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# Update on HIV Diagnostic Technologies

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The findings and conclusions in this presentation are those of the author and do not necessarily represent the views of the Centers for Disease Control and Prevention



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# MORBIDITY AND MORTALITY WEEKLY REPORT

## *Recommendations and Reports*

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# Interpretation and Use of the Western Blot Assay for Serodiagnosis of Human Immunodeficiency Virus Type 1 Infections



# Diagnostic Algorithm: 1989

- The Public Health Service recommends that no positive test results be given to clients/patients until a screening test has been repeatedly reactive (i.e., greater than or equal to two tests) on the same specimen and a supplemental, more specific test such as the Western blot has been used to validate those results





## 1989 Almanac

- Berlin Wall dismantled
- Tiananmen Square
- Exxon Valdez
- U.S. invades Panama

# MNWR™

MORBIDITY AND MORTALITY WEEKLY REPORT

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- 211 Update: HIV Counseling and Testing Using Rapid Tests — United States, 1995
- 215 Strategies for Providing Follow-Up and Treatment Services in the National Breast and Cervical Cancer Early Detection Program — United States, 1997
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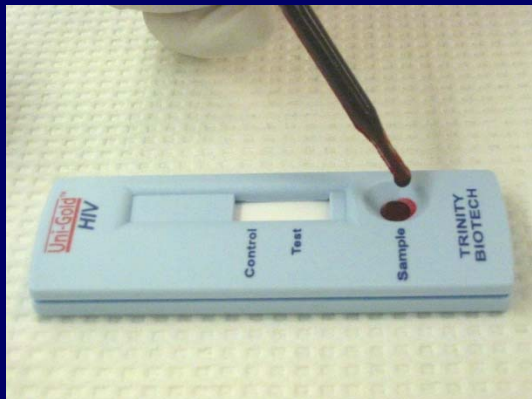
## Update: HIV Counseling and Testing Using Rapid Tests — United States, 1995

Approximately 25 million persons each year in the United States are tested for antibody to human immunodeficiency virus (HIV). Publicly funded counseling and testing (CT) programs conduct approximately 2.5 million of these tests each year. CT can have important prevention benefits (1); however, in 1995, 25% of persons testing HIV-positive and 33% of persons testing HIV-negative at publicly funded clinics did not return for their test results (2). Rapid tests to detect HIV antibody can be performed in an average of 10 minutes (3), enabling health-care providers to supply definitive

# Recommendation ...and a Promise

- Health-care providers should provide preliminary positive test results before confirmatory results are available in situations where tested persons benefit.
- When additional rapid tests become available for use in the United States, the PHS will re-evaluate algorithms using specific combinations of two or more rapid tests for screening and confirming HIV infection.





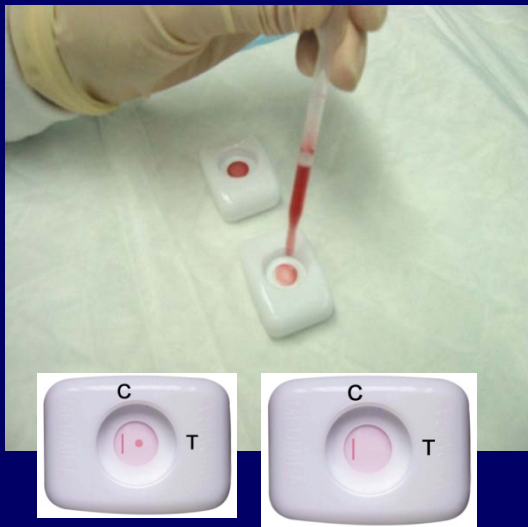
**Uni-Gold Recombigen**



**Multispot HIV-1/HIV-2**



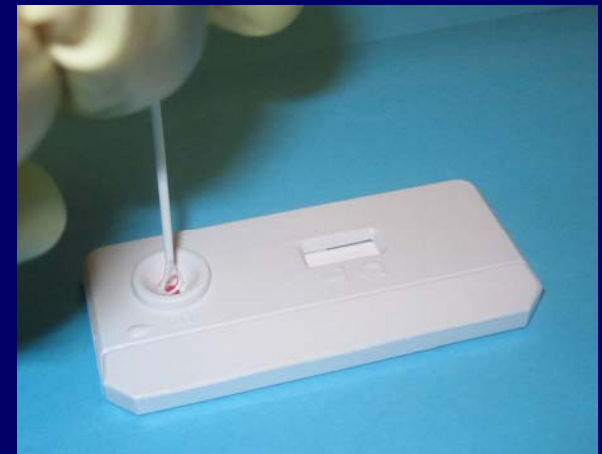
**Clearview Complete HIV 1/2**



**Reveal G3**

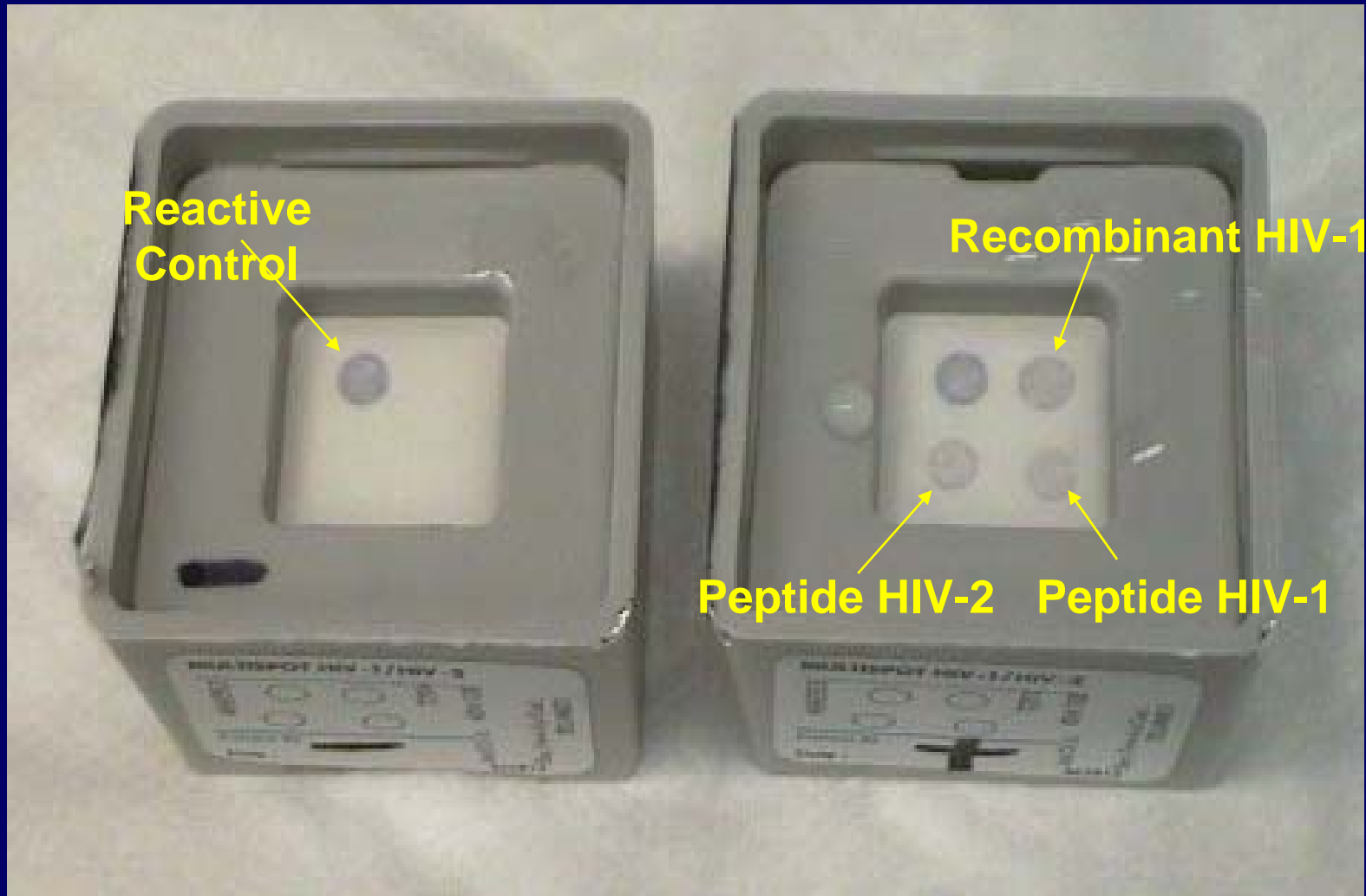


**OraQuick Advance**



**Clearview HIV 1/2 Stat Pak**

# Multispot: Differentiates HIV-1 from HIV-2





# FDA-Approved Rapid HIV Tests

Sensitivity  
(95% C.I.)

Specificity  
(95% C.I.)

## Oral fluid

OraQuick Advance

99.3 (98.4 - 99.7)

99.8 (99.6-99.9)

## Whole blood

Un-Gold Recombigen

100 (99.5 - 100)

99.7 (99.0 - 100)

Clearview Stat-Pak

99.7 (98.9 - 100)

99.9 (98.6 - 100)

Clearview Complete

99.7 (98.9 - 100)

99.9 (98.6 - 100)

## Serum/plasma

Reveal G3

99.8 (99.2 - 100)

99.9 (98.6 - 100)

Multispot

100 (99.9 - 100)

99.9 (99.8 - 100)



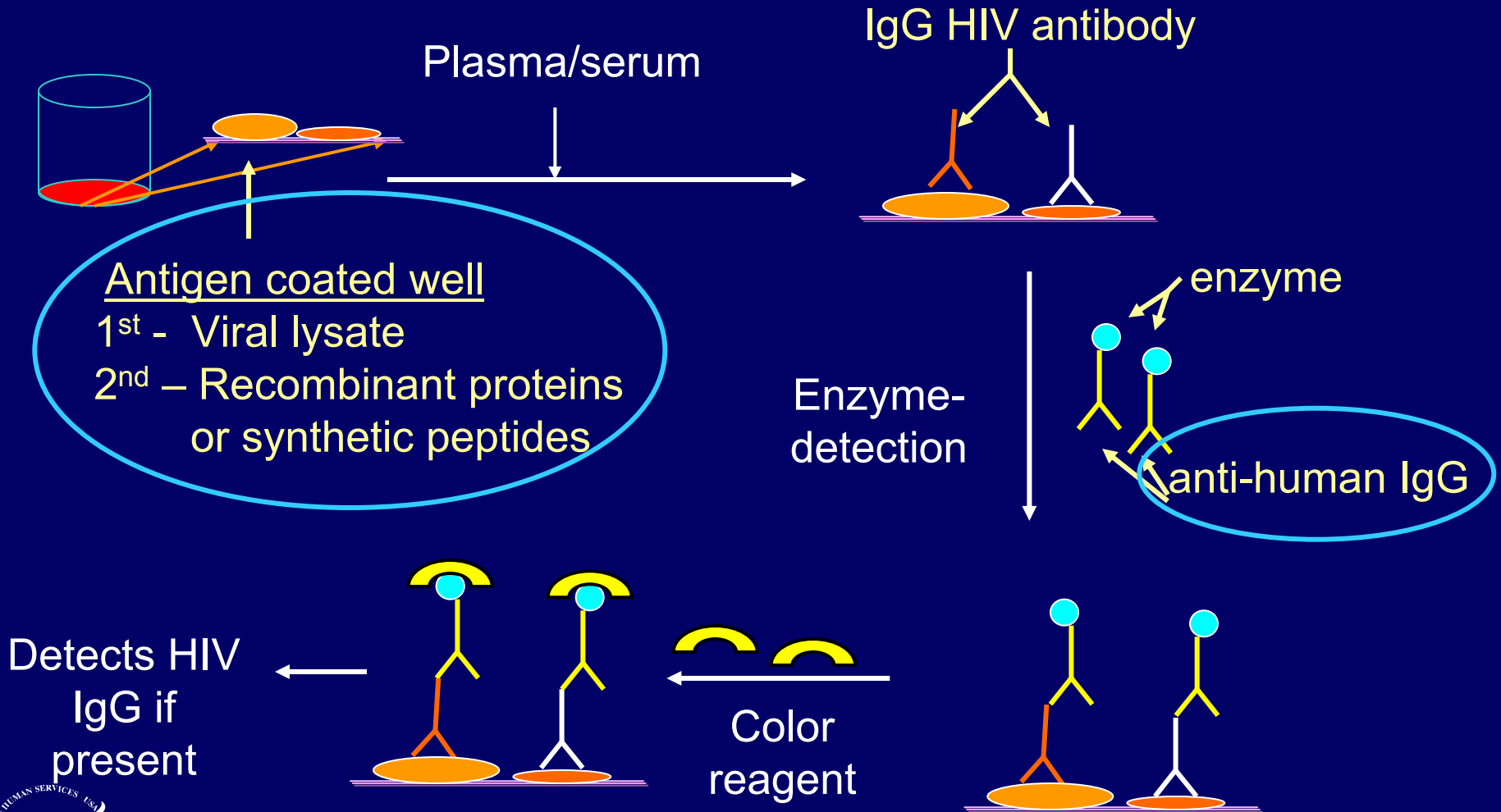
# Process for Developing New HIV Testing Algorithms

- APHL/CDC HIV Algorithm Workgroups
  - Point of care (POC)
  - Laboratory
- Data gathering –retrospective and prospective
- Proposed Algorithms available at

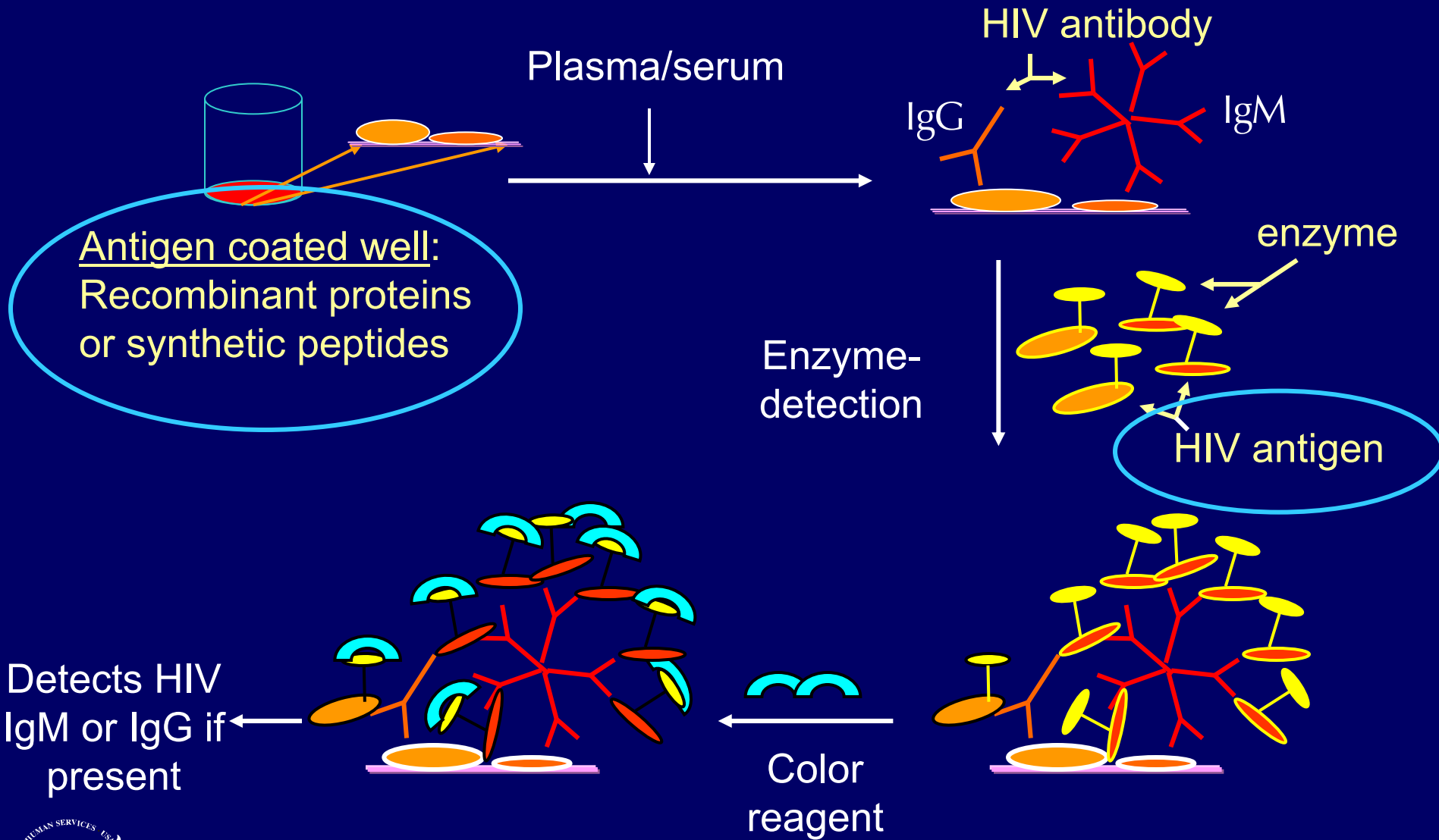
[www.hivtestingconference.org](http://www.hivtestingconference.org)



