

# 2016 HIV DIAGNOSTICS CONFERENCE

MARCH 21-24, 2016 • ATLANTA, GA

*The New Landscape of HIV  
Testing in Laboratories,  
Public Health Programs  
and Clinical Practice*

## US HIV DIAGNOSTIC TEST TIMELINE

- 1985 Whole Viral lysate IA (1st generation)
- 1987 HIV-1 Western Blot
- 1989 p24 Antigen Assay
- 1990 HIV-2 IA  
HIV-1 IA for Dried Blood Spots
- 1991 Synthetic Peptide IA (2nd generation)
- 1992 IgM Sensitive Antibody Sandwich IA (3rd generation)  
HIV-1 IFA  
CLIA-Moderate Complexity HIV-1 Rapid IA
- 1994 Collection Device and HIV-1 IA for Oral Fluid
- 1996 HIV-1 IA for Urine  
HIV-1 Home Specimen Collection  
Diagnostic System  
Quantitative HIV-1 Viral Load Assay
- 2002 Rapid HIV-1 IA for Whole Blood, Plasma (Waived 2003 for whole blood, 2004 for Oral Fluid)
- 2003 IAs to Include Group O Detection
- 2004 Rapid IA Differentiates HIV-1 from HIV-2
- 2006 Random Access Microparticle  
Chemiluminometric IA  
Qualitative HIV-1 Nucleic Acid Test for Diagnostic Use
- 2010 HIV-1/2 Antigen Antibody Combination IA (4th generation)
- 2012 CLIA-Waived Rapid IA Provides Immediate Test Results  
Over-the-counter HIV-1/2 Rapid IA for Oral Fluid Dual Path  
Rapid IA (Waived 2014)
- 2013 Rapid IA Differentiates HIV-1 from HIV-2  
Relabeled for Supplemental Use  
HIV-1/2 Antigen Antibody Combination  
Rapid IA (Waived 2014)
- 2014 Supplemental Dual Path Rapid IA  
Differentiates  
HIV-1 from HIV-2 with Reader
- 2015 Fully automated Ag/Ab Differentiation  
Screening Test

— PRESENTED BY —



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# WELCOME

Dear Colleagues,

Welcome to Atlanta and the 2016 HIV Diagnostics Conference, presented by the Centers for Disease Control and Prevention (CDC), the Association of Public Health Laboratories (APHL), the American Sexual Health Association (ASHA) and the American Sexually Transmitted Diseases Association (ASTDA). We are excited that you are here and sincerely hope the conference provides you with valuable knowledge related to the new and ever-changing landscape of HIV diagnostics.

It has been an exciting time since our last Conference in 2012! The long awaited recommendations for an updated laboratory testing algorithm were released by CDC in conjunction with APHL in 2014 and since this time the recommendations have been implemented in many locations. In addition to the guidelines, we have also seen the launch of additional new technologies that have the potential to further change how and where we test for HIV.

During the conference we hope to highlight the successes associated with the updated laboratory algorithm and technology, as well as the hurdles and challenges we still face to fully implement and take advantage of all of the new advances in the field of HIV diagnostics. We will also provide a brief glimpse into new technologies that are on the horizon and welcome feedback on the path forward.

Networking, partnerships, and informal exchange of ideas are also vital factors for making the conference a success and for continuing the process of improving HIV diagnosis. We encourage engagement between presenters, attendees and exhibitors, as this has been a critical component of past conferences and has helped pave the way to where we are in the field.

On behalf of the planning committee, we welcome you back to Atlanta, look forward to your participation and hope you find the conference engaging and rewarding.

