differentiation								
	BioPlex 2200 HIV Ag-Ab Result							
Population	HIV-1 Ab	HIV-2 Ab	HIV Ab Reactive,	% Differentiation				
	Reactive	Reactive	Undifferentiated	Capability				
HIV-1 Known Positive	1742	0	0	100				
HIV-2 Known Positive	0	187	13	93.5				



Organ Donor Samples (Sensitivity and Specificity)







BioPlex 2200 HIV Ag-Ab Assay Summary



- Independent measurements of antibodies and antigen
- Differentiates HIV-1 and HIV-2
- Detects and reports individual analytes

✓ Distinguishes early infection (acute/primary HIV-1)
✓ Potentially directs follow up (supplemental) testing



Q: How many analytes are in the assay kit?

A: The BioPlex 2200 HIV Ag-Ab assay has four (4) analytes:

HIV-1 Ab (group M) HIV-1 Ab (group O) HIV-2 Ab HIV-1 p24 Ag

The HIV-1 Ab results (groups M and O) are combined to give a single composite result.

The HIV Ag-Ab overall result uses the HIV-1 Ab composite result plus HIV-2 Ab and HIV-1 p24 Ag results to give a single result.

Q: What are the HIV Ag-Ab reportable results?

A: The kit reports the following for each sample:

HIV Ag-Ab (overall result of all assays below) with HIV-1 Ab (composite result of HIV-1 group M and O assays) HIV-2 Ab HIV-1 p24 Ag

Q: Why do you call it a 5th generation assay?

- A: The "5th generation" nomenclature is being used to signify the advancement of 4th generation assays that can differentiate HIV-1 p24 Antigen from Antibody(s). The BioPlex 2200 HIV Ag-Ab assay has the unique ability to differentiate HIV-1 p24 Ag, HIV-1 Ab and HIV-2 Ab; the first of its kind according to the FDA.
- Q: Why are the group M and O results not individually reported?
- A: Even though they are individually calibrated and controlled, there is too much cross talk (cross reactivity) between the beads to accurately distinguish between the two results. Hence, the system uses an algorithm of the 2 results to give a single HIV-1 Ab result.



FAQs

Q: Can the 3 individual results be reported without the overall result?

- A: No. Per the FDA, all results must be reported. In SW v4.2 release, a Test Group can be created under Setup, Test Group Setup to create a specific group to automatically order and report all assays. In SW v4.3 reporting of all results will be enforced and a Test Group is no longer recommended / needed.
- Q: How can you report the individual assay results from the overall HIV Ag-Ab result?
- A: All assays are to be resulted and reported. However, when an HIV Ag-Ab overall result is non-reactive, only the HIV Ag-Ab overall result is required to be reported. If an HIV Ag-Ab overall result is repeatedly REACTIVE, all individual results must be reported. At the very least, the individual(s) REACTIVE result should be reported. This is enforced in SW v4.3 and needs to be mitigated in SW v4.2.

Q: How many IQ beads are in the HIV Ag-Ab assay?

A: There are 3 IQ beads – Serum Verification Bead (SVB), Internal Standard Bead (ISB), and Signal Normalization Bead (SNB). There is no Reagent Blank Bead (RBB).

Q: Why is there not an RBB?

A: The HIV assay has very low non-specific binding which obviates the need for a RBB. Review the assay principle section. Notice the streptavidin PE binds only to the Biotin of Conjugate 1; and does not bind directly to any IgG.

Q: What do I tell my customer when they ask why RBB adds value to other kits and not HIV?

A: Best practices for IQ beads are evaluated on a product by product basis, and it was determined that inclusion solely of SVB, ISB and SNB would provide a more robust test kit. Bio-Rad R&D data supports the use of the RBB in other assays.



BIOPLEX 2200 SYSTEM

Q: What does the SNB do?

A: Signal Normalization Bead (SNB) serves two functions:

- It is used to normalize assay signals into a fluorescence ratio (FR) controlling for minor RV processing and sample matrix variations
- It prevents results from being reported if there are major RV processing errors or large sample matrix affects by comparing the SNB signal of each RV to the calibration SNB signal

Q: What is the dead volume requirement to run the kit?