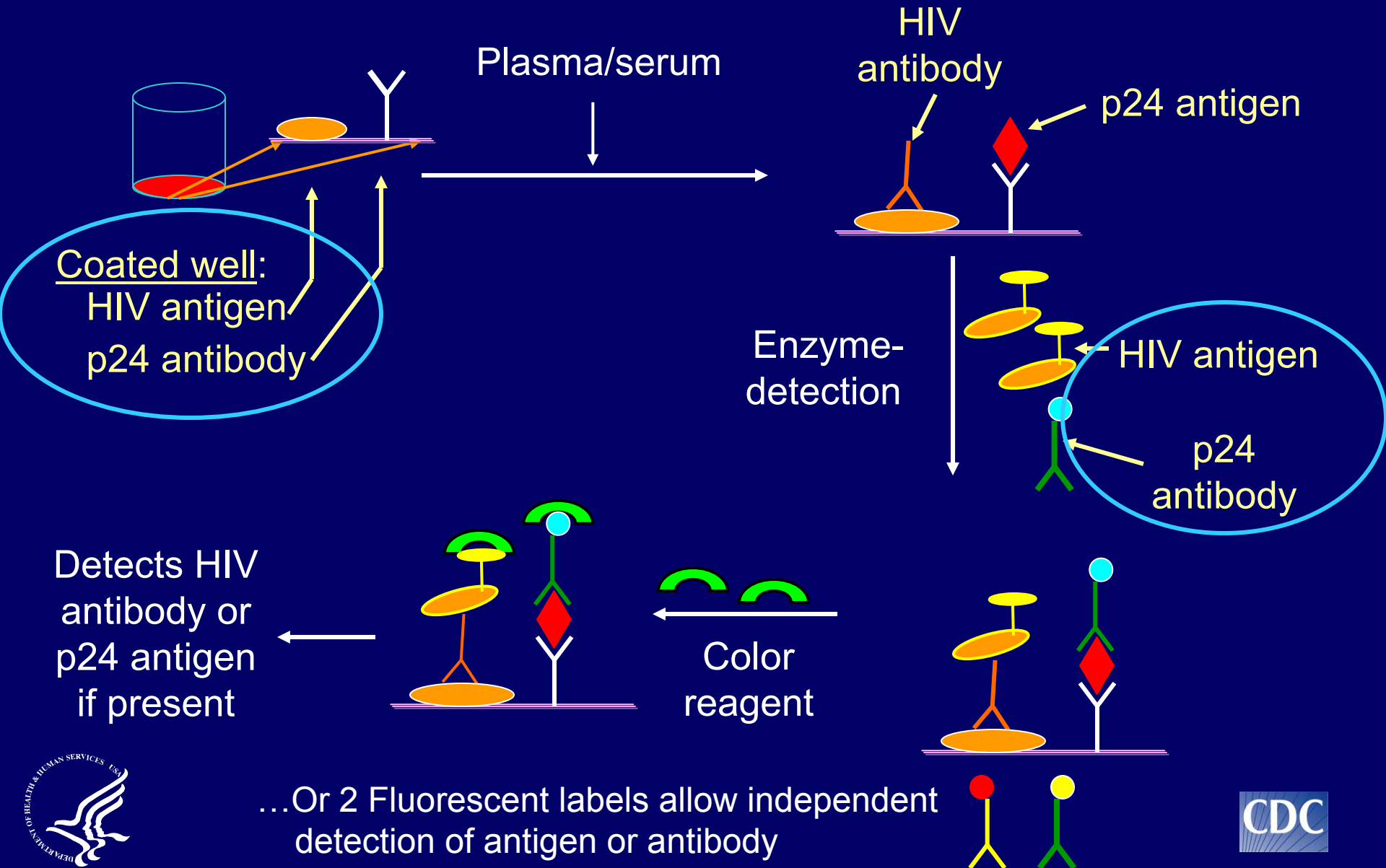
# 1<sup>st</sup> and 2<sup>nd</sup> Generation "Indirect" EIA



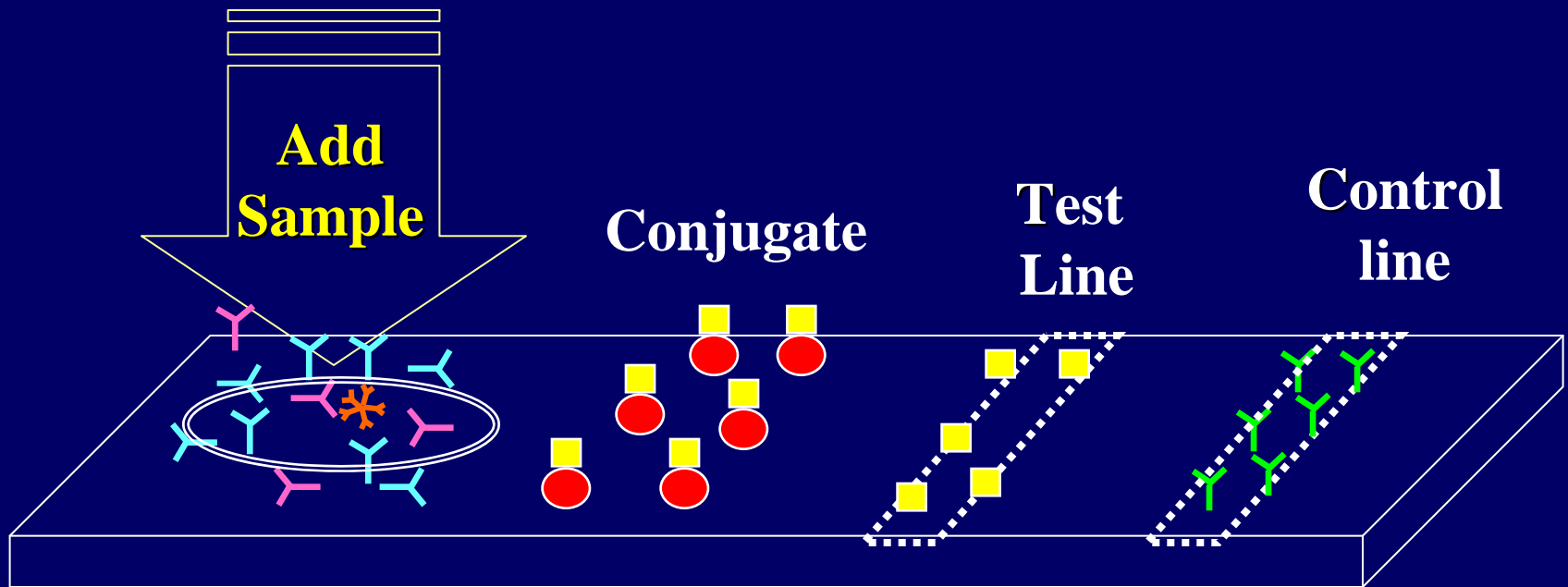
# 3<sup>rd</sup> Generation "Sandwich" EIA



# 4<sup>th</sup> Generation Combination EIA



# Rapid HIV Diagnostics: Lateral Flow Devices



**IgG anti-HIV**  
**IgG Antibodies**  
**IgM anti-HIV**



**Colloidal gold**  
conjugated to  
- **protein A**



**HIV antigen**

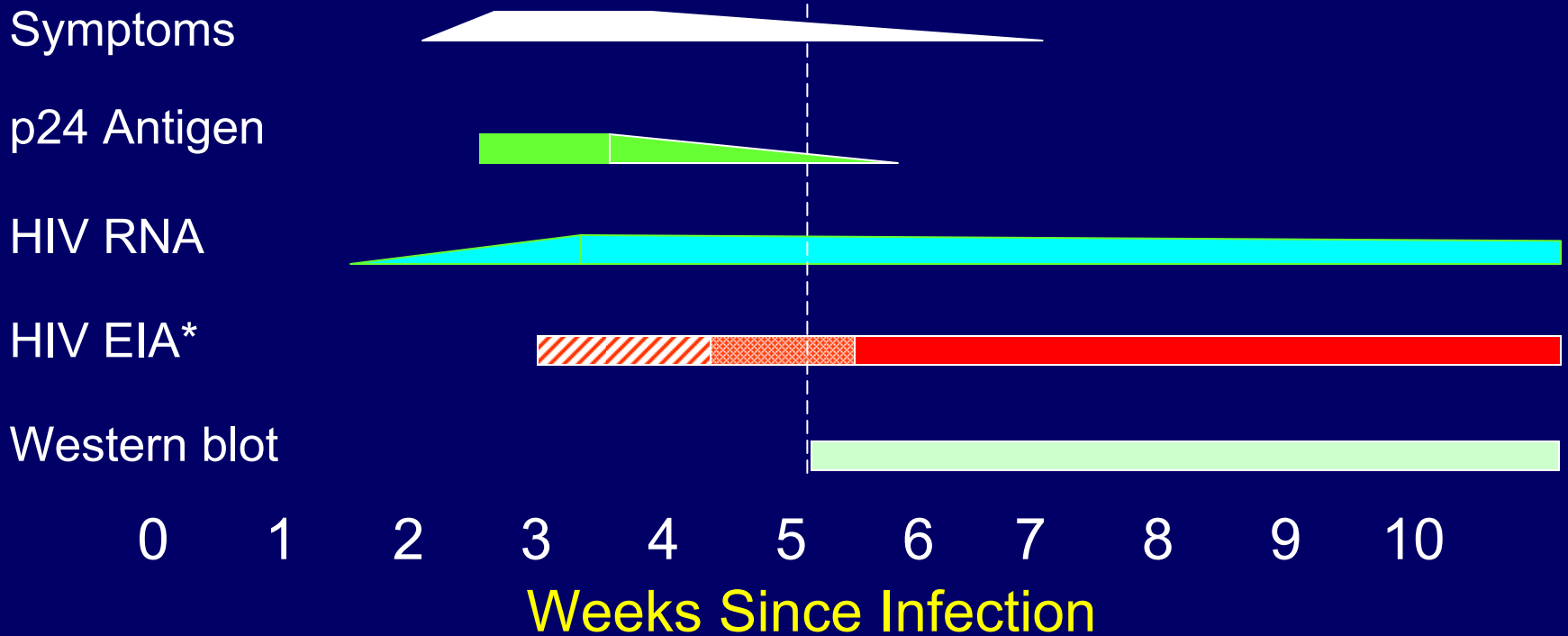


**Anti-IgG**  
**antibodies**

- **HIV antigen (*Unigold, Determine*)**



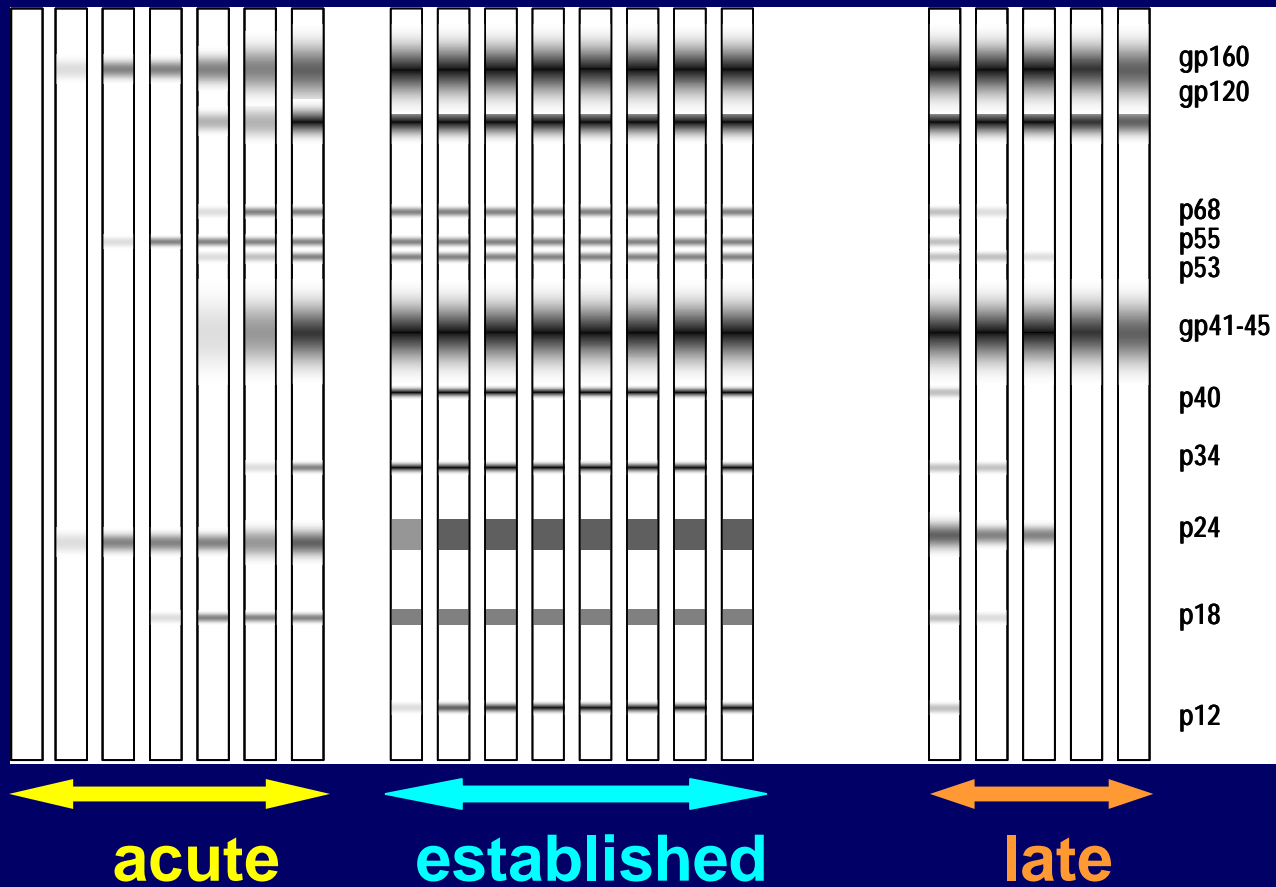
# Detection of HIV by Diagnostic Tests



-  \*3<sup>rd</sup> generation, IgM-sensitive EIA
-  \*2<sup>nd</sup> generation EIA
-  \*viral lysate EIA

After Fiebig et al, AIDS 2003;  
17(13):1871-9





1wk 2wk 3wk 6wk 2mo 6mo 1yr 2yr 3yr +8yr





# HIV Antigens in EIAs

Abbott HIVAB HIV-1/2	P24, Gp41, Gp120, Gp36
Genetic Systems rLAV	Viral lysate, Gp41
Gen Sys HIV-1/HIV-2 Plus O	P24, Gp160, Gp36, "O"
Siemens Advia HIV 1/0/2	P24, Gp41, Gp36
Ortho Vitros ECI	P24, Gp41, Gp120, Gp36

# HIV Antigens in Rapid Tests

OraQuick	Gp41, Gp36
Reveal	Gp41, Gp120, Gp36, Gp38
Unigold	Gp41, Gp120
Clearview Stat Pak*	Gp41, Gp120, Gp36
Clearview Complete*	Gp41, Gp120, Gp36
Multispot	sGp41, rGp41, Gp36
Determine	rGp41, sGp41, Gp120, Gp36

*\*Identical antigens*

# HIV Screening in Pregnant Women

- Rapid HIV testing of pregnant women in labor for whom no HIV test results are available;
- 7680 women screened
  - 54 (0.7%) new HIV infections identified
  - 6 false positive OraQuick tests, no false negatives
  - 15 false-positive EIAs: 7 p24 only, 8 WB negative
- Specificity: OraQuick 99.92%; EIA 99.80%
- Positive Predictive value: OraQuick 90%; EIA 76%

*Bulterys et al, JAMA July 2004*



# Indeterminate Western Blots

- 89 EIA RR, WB Indeterminate
  - 55 (62%) with p24
    - 4 with p24 seroconverted, all high risk
    - 0 low risk p24 patients seroconverted
- 168 uninfected, healthy vaccine trial volunteers
  - 52 (32%) EIA-neg, WB indeterminate
    - 24 (47%) with p24

- Celum et al, Arch Int Med 1994  
- Midthum et al, JID 1990



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# Diagnostic Assays Recently Approved by the FDA

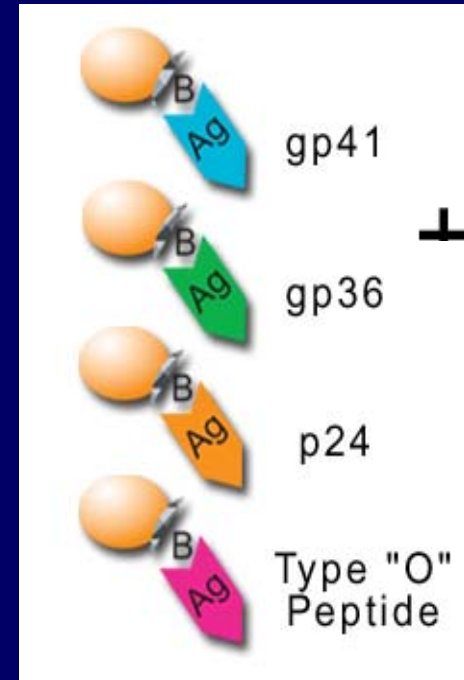


# The ADVIA<sup>®</sup> Centaur<sup>™</sup> Random Access HIV 1/O/2 Enhanced (EHIV)



# Siemens HIV 1/O/2 Enhanced (EHIV)

- 50  $\mu$ l specimen
- 3<sup>rd</sup> generation “sandwich” format
- Random access chemiluminescent immunoassay
- FDA-approved July 2006