Monica M. Parker, PhD  
*New York State Department of Health  
Co-Chair, 2016 HIV Diagnostics Conference*

S. Michele Owen, PhD  
*Centers for Disease Control and Prevention  
Co-Chair, 2016 HIV Diagnostics Conference*



# 2016 HIV DIAGNOSTICS CONFERENCE COMMITTEE

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*New York State Department of Health*

**S. Michele Owen, PhD**

*Centers for Disease Control and Prevention*

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*American Sexually Transmitted Diseases Association*

**Laura G. Wesolowski, PhD**

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**Kelly Wroblewski MPH, MT (ASCP)**

*Association of Public Health Laboratories*

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*Florida Bureau of Public Health Laboratories*

**Barbara Body, PhD, D (ABMM)**

*Laboratory Corporation of America*

**Pollyanna R. Chavez, PhD**

*Centers for Disease Control and Prevention*

**Kevin P. Delaney, PhD**

*Centers for Disease Control and Prevention*

**Steve F. Ethridge, MT (ASCP)**

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**Indira K. Hewlett, PhD**

*U.S. Food and Drug Administration*

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**Christopher D. Pilcher, MD**

*University of California, San Francisco*

**Liisa M. Randall, PhD**

*National Alliance of State and Territorial AIDS Directors*

**Benjamin Tsoi, MD, MPH**

*New York City Department of Health and Mental Hygiene*

## PHYSICIAN PLANNER

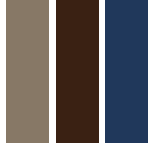
**Philip J. Peters, MD**

*Centers for Disease Control and Prevention*

## CONFERENCE MANAGER

**Lynn Barclay**

*American Sexual Health Association*



## ACKNOWLEDGEMENTS

The Conference Committee wants to sincerely thank the following individuals for their commitment to the success of this conference:

**Kelly Curtis, PhD**

**Joanne Stekler, MD, MPH**

**Anne M. Gaynor, PhD**

**Linda M. Styer, PhD**

**William A. Meyer III, Ph.D., D (ABMM), MLS (ASCP)**

**Barbara Werner, PhD**

**Marc Pitasi, MPH**

**Fred Wyand**



# DEDICATIONS

The Conference Committee dedicates the 2016 HIV Diagnostics Conference to 4 recent retirees from the public health arena:

**Spencer Berry Bennett, MPH**

**Elliot Cowan, PhD**

**Bernard M. Branson, MD**

**Barbara Warner, PhD**

These incredible individuals have contributed tremendously to the field of HIV diagnostics in the United States. The following pages give us a glimpse of their accomplishments and impact.





## Spencer Berry Bennett, MPH

Berry served as a virologist for the Florida Bureau of Public Health Laboratories from 1977 to 2015. He organized and led a new department in 1985 with a focus on HIV diagnostic testing. The Retrovirology Unit has developed and provides a comprehensive HIV clinical management testing program (HIV-1 viral load, CD4/CD8 immunocytometry and HIV-1 genotyping services) in addition to advanced HIV-1/2 Ag/Ab diagnostic services. The Florida Bureau of Public Health Laboratories is proud of its commitment to providing HIV diagnostic and clinical management services to their Florida clients.

Berry is a passionate public health professional who has contributed to HIV testing at the state level and beyond. As part of the APHL HIV/HCV Testing Subcommittee, he was instrumental in the development of the CDC/APHL laboratory HIV algorithm guidance which recommends the use of HIV-1/HIV-2 antigen/antibody testing. Florida was one of the first public health laboratories in the nation to adopt the algorithm, and the transition to the algorithm was successful largely due to Berry's tireless efforts and collaboration with surveillance staff. Further, his laboratory provides nucleic acid testing to 20 public health laboratories using the algorithm.

Berry is a recognized HIV diagnostics expert. He has educated colleagues, students and healthcare professionals about HIV testing, and has presented in national teleconferences. He assisted colleagues in Ukraine to develop their HIV algorithm through a twinning initiative with APHL. Berry is a contributing or first author on seminal HIV diagnostics publications. He has presented his work at several HIV Diagnostics Conferences and chaired the 2012 planning committee.