A: The sample volume required to run the assay is 40 μL. However, the minimum volume requirements will vary by tube size. A Minimum Volume for HIV Ag-Ab Assay Guide is available for reference: PN 12000544.

Q: What are the reported units and nomenclature?

A: Index Values – IDX. Reactive and Non-Reactive. There is no Gray Zone result (it is only available OUS).

NOTE: All initial reactive results must be repeated in duplicate.

Q: Are International Standards available?

- A: No. There are no known international standards at this time. However, to calculate the Limit of Detection (analytical sensitivity) two know standards were used: WHO and French ANSM.
- Q: Once a kit is opened, how long is it stable?
- A: As long as the kit is stored appropriately at 2-8°C, the open kit is stable for 60 days. Calibrators have 30 days open vials stability and controls have 60 days when stored at 2-8°C.

Q: Can I test both serum and plasma samples in these assays?

A: Yes, the BioPlex 2200 HIV Ag-Ab assay has been validated for use with serum or plasma. There are exceptions to plasma. See Supported Specimen Type and Handling section for details.

BIO RAD



- Q: Can I use Serum Separator Tubes (SST) or Plasma Separator Tubes (PST) for samples?
- A: Yes, the BioPlex 2200 HIV Ag-Ab assay has been validated for use with SST and lithium heparin PST.
- Q: Can I use serum samples for organ donor testing?
- A: No, the BioPlex 2200 HIV Ag-Ab assay has only been validated for use with plasma.
- Q: How do the BioPlex 2200 HIV Ag-Ab assays handle the prozone effect?
- A: Prozone only affects 1-step assays and the HIV assays are 2-step indirect assays with a wash step.
- Q: What is the real throughput of the BioPlex 2200 HIV Ag-Ab kit?
- A: 84 Samples per hour and approximately 60 minutes to first result.
- Q: How do I explain the differences between the IDD GS HIV Combo EIA kit and the BioPlex HIV Ag-Ab kit?
- A: The best way to describe the difference is in the technology that is used. The GS HIV Combo is done on a microtiter plate enzyme immunoassay (EIA), while the BioPlex is done using a multiplex flow immunoassay methodology. The assay methodology greatly resembles traditional EIA, but permits simultaneous detection and identification of assay. In addition, there are some subtle variations in some of the antigens / antibodies used, as well as differences in the conjugates and label (read via fluorescence).





Q: What is the carryover of the assay?

- A: There is minimal carryover: ≤ 1 part per million (ppm). This translates into ≤ 0.1 Index value difference. An OUS white paper is available to summarize the information. In addition, a carryover procedure is now available to help labs determine their own carryover. See LB001328.
- Q: Can I program the BioPlex System to automatically reflex to the individual results from a reactive HIV Ag-Ab result?
- A: In SW v4.2, this must be mitigated and can be done by creation of a Test Group. In SW v4.3, this will automatically be done with each order.
- Q: What 3rd party HIV panel should I recommend to my customers?
- A: Various commercially available panels can be used with the HIV Ag-Ab that will demonstrate its ability to detect earlier seroconversions than competitive products. See Sales Tools, section 7.3.
- Q: Where does the HIV Ag-Ab assay fit in the current CDC HIV testing algorithm?
- A: The HIV Ag-Ab assay is intended to be used at the beginning or first portion of the algorithm. That is, it falls under the category of HIV-1/2 antigen / antibody combination immunoassay. See US HIV Testing Algorithm, section 8.3.
- Q: What do I say if my customers say they won't run the Geenius or other antibody differentiation supplemental assay?
- A: CDC published in June 2014 the Laboratory Testing Algorithm for the Diagnosis of HIV Infection. Customers should follow the recommendations as outlined in the document, where supplemental testing should follow every repeatedly reactive diagnostic "combo" test. The HIV Ag-Ab assay is not designed to be a supplemental assay and is not labeled as such. Customers would be using our product off-label should they choose to ignore our intended use statement and CDC testing guidelines.