On-board Refrigeration of 30 Different Assays







STAT sample requests without pausing  
Results in ~60 minutes

# Ortho VITROS ECI/ECiQ

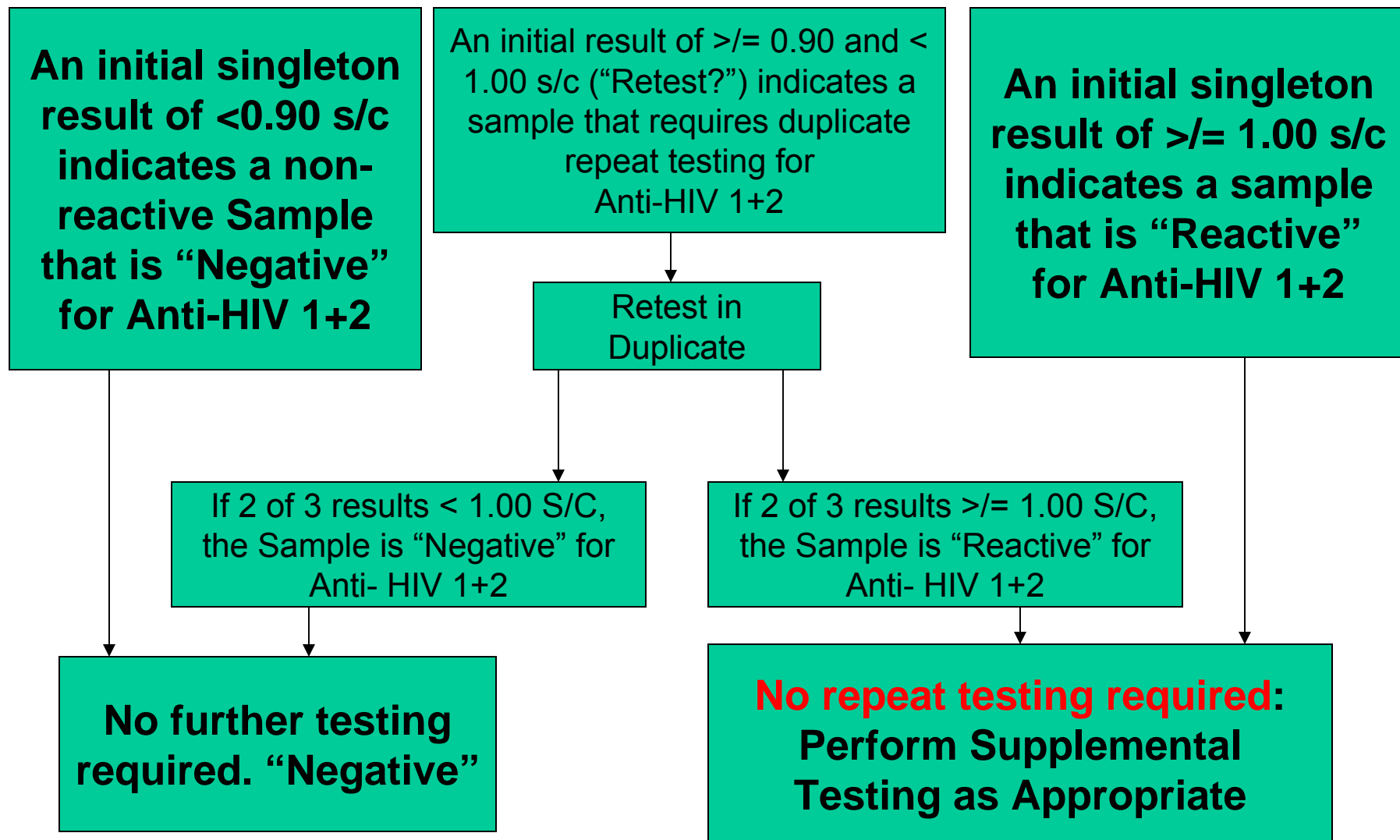


# Ortho VITROS Anti-HIV 1 + 2

- 80  $\mu$ l specimen, random access
- 3<sup>rd</sup> generation chemiluminescent immunoassay
  - **HIV 1 Env 13** - gp 120 and gp 41 region
  - **HIV-1 Env 10** - gp41 region which extends beyond the C-terminus of Env 13
  - **HIV-1 p24** - full length core protein of HIV-1
  - **HIV-2 Env AL** - region from gp 36 of HIV-2
- FDA approved March 2008



# Result Algorithm





# **APTIMA HIV-1 RNA Qualitative Assay**

**Gen-Probe Incorporated**

- **Target capture specimen processing**
- **Transcription-Mediated Amplification (TMA)**
- **Dual Kinetic Assay**
  
- **FDA approved September 2006**

# Qualitative RNA Assay: Intended Use

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- Aid to HIV-1 diagnosis
- Diagnosis of acute HIV-1 infection in antibody-negative persons
- Confirmation of HIV-1 infection in antibody-positive persons when it is reactive



# Clinical Syndrome of Acute HIV

- 40-90% develop symptoms of Acute HIV
- 50%-90% with symptoms seek medical care
- Of those diagnosed with Acute HIV, 50% of patients seen at least 3 times before diagnosis

- Kahn et al, NEJM 1998

- Weintrob et al, Arch Int Med 2003



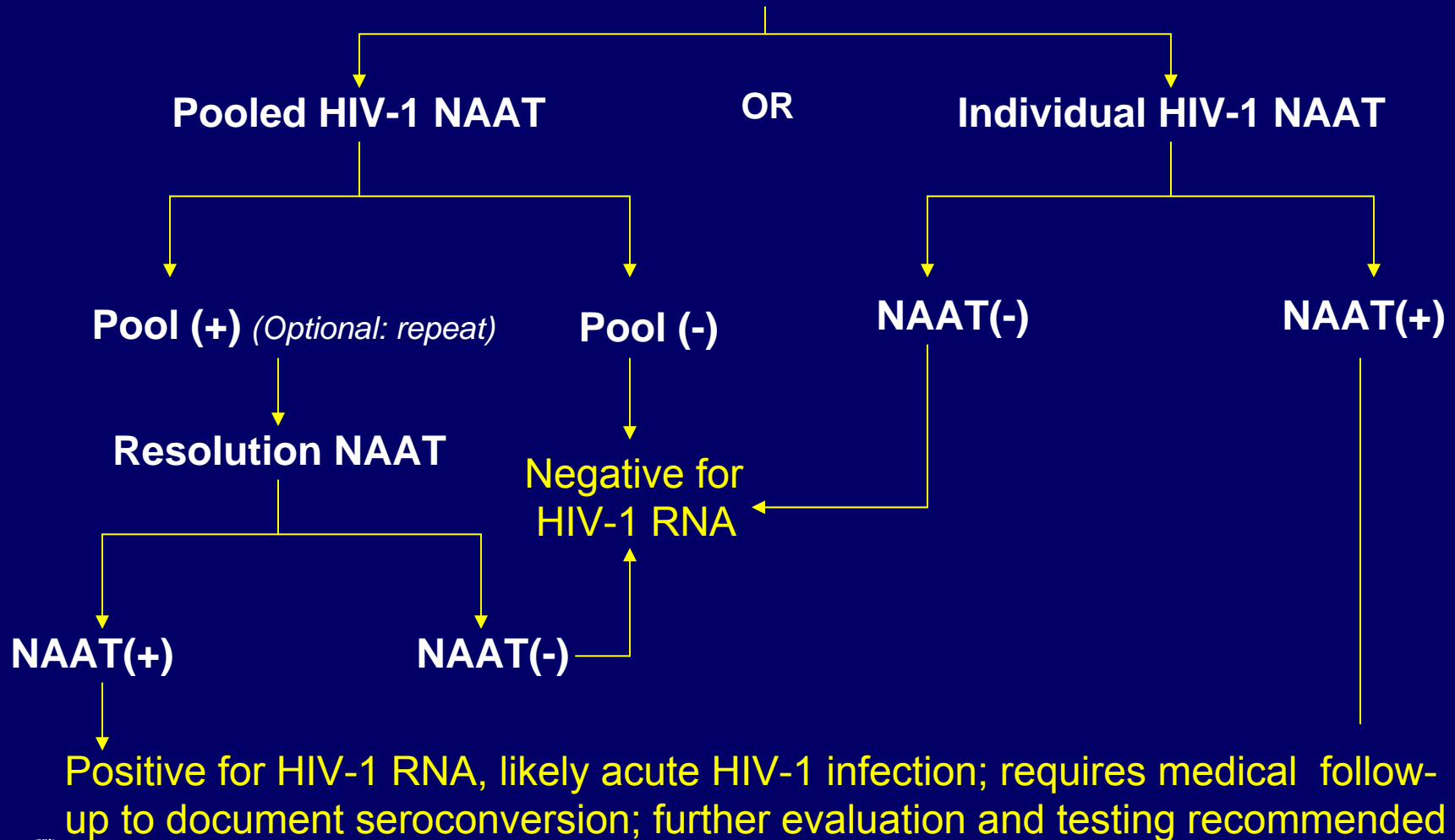
# Pooled RNA Screening for Early HIV Infection





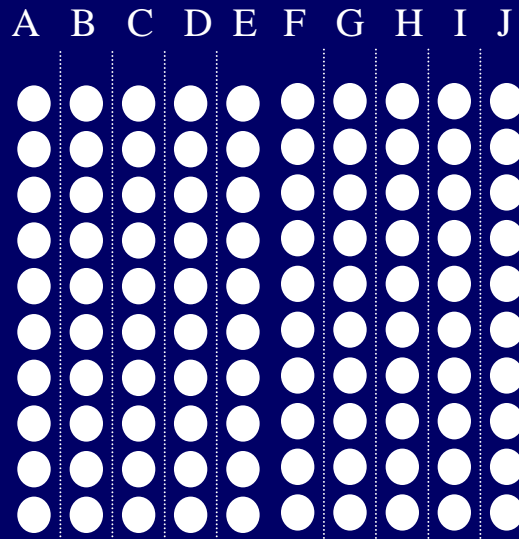
# Algorithm 4. Acute HIV Infection Testing

Non-reactive HIV-1 or HIV-1/2 Immunoassay

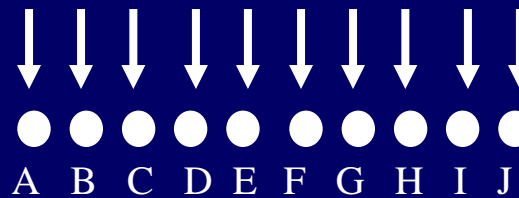


# Pooled NAAT Screening for Early HIV Infection

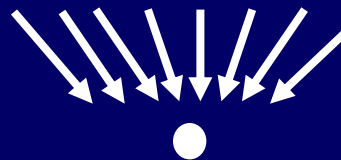
100  
Individual  
specimens  
(HIV antibody negative)



10 Pools of 10



1 Screening  
Pool

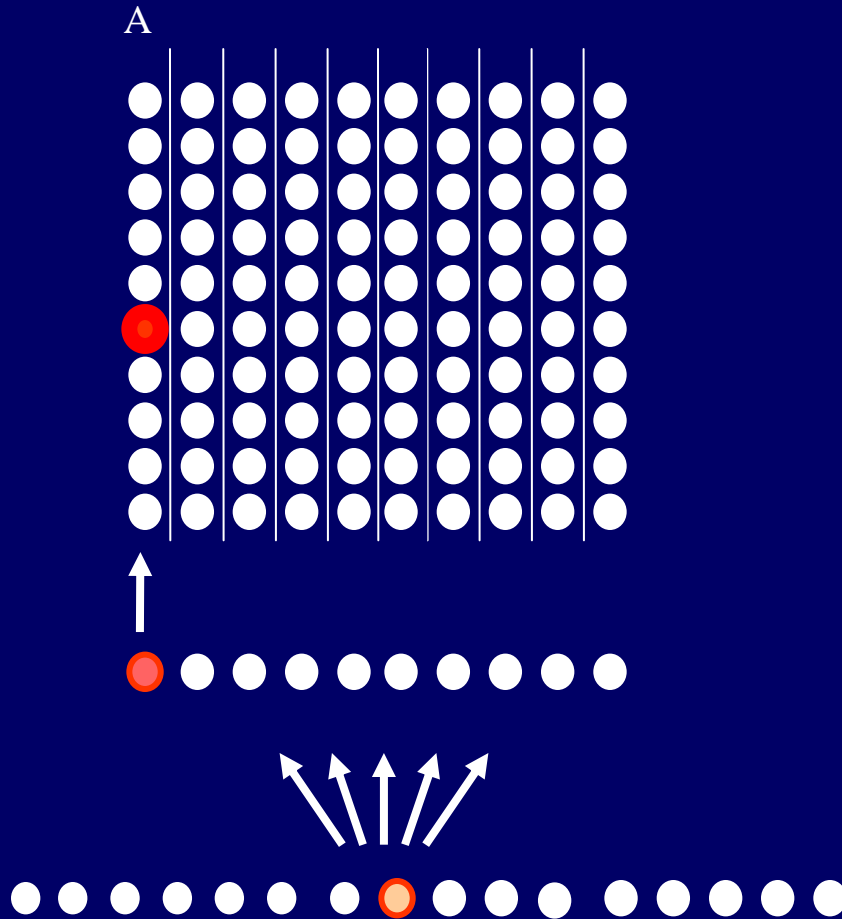


# Resolution Testing

Individual NAAT testing on 10 specimens

10 pools of 10 tested with NAAT

Screening Pools of 100 specimens tested with NAAT



# Yield from Pooled RNA Screening

<u>Site</u>	<u>Number tested</u>	<u>HIV Ab+</u>	<u>RNA+/ Ab-</u>
N.C. - 2003	109,250	583 (0.5%)*	23 (0.02%)

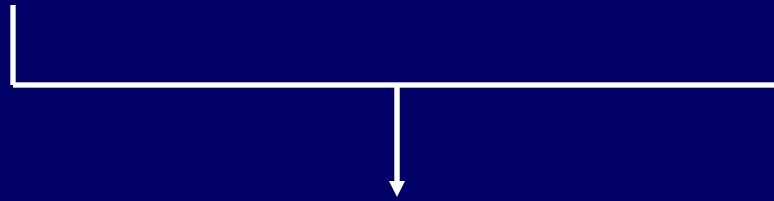
\*Screened with Vironostika EIA



# CDC AHI Study: Pooling Procedure

## 1-Stage Pooling

16 Specimens



1 Master Pool

# Yield from Pooled RNA Screening

<u>Site</u>	<u>Number tested</u>	<u>HIV Ab+</u>	<u>RNA+/ Ab-</u>
N.C. - 2003	109,250	583 (0.5%)*	23 (0.02%)
Florida - 2007	45,288	561 (1.2%) <sup>†</sup>	11 (0.02%)
L.A. - 2007	30,289	354 (1.2%)*	28 (0.09%)

\*Screened with Vironostika EIA

<sup>†</sup>Screened with Bio-Rad 1-2 Plus O



# Yield from Pooled RNA Screening

<u>Site</u>	<u>Number tested</u>	<u>HIV Ab+</u>	<u>RNA+/ Ab-</u>
N.C. - 2003	109,250	583 (0.5%)*	23 (0.02%)
Florida - 2007	45,288	561 (1.2%) <sup>†</sup>	11 (0.02%)
L.A. - 2007	30,289	354 (1.2%)*	28 (0.09%)
L.A. - 2007	30,289	366 (1.2%) <sup>†</sup>	16 (0.05%)

\*Screened with Vironostika EIA

<sup>†</sup>Screened with Bio-Rad 1-2 Plus O



# Yield from Targeted RNA Screening

<u>Site</u>	<u>Number tested</u>	<u>HIV Ab+</u>	<u>RNA+ / Ab-</u>
SFCC - 2004	3,789	125 (3.2%)	11 (0.3%)
L.A. - 2004	2,523	22 (0.9%)	1 (0.05%)
Atlanta - 2004	2,202	66 (2.9%)	4 (0.2%)
Seattle - 2005	3,525	81 (2.3%)	7 (0.2%)
SFCC-RT 2007	1,092	82 (7.5%)	11 (1.1%)



# Abbott Architect 4<sup>th</sup> generation EIA

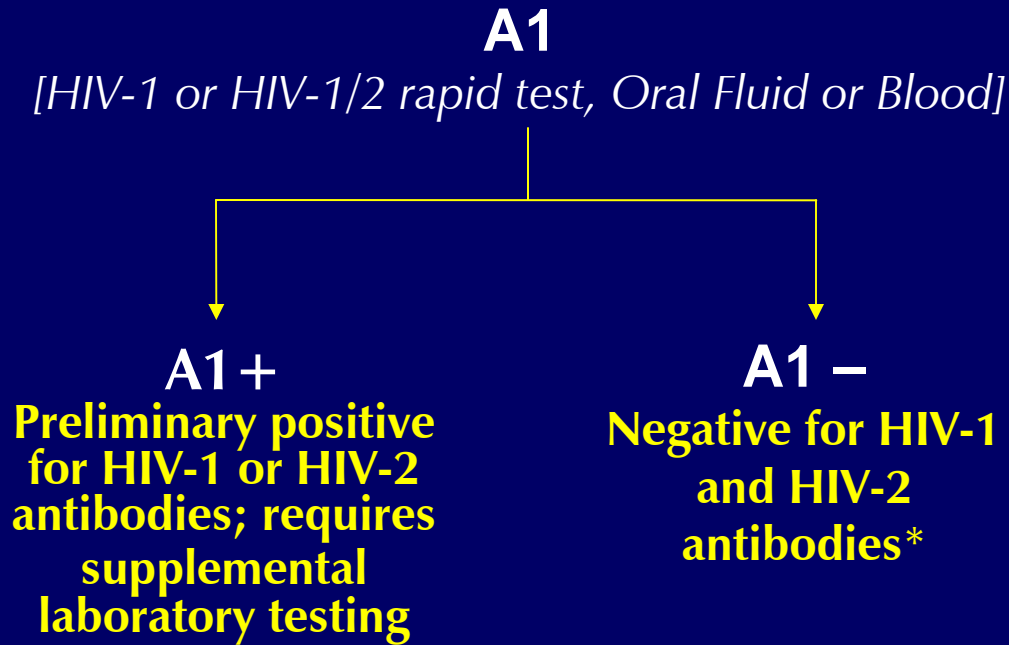


# 3<sup>rd</sup> vs. 4<sup>th</sup> generation HIV serology

	2005	2006	2007	<i>Total</i>
Newly identified HIV cases	289 (22,532)	230 (11,275)	250 (9,376)	769 (43,183)
<b>Total AHI cases</b>	<b>53</b> (18.3%)	<b>43*</b> (18.6%)	<b>30*</b> (12%)	<b>126</b> (16.3%)
3 <sup>rd</sup> generation EIA	35 (66%)	28 (67%)	17 (56.5%)	80 (63.2%)
4 <sup>th</sup> generation EIA	49 (92%)	42 (97.7%)	27 (90%)	118 (93.2%)

- Cunningham P, unpublished data, Australia

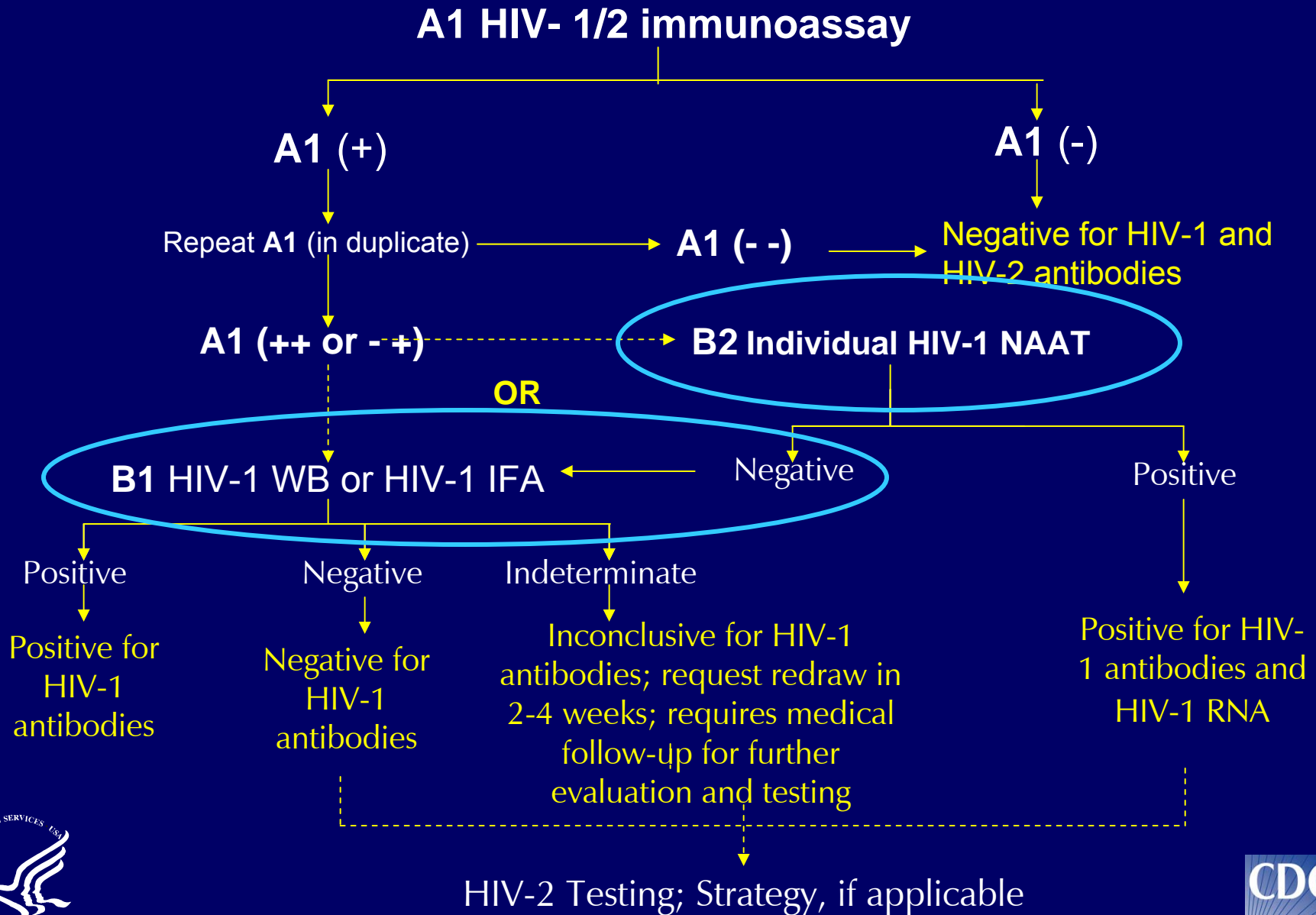
# POC Algorithm 1: Single Rapid Test for HIV Screening



\*If using an HIV-1 only rapid test, Negative for HIV-1 antibodies only



# Lab Algorithm 2: HIV-1/2 EIA/WB/IFA/NAAT



# CDC Alternative Algorithm Study

- Infected and uninfected U.S. blood donors: 997
  - 621 HIV+, 513 HIV-, 41 Indeterminate
- International: 178 total, 128 non-B subtypes
  - Blood donors: 64
  - CDC Cameroon study: 114
- Seroconversion panels:
  - 183 specimens from 15 pts
- HIV-2 specimens: 32

*Owen et al, J. Clin. Microbiol. doi:10.1128/JCM.02196-07 March 2008*



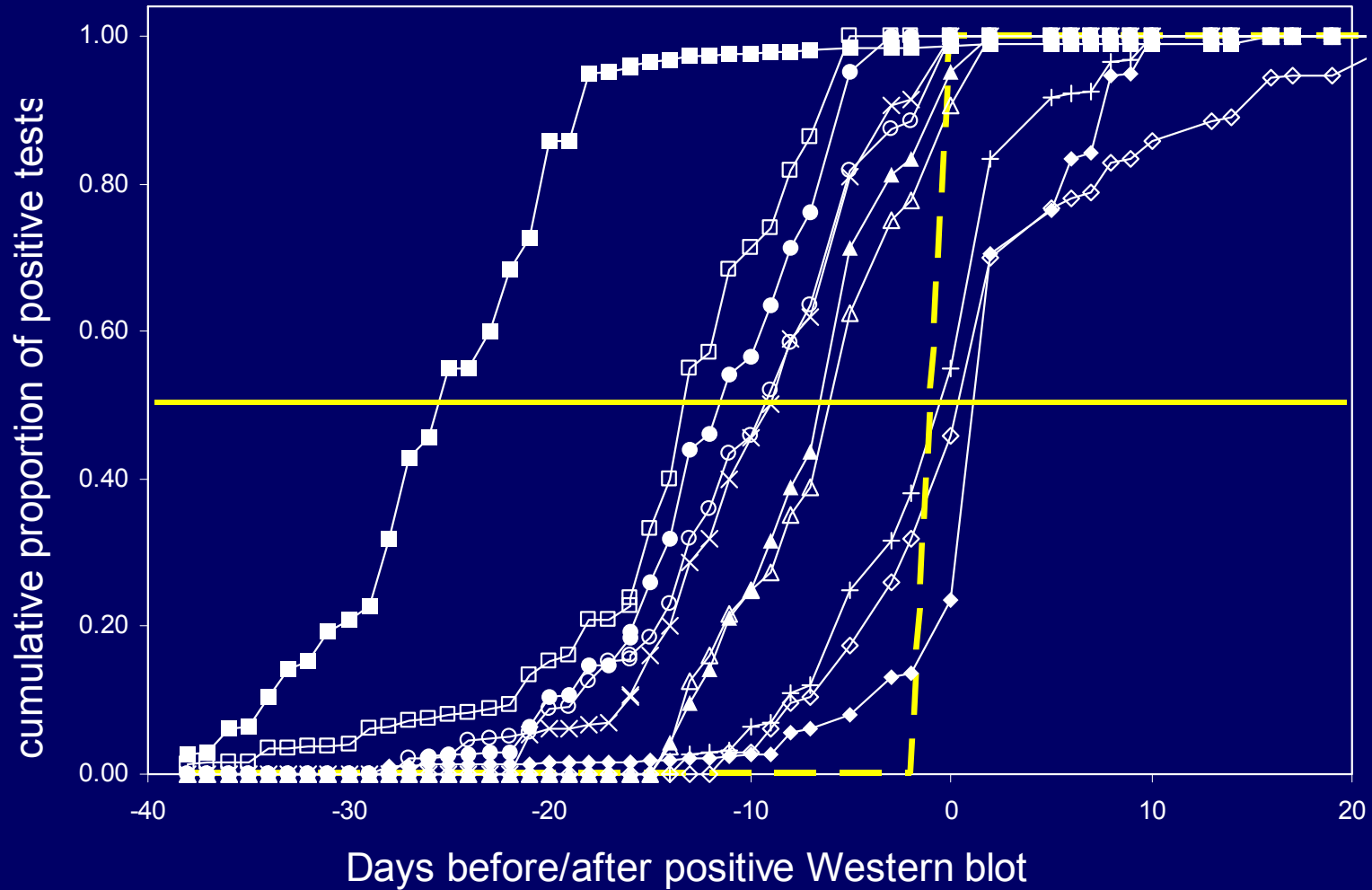
# CDC Alternative Algorithm Study

Test	621 HIV+, 513 HIV-	Sensitivity	Specificity
Genetic Systems HIV-1/2+O		99.8	99.4
Abbott rDNA		99.4	97.7
Vironostika HIV-1 + O		99.7	99.0
Genetic Systems HIV-1/2 peptide		98.7	99.8
Genetic Systems rLAV		97.4	100.0
Vironostika HIV-1 microelisa		99.0	98.4
Oraquick Advance		98.6	99.8
Reveal G2		99.0	99.8
Uni-Gold Recombigen		98.4	99.4
Procleix [ <i>Aptima</i> ]		97.4	99.6
CDC RNA		95.8	99.4
Ampliscreen		92.6	96.9

Owen et al, *J. Clin. Microbiol.* doi:10.1128/JCM.02196-07 March 2008



# Current Assays with 15 Seroconverter Panels

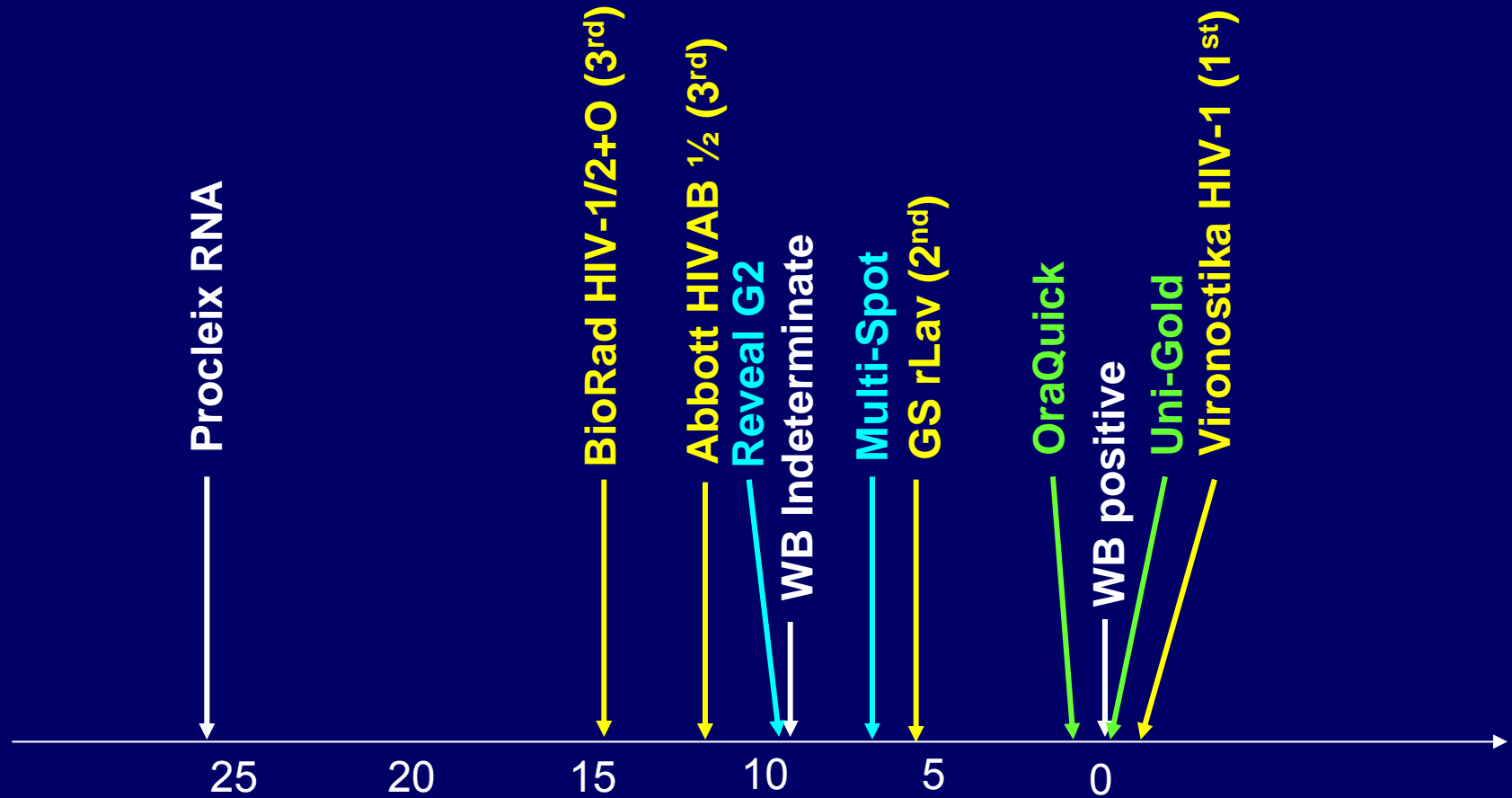


183 specimens from 15 seroconverters

Owen et al, *J. Clin. Microbiol.* doi:10.1128/JCM.02196-07 March 2008



# Current Assays with 15 Seroconverter Panels



Days before Western blot positive when 50% of Specimens Reactive

185 specimens from 15 seroconverters

Owen et al, *J. Clin. Microbiol.* doi:10.1128/JCM.02196-07 March 2008





/ironostika		Viral Load	HIV-1/2/O	UG	MS	OQ	SP
EIA Result	WB	copies/ml	EIA Result	RT	RT	RT	RT
NR	I	5,770	NR	NR	NR	NR	NR
NR	I	≥500,000	NR	NR	NR	NR	NR
NR	I	12,183	R	R	NR	NR	NR
NR	N	77	NR	NR	NR	NR	NR
NR	I	6,373	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	12,852	NR	NR	NR	NR	NR
NR	I	14,062	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	R	R
NR	N	3,921	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	NR	NR	NR
NR	N	≥500,000	NR	R	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	1,177	NR	NR	NR	NR	NR
NR	N	>500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	43,173	NR	NR	NR	NR	NR
NR	I	30,734	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	102,288	NR	NR	NR	NR	NR
NR	N	327,333	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	389,850	NR	NR	NR	NR	NR
NR	I	413,186	NR	R	R1	NR	NR
NR	I	446,770	NR	NR	NR	NR	NR
NR	N	358,030	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	427,490	NR	NR	NR	NR	NR
NR	N	210,204	R	R	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR

■ 42 RNA+ specimens, screening test negative:

- Vironostika 22
- Oraquick 17
- Bio-Rad 3

*Louie et al, J Clin Microbiol 2008*



/ironostika		Viral Load	HIV-1/2/O	UG	MS	OQ	SP
EIA Result	WB	copies/ml	EIA Result	RT	RT	RT	RT
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NR	N	12,852	NR	NR	NR	NR	NR
NR	I	14,062	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	R	R
NR	N	3,921	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	NR	NR	NR
NR	N	≥500,000	NR	R	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	1,177	NR	NR	NR	NR	NR
NR	N	>500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	43,173	NR	NR	NR	NR	NR
NR	I	30,734	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	102,288	NR	NR	NR	NR	NR
NR	N	327,333	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	389,850	NR	NR	NR	NR	NR
NR	I	413,186	NR	R	R1	NR	NR
NR	I	446,770	NR	NR	NR	NR	NR
NR	N	358,030	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	427,490	NR	NR	NR	NR	NR
NR	N	210,204	R	R	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR

■ 42 RNA+ specimens, screening test negative:

- Vironostika 22
- Oraquick 17
- Bio-Rad 3

■ Number detected by:

- Western blot 0
- Bio-Rad Plus O 22

*Louie et al, J Clin Microbiol 2008*



/ironostika		Viral Load	HIV-1/2/O	UG	MS	OQ	SP
EIA Result	WB	copies/ml	EIA Result	RT	RT	RT	RT
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NR	I	≥500,000	NR	NR	NR	NR	NR
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NR	N	77	NR	NR	NR	NR	NR
NR	I	6,373	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	12,852	NR	NR	NR	NR	NR
NR	I	14,062	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	R	R
NR	N	3,921	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	NR	NR	NR
NR	N	≥500,000	NR	R	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	1,177	NR	NR	NR	NR	NR
NR	N	>500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	43,173	NR	NR	NR	NR	NR
NR	I	30,734	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	102,288	NR	NR	NR	NR	NR
NR	N	327,333	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	389,850	NR	NR	NR	NR	NR
NR	I	413,186	NR	R	R1	NR	NR
NR	I	446,770	NR	NR	NR	NR	NR
NR	N	358,030	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	427,490	NR	NR	NR	NR	NR
NR	N	210,204	R	R	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR

■ 42 RNA+ specimens, screening test negative:

- Vironostika 22
- Oraquick 17
- Bio-Rad 3

■ Number detected by:

- Western blot 0
- Bio-Rad Plus O 22
- Unigold 11

*Louie et al, J Clin Microbiol 2008*



EIA Result	WB	copies/ml	EIA Result	RT	RT	RT	RT
NR	I	5,770	NR	NR	NR	NR	NR
NR	I	≥500,000	NR	NR	NR	NR	NR
NR	I	12,183	R	R	NR	NR	NR
NR	N	77	NR	NR	NR	NR	NR
NR	I	6,373	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	12,852	NR	NR	NR	NR	NR
NR	I	14,062	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	R	R
NR	N	3,921	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	NR	NR	NR
NR	N	≥500,000	NR	R	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	1,177	NR	NR	NR	NR	NR
NR	N	>500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	43,173	NR	NR	NR	NR	NR
NR	I	30,734	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	102,288	NR	NR	NR	NR	NR
NR	N	327,333	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	389,850	NR	NR	NR	NR	NR
NR	I	413,186	NR	R	R1	NR	NR
NR	I	446,770	NR	NR	NR	NR	NR
NR	N	358,030	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	427,490	NR	NR	NR	NR	NR
NR	N	210,204	R	R	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	≥500,000	R	R	R1	NR/NR	NR

■ 42 RNA+ specimens, screening test negative:

- Vironostika 22
- Oraquick 17
- Bio-Rad 3

■ Number detected by:

- Western blot 0
- Bio-Rad Plus O 22
- Unigold 11
- Multispot 7

*Louie et al, J Clin Microbiol 2008*



Vironostika		Viral Load copies/ml	HIV-1/2/O EIA Result	UG	MS	OQ	SP
EIA Result	WB			RT	RT	RT	RT
NR	I	5,770	NR	NR	NR	NR	NR
NR	I	≥500,000	NR	NR	NR	NR	NR
NR	I	12,183	R	R	NR	NR	NR
NR	N	77	NR	NR	NR	NR	NR
NR	I	6,373	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	12,852	NR	NR	NR	NR	NR
NR	I	14,062	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	R	R
NR	N	3,921	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	NR	NR	NR
NR	N	≥500,000	NR	R	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	1,177	NR	NR	NR	NR	NR
NR	N	>500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	43,173	NR	NR	NR	NR	NR
NR	I	30,734	NR	NR	NR	NR	NR
NR	N	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	R	R	R1	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	102,288	NR	NR	NR	NR	NR
NR	N	327,333	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	I	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	389,850	NR	NR	NR	NR	NR
NR	I	413,186	NR	R	R1	NR	NR
NR	I	446,770	NR	NR	NR	NR	NR
NR	N	358,030	NR	NR	NR	NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR
NR	N	427,490	NR	NR	NR	NR	NR
NR	N	210,204	R	R	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR	NR
NR	N	≥500,000	NR	NR	NR	NR/NR	NR
NR	N	≥500,000	R	NR	NR	NR	NR

■ 42 RNA+ specimens, screening test negative:

- Vironostika 22
- Oraquick 17
- Bio-Rad 3

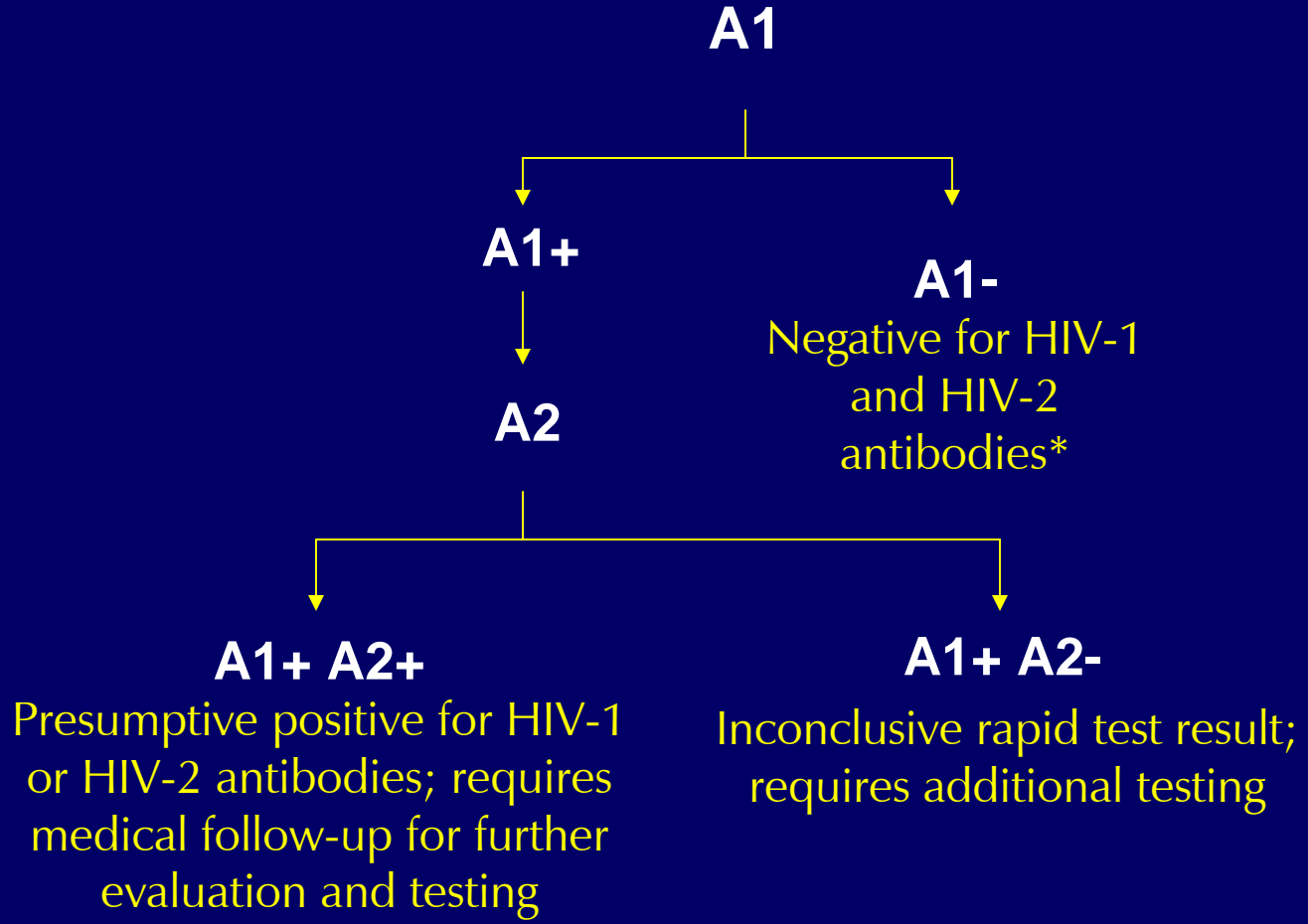
■ Number detected by:

- Western blot 0
- Bio-Rad Plus O 22
- Unigold 11
- Multispot 7
- Stat-Pak 1
- OraQuick 1

*Louie et al, J Clin Microbiol 2008*

# POC Algorithm 2: Two Rapid Tests in Sequence on Blood

[A1 and A2 must be different rapid tests]

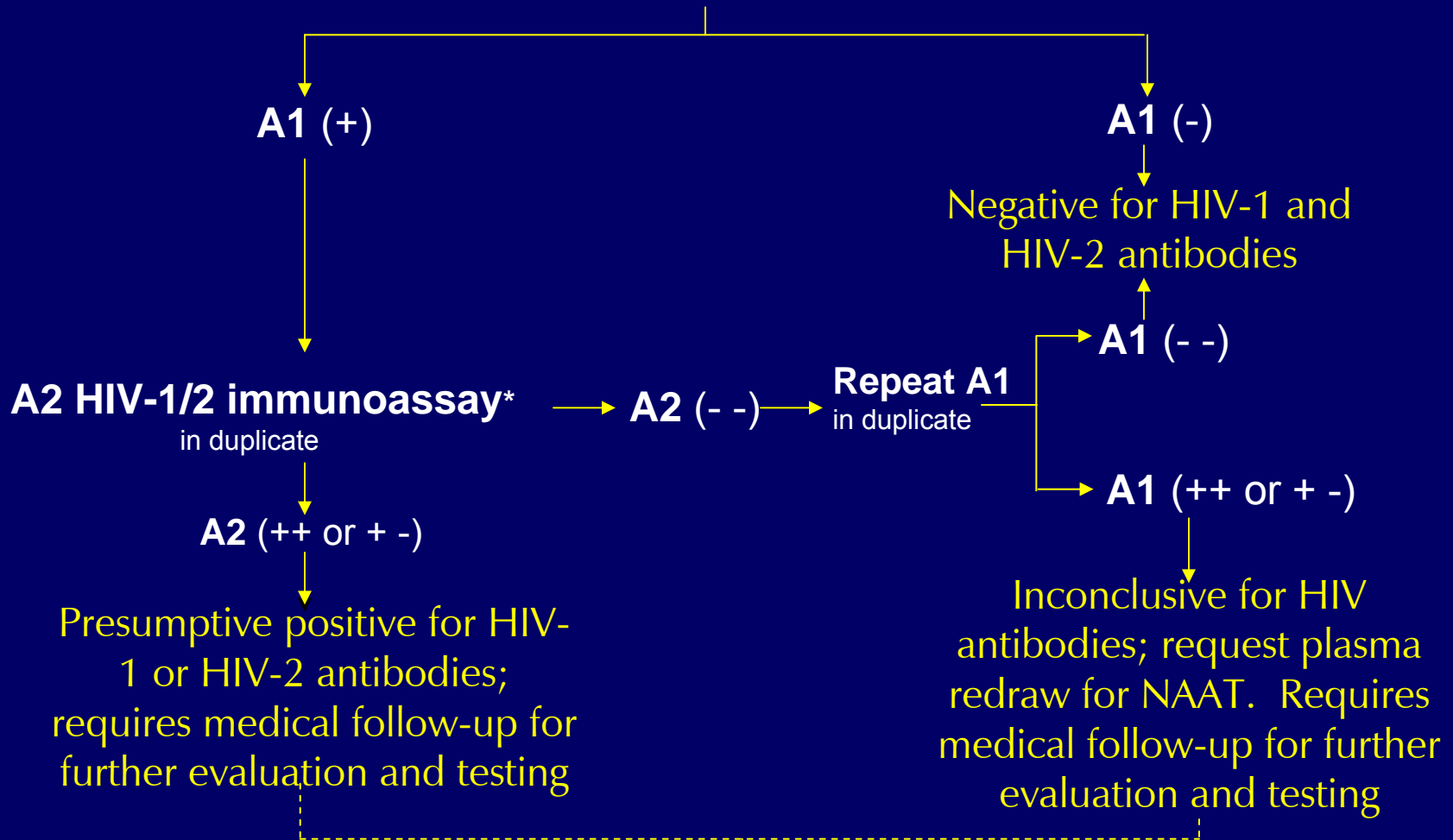


\*If using an HIV-1 only rapid test, Negative for HIV-1 antibodies only



# Lab Algorithm 3. HIV-1/2 Dual Immunoassay

## A1 HIV-1/2 Immunoassay



HIV-2 Testing; Strategy, if applicable



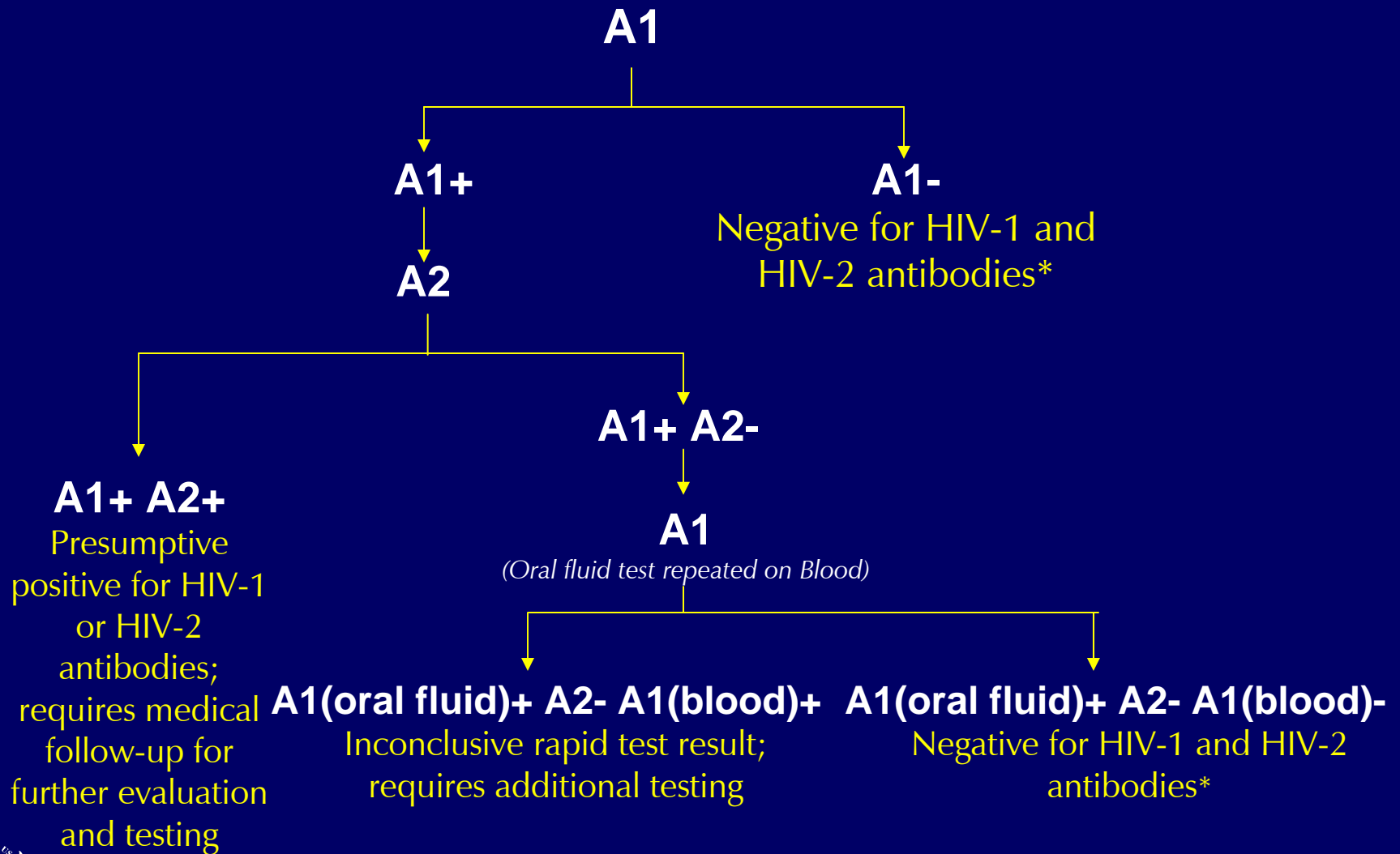




# Sensitivity – Optimized Algorithm (either test positive)

	GS HIV-1/2+O	Abbott	Vir HIV-1+O	GS HIV-1/2 peptide	GS rLAV	Vir HIV-1	Oraquick	Reveal	Uni-Gold	Procleix	CDC RNA	Ampliscreen
<b>GS HIV-1/2+O</b>	99.8 / 99.4	99.8	99.8	99.8	99.8	99.8	99.8	99.8	99.8	100.0	100.0	100.0
<b>Abbott</b>	97.5	99.4 / 97.7	99.8	99.5	99.7	99.5	99.5	99.5	99.5	99.5	99.5	99.5
<b>Vir HIV-1+O</b>	98.4	96.7	99.7 / 99.0	99.7	99.7	99.7	99.7	99.7	99.8	99.8	99.8	99.8
<b>GS HIV-1/2 peptide</b>	99.2	97.5	98.8	98.7 / 99.8	98.9	99.4	98.7	99.0	99.1	99.0	98.9	98.9
<b>GS rLAV</b>	99.4	97.7	99.0	99.8	97.4 / 100	99.2	98.9	99.2	98.9	99.2	99.0	99.0
<b>Vir HIV-1</b>	97.9	96.3	97.7	98.2	98.4	99.0 / 98.4	99.4	99.4	99.3	99.4	99.4	99.4
<b>Oraquick</b>	99.2	97.5	98.8	99.6	99.8	98.2	98.6 / 99.8	99.0	99.1	99.0	98.9	98.9
<b>Reveal</b>	99.2	97.5	98.8	99.6	99.8	98.2	99.6	99.0 / 99.8	99.5	99.2	99.2	99.2
<b>Uni-Gold</b>	99.0	97.3	98.8	99.2	99.4	97.8	99.2	99.2	98.4 / 99.4	99.3	99.1	99.1
<b>Procleix</b>	99.0	97.3	98.6	99.4	99.6	98.1	99.4	99.4	99.0	97.4 / 99.6	97.6	97.4
<b>CDC RNA</b>	98.8	97.1	98.4	99.2	99.4	97.9	99.2	99.2	98.8	99.0	95.8 / 99.4	96.9
<b>Ampliscreen</b>	96.3	94.5	95.9	96.7	96.9	95.3	96.7	96.7	96.3	96.5	96.3	92.6 / 96.9

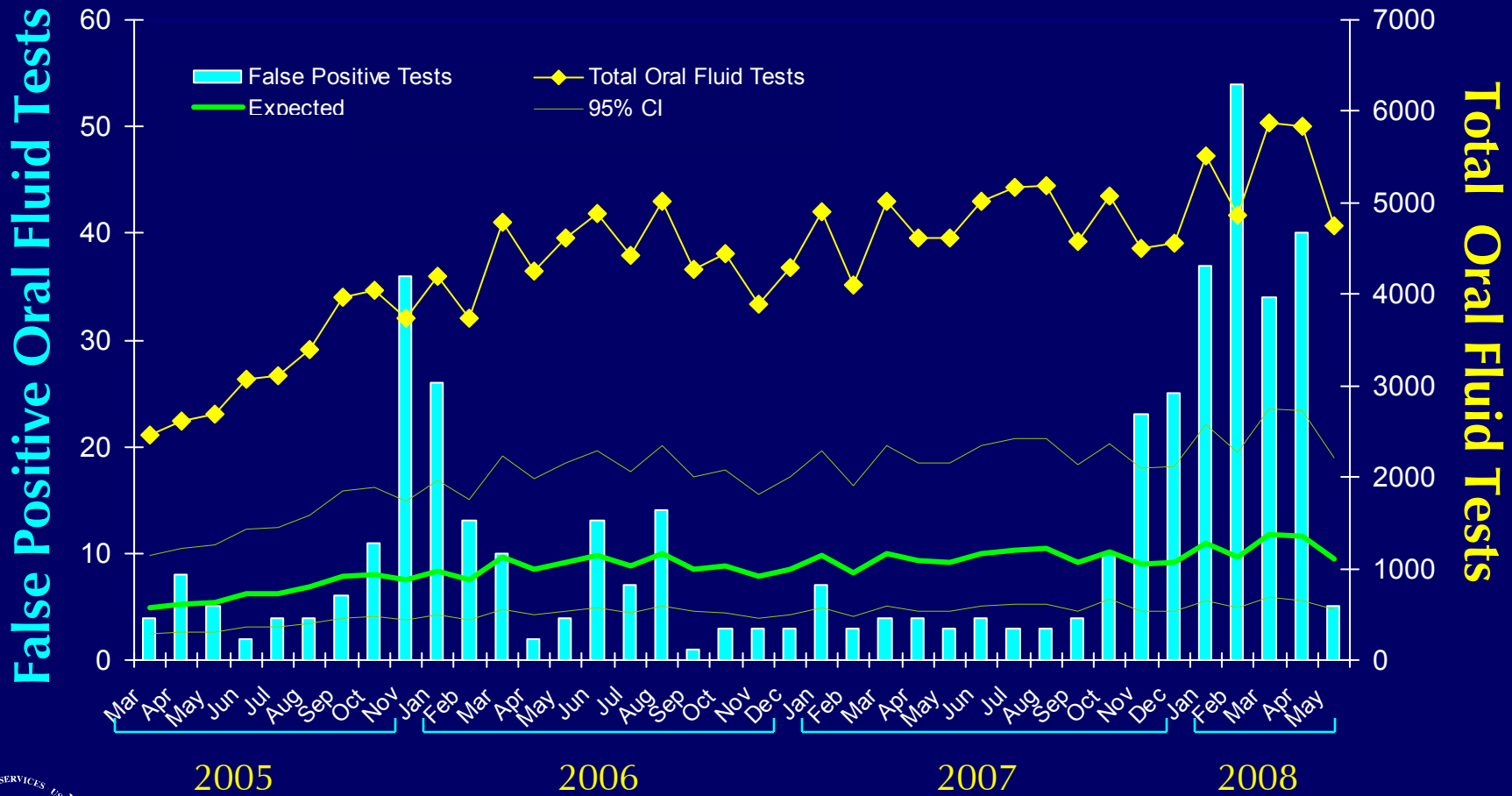
# Algorithm 3. Initial Oral Fluid Rapid HIV Test



\*If using an HIV-1 only rapid test, Negative for **HIV-1 antibodies only**



# False Positive Oral Fluid Rapid Tests New York City STD Clinics 2005-2008



- MMWR June 20, 2008



# Finger Stick Blood after OF Reactive

*NY City STD Clinics, March 2005- April 07*

- 133,832 oral fluid rapid tests
  - 1720 (1.2%) reactive
    - 1664 with confirmatory results
    - 368 false positive (PPV 77%)
  - 1194 with immediate finger stick, same test
    - 850 concordantly reactive on OF and fingerstick
      - 840 confirmed positive (PPV 98.9%)
    - 344 OF-reactive, finger stick negative
      - 1 positive by WB

*- MMWR June 20, 2008*



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# On the Horizon...

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Multi-analyte  
rapid test



Ag-Ab combo

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# Current and Upcoming Tests for Detecting Recent Infection and Estimating Incidence

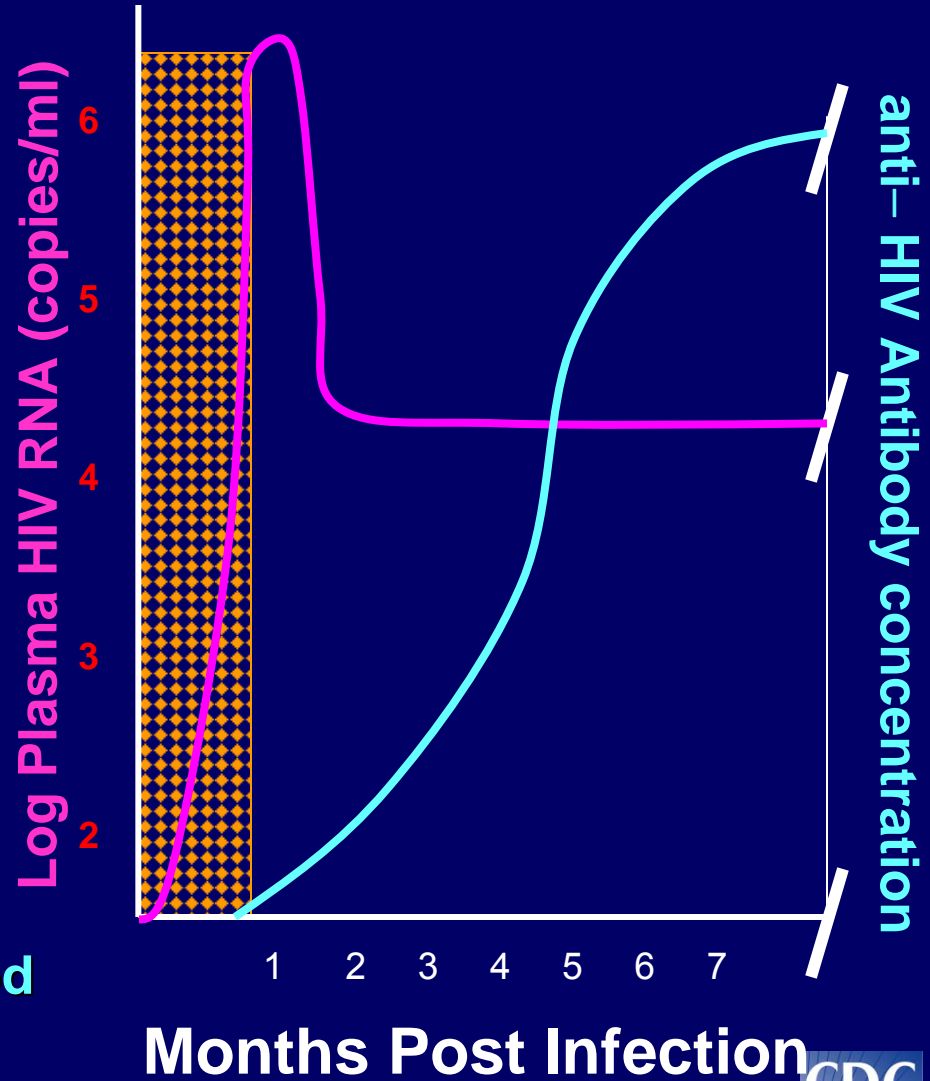


# Current Assays for Recent Infection

- **Virus+ Antibody -**
- **Antibody Avidity**
- **Antibody Titer**

Most accurate assay

but has the smallest window period



Months Post Infection

Quinn 2000 *AIDS*; 14: 2751

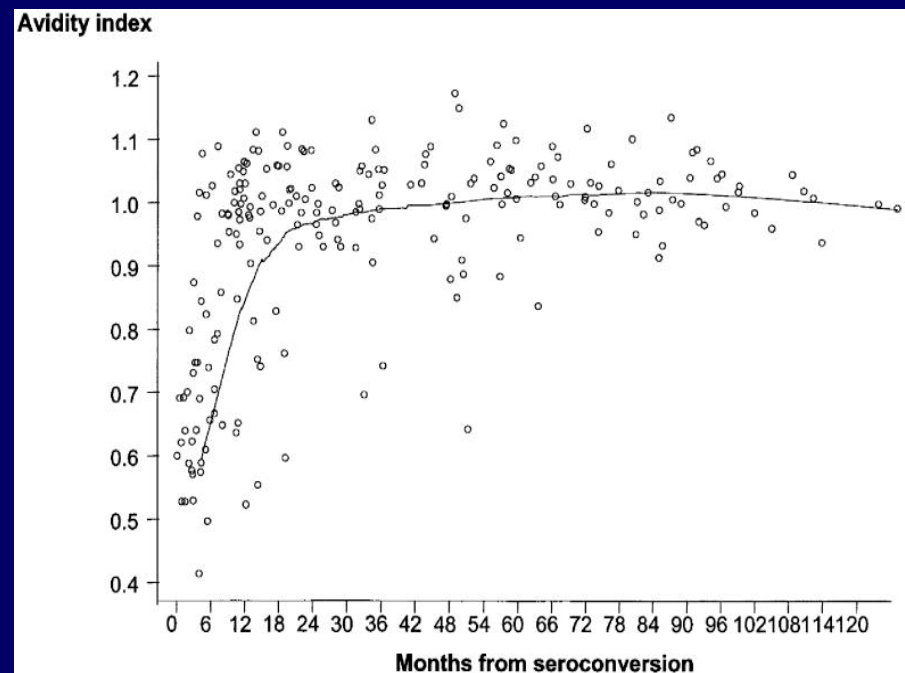




# Current Assays for Recent Infection

- **Virus+ Antibody -**
- **Antibody Avidity**
- **Antibody Titer**

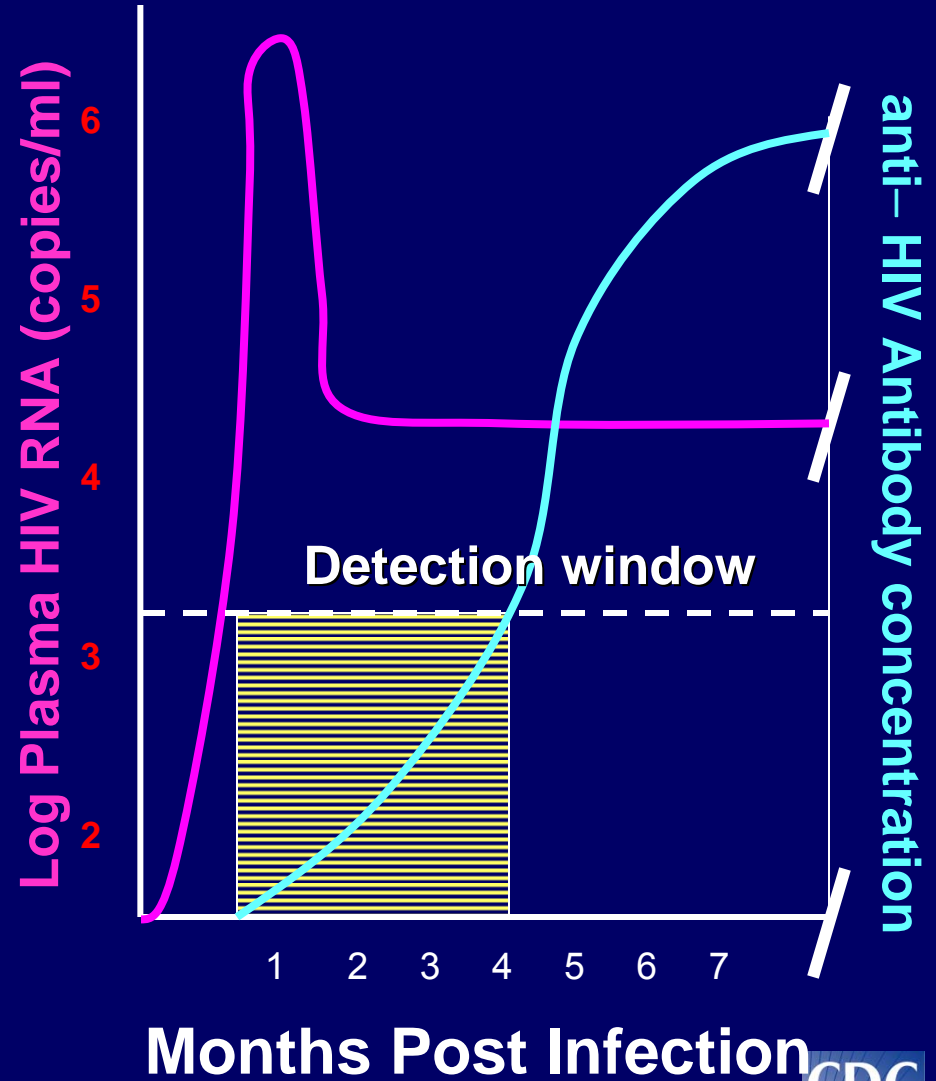
## Maturation of Antibody Response



Suligoi B, 2003 *JAIDS*; 32:424.

# Current Assays for Recent Infection

- **Virus+ Antibody -**
- **Antibody Avidity**
- **Antibody Titer**



Months Post Infection

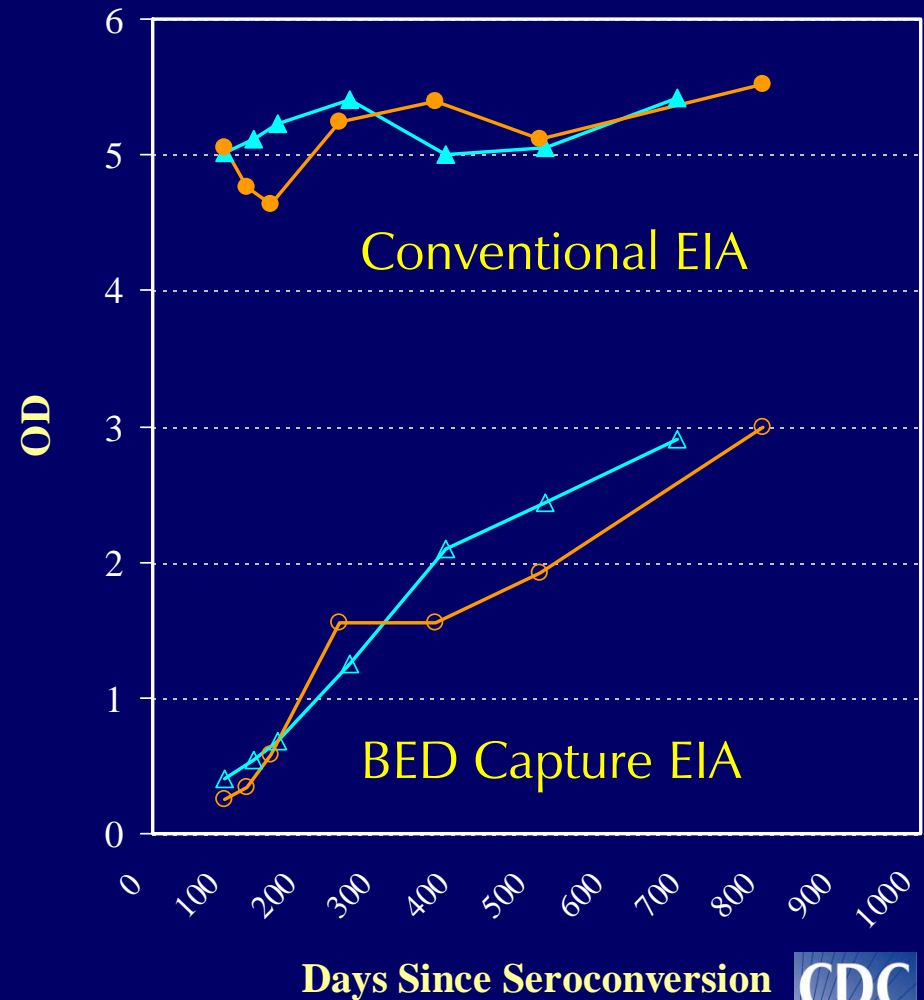


Janssen RS, *JAMA* 1998;280:42

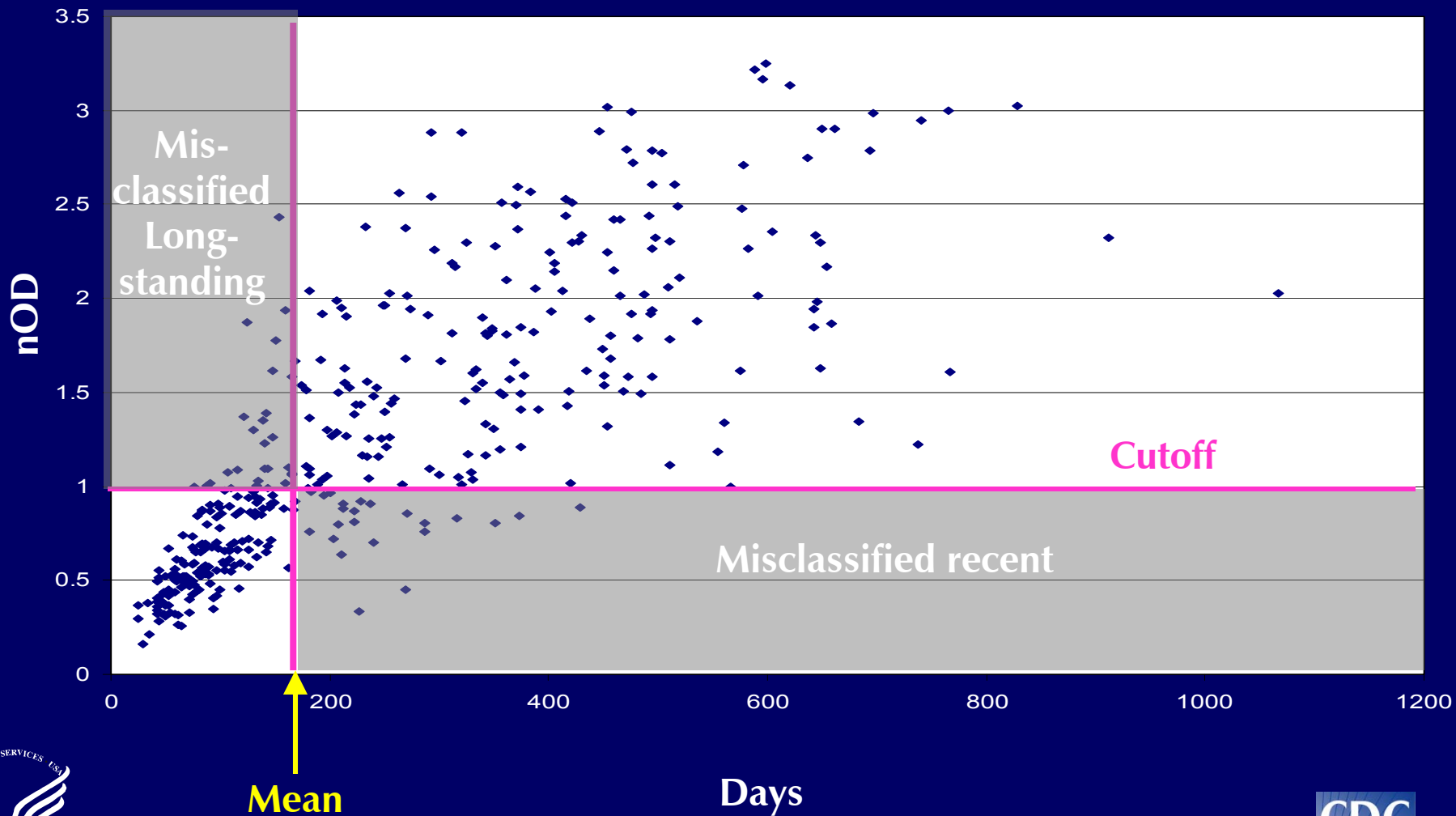


# Current Assays for Recent Infection

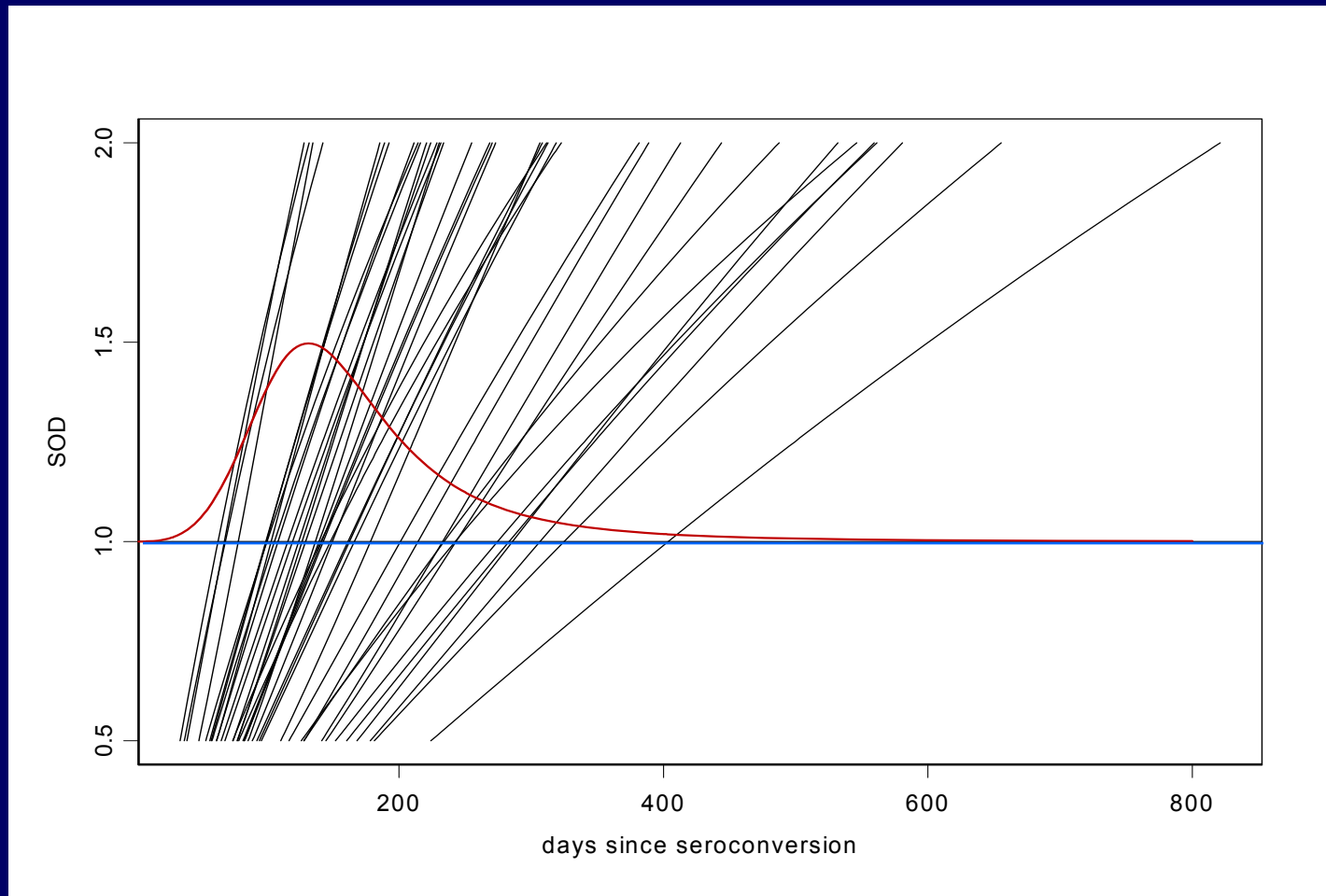
- **Virus+ Antibody -**
- **Antibody Avidity**
- **Antibody Titer**
  - **Proportion**



# Window Period Estimates: Incidence

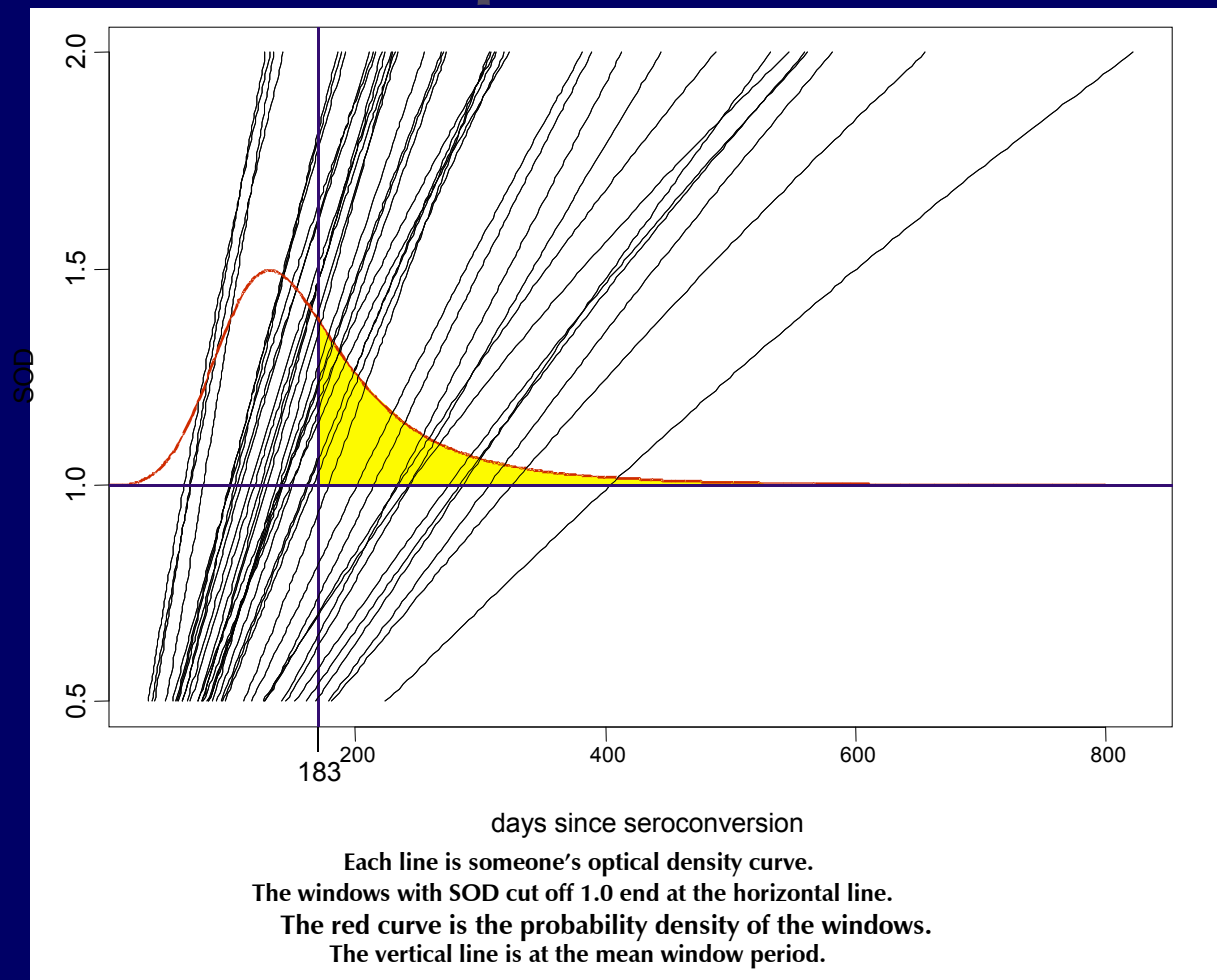


# Distribution of Individual Window Periods

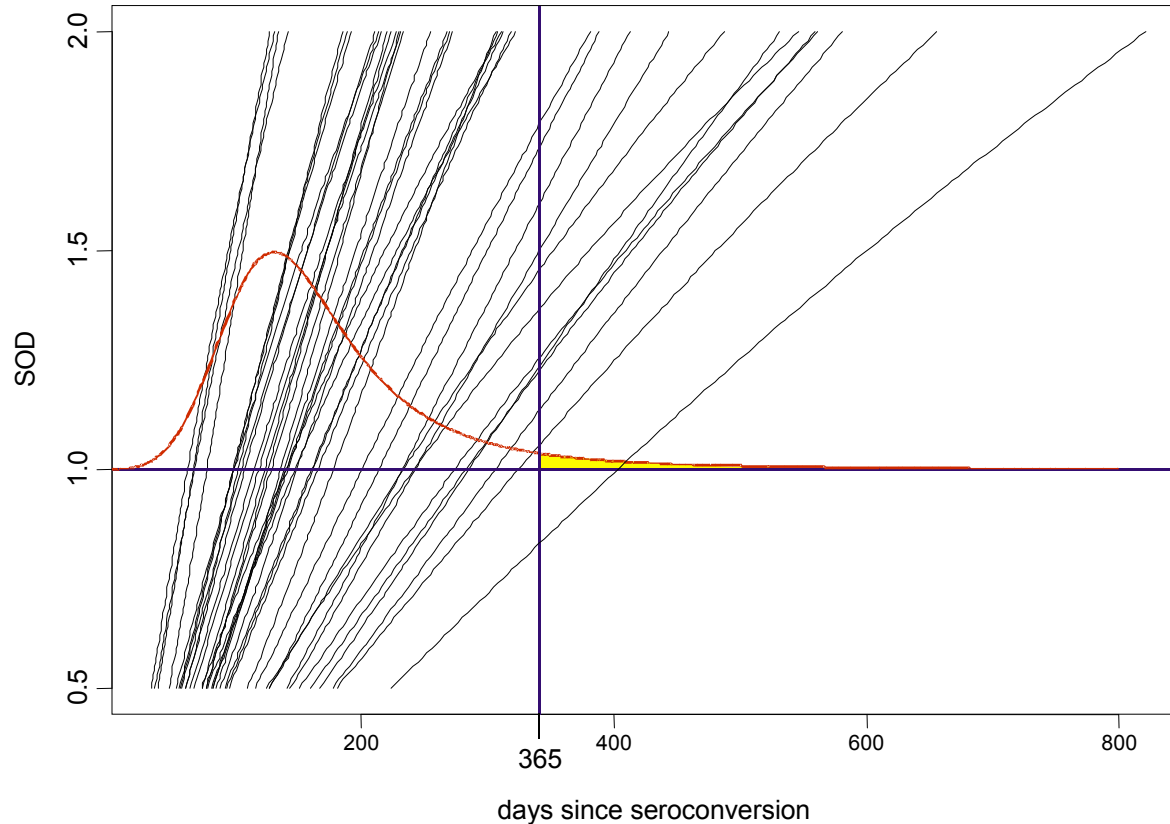


# Proportion of persons with time from seroconversion to test longer than mean window

period



# Proportion of individuals with time from seroconversion to test greater than 1 year



Each line is someone's optical density curve.  
The windows with SOD cut off 1.0 end at the horizontal line.  
The red curve is the probability density of the windows.  
The vertical line is at one year from seroconversion.

# Current Assays for U.S.

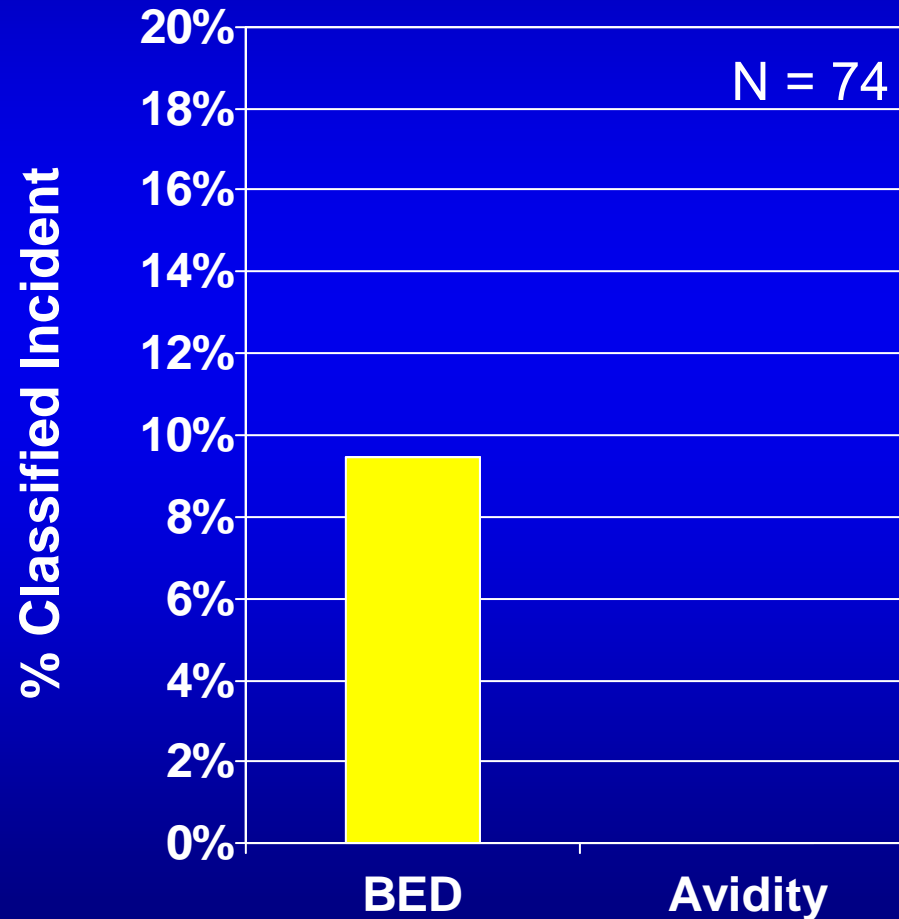
- Titer (less sensitive):
  - Vironostika (discontinued)
  - Vitros Eci
- Avidity
  - BioRad HIV 1/2 Plus O
  - Vitros
- Proportion
  - BED (incidence surveillance only)





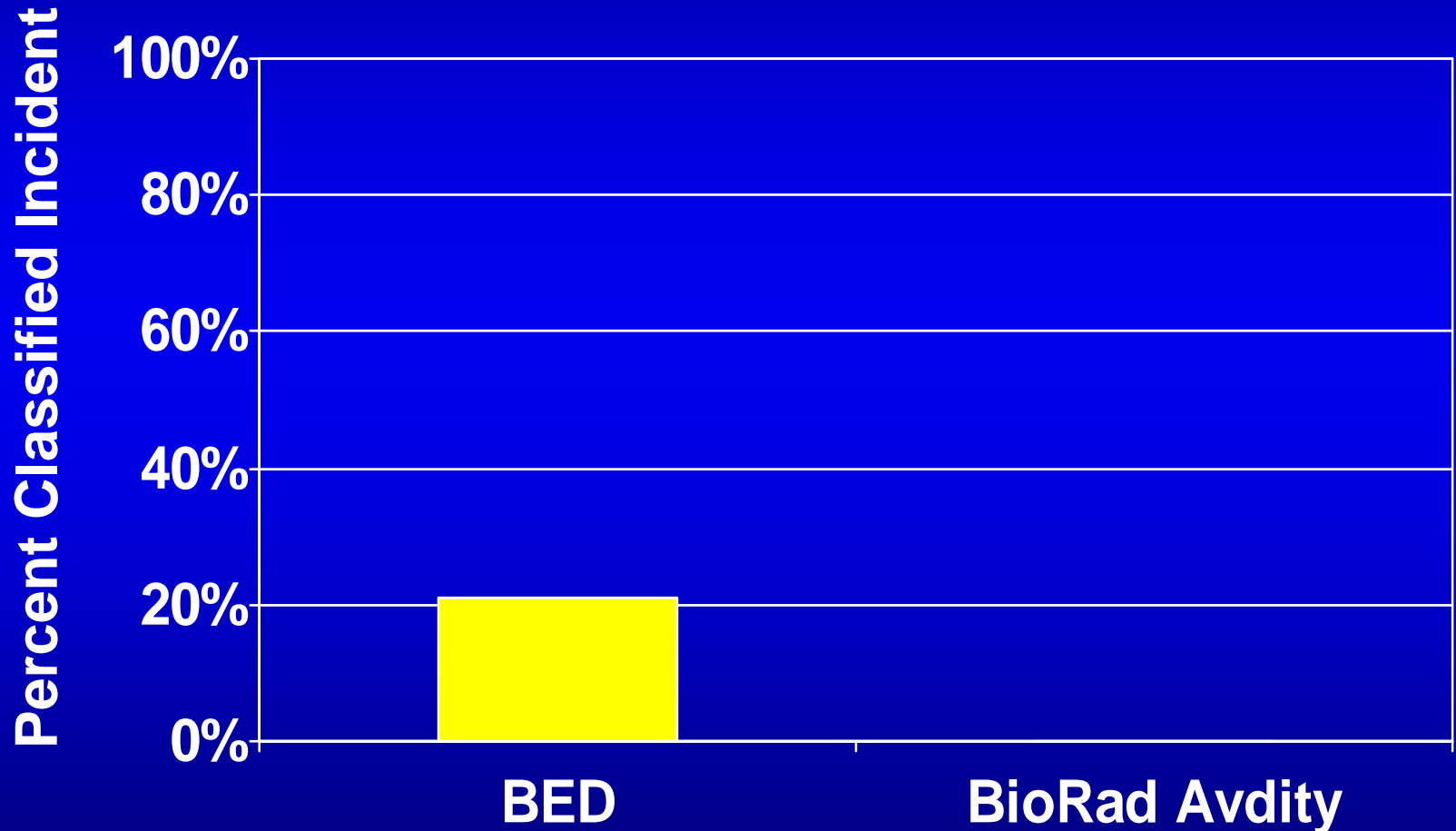
# BED vs. Avidity - False Incident Chronic Infection (no ARVs, no AIDS)

JHU Moore Clinic



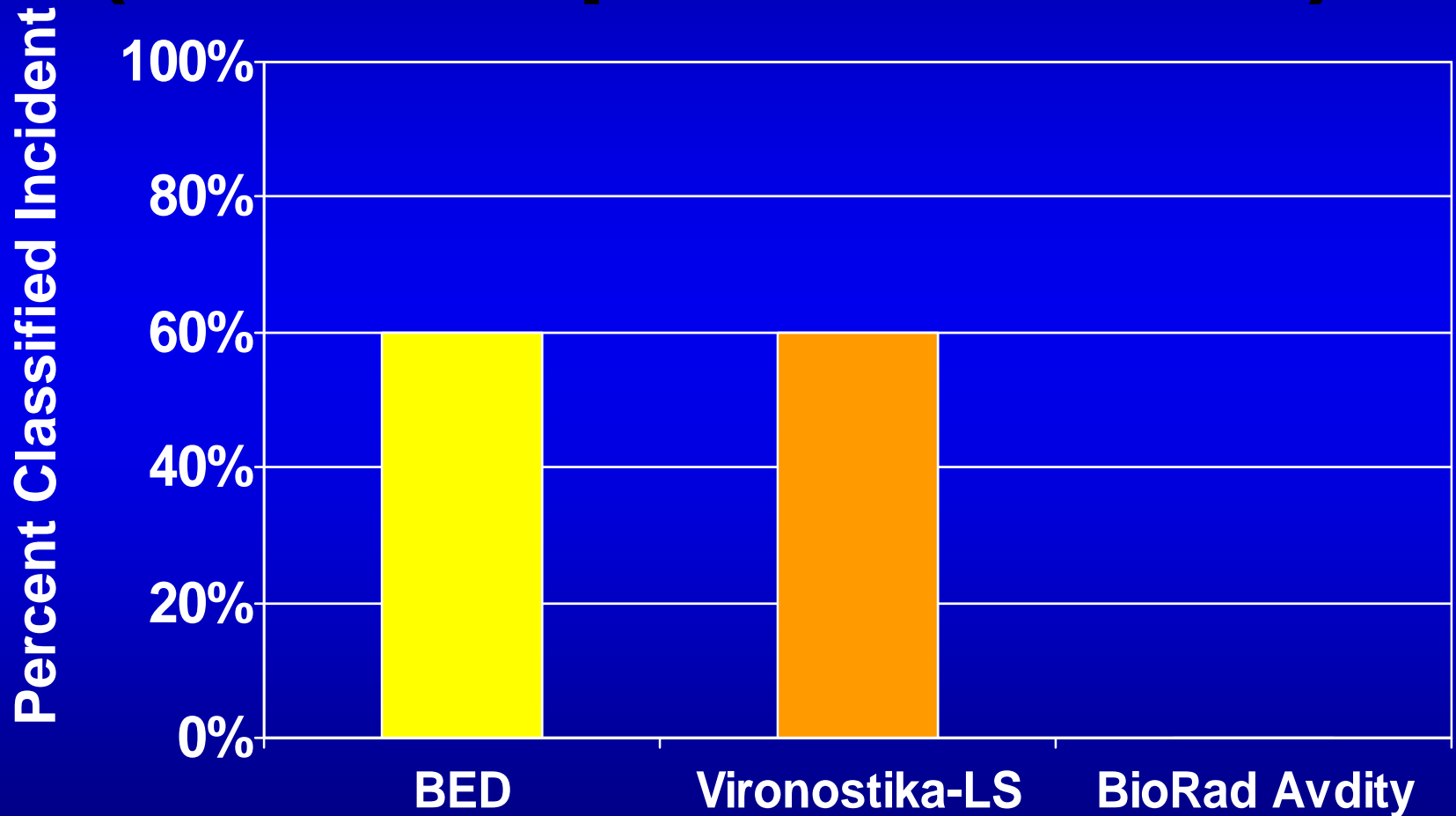
# Misclassification of Chronically Infected Virally Suppressed Subjects on ARVs

(VL < 50 cps/ml, CD4 > 500 cells / ml)



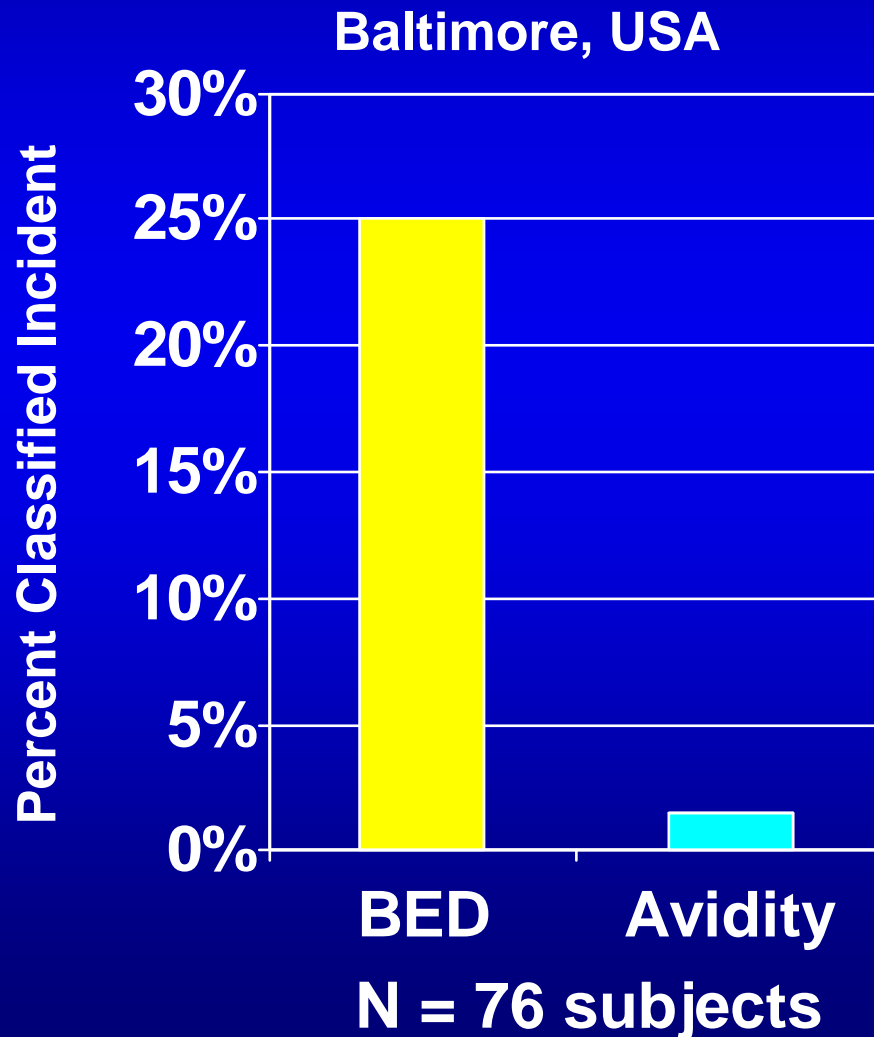
N = 134 samples

# Misclassification of Elite Suppressors (VL < 50 cps/ml no ARVs)

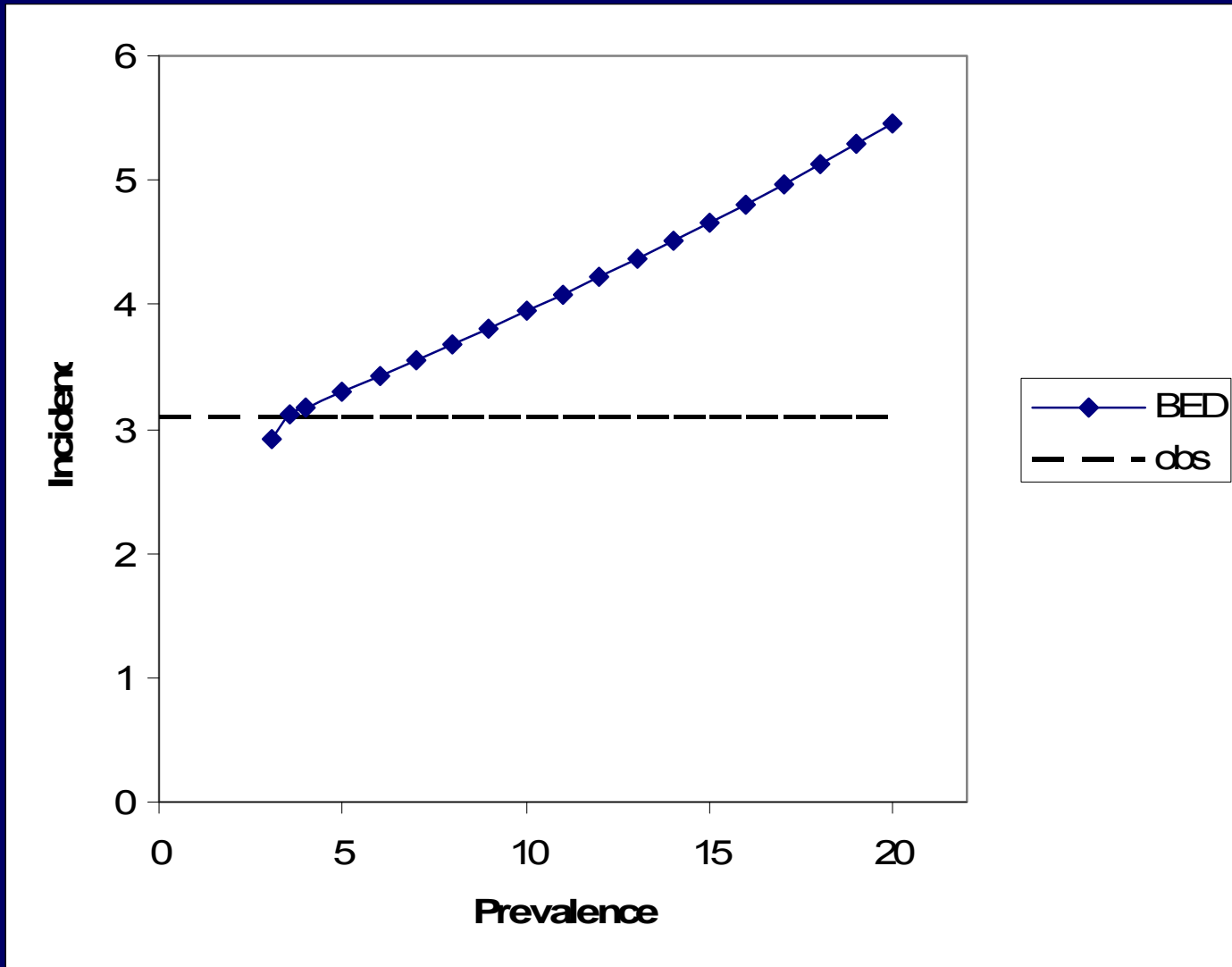


N = 16 samples

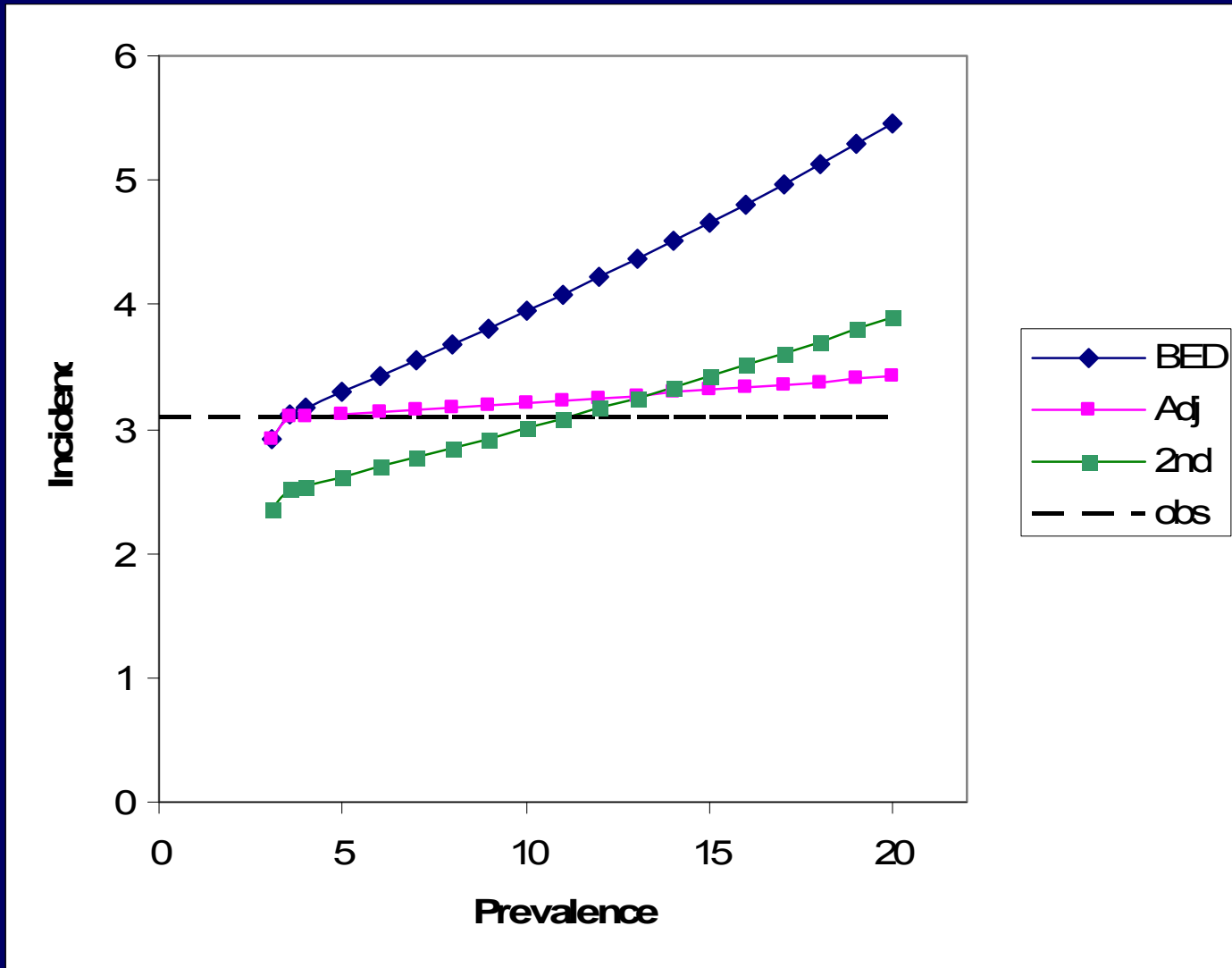
# Misclassification of AIDS Patients (CD4 < 50 cells / ml)



# Simulated Increasing Prevalence: VAX004 Trial



# Adjustments Applied to VAX004 Trial Simulation



# Discussion Topics

- Do we want to do away with the Western blot?
- What do settings want from POC?
- What do clinicians want from laboratories, e.g.:
  - “Preliminary positive” EIA results?
- Context-specific issues, e.g.:
  - Pregnancy, diagnosis, etc.
- What data do we need?