Berry has a positive attitude and is always willing to lend a hand by providing his expertise, support or encouragement. He was a member of the Florida Consortium on HIV/AIDS Research, and served on their Executive Advisory Board. He was on the advisory committee of the Florida State College Jacksonville, Medical Laboratory Technician Program. He was a member of the Florida Public Health Association, serving as a Member at Large and co-Chair of the HIV/AIDS section, and served as the President of the Jacksonville Area Microbiology Society (JAM), 2013-2015. Those who have worked with Berry know what a pleasure it is, and we are grateful for his contributions to the field.



## Bernard M. Branson, MD

Dr. Branson's career has been unconventional but notable, dating back to Northwestern University Medical School, when he started a pastry business – Let Them Eat Cake! He conceived tactics (such as a costumed Marie Antoinette who dispensed samples) that helped the enterprise grow. Bernie trained in Medicine and Pediatrics at UNC. In 1978, brought to Baltimore by the National Health Service Corps, he served as Director of Pediatrics at the East Baltimore Medical Plan, and, along with community members, founded the volunteer STD Clinic for the Gay Community Center of Baltimore. As the clinic grew, Bernie worked as the DJ at an after-hours disco to raise money to buy a new facility at Chase Street and Brexton Alley. Chase-Brexton Health Services has become the largest HIV and LGBT health services provider in MD. Bernie also served as Medical Director of Baltimore City's Head Start Program.



In 1983, the first cases of AIDS appeared in Baltimore. Bernie was in private practice in Internal Medicine and Pediatrics, and on the faculty at Johns Hopkins. Many of the first adults and children with AIDS in Maryland were in his practice. Patients and their families, confronting this frightening and fatal new disease, began to meet after hours in Bernie's office. These support groups grew and morphed into HERO, the Health Education Resource Organization, a community based-organization that, under Bernie's leadership, initiated the Maryland state AIDS hotline and instituted the state's anonymous HIV counseling and testing program. HERO lasted for 25 years as the largest HIV-related CBO in Baltimore. Bernie found time to produce HIV continuing medical education programs with the Physicians Association for AIDS Care, and by 1990, he was producing a public-access cable show, "HIV Update," in 42 US cities.

In 1984, Bernie prompted the formation of the first study Community Advisory Board to resolve a difference of opinion over the Baltimore component of the MACS study. (The protocol developers did not want to screen participating gay men for STDs; the community sided with Bernie.) In 1985 he co-founded Our Friends Place, a child-abuse prevention program that utilized community volunteers and a Baltimore City Head Start center, and he became Principal Medical Consultant for Job Corps, designing the HIV screening and monitoring protocols for the 65,000 adolescents entering this residential Department of Labor training program each year. In 1988, while interim Director of Pediatrics at Harbor Hospital Center, Bernie established the first-ever Sick Child Daycare Center in the hospital's pediatric ward.

In 1990 Bernie joined CDC, and began to design and conduct operational research projects on HIV prevention, counseling, and testing. In the 1990s, he provided technical assistance on HIV surveillance through the Caribbean and Central America. By 1992, he authored the first CDC guidelines on early intervention for HIV infection, and then spearheaded the effort to change PHS and FDA regulations to facilitate introduction of rapid HIV tests with CLIA waiver into the US. As DHAP's Associate Director for Laboratory Diagnostics, he organized the first HIV Diagnostics Conference in 2005 to address the changing HIV diagnostic landscape, and in 2006 served as lead author for CDC's 2006 updated recommendations for HIV routine screening. At the 2010 Diagnostics conference, Bernie proposed the updated HIV testing algorithm that culminated in the 2014 release of Updated Recommendations for Testing for the Diagnosis of HIV Infection – the first in 25 years. During his career, Bernie co-authored over 100 articles, mentored numerous protégés, and became known as the "HIV testing guru."





## Elliot Cowan, PhD

*and the story of the journey of the Accidental Regulator...*

On Elliot Cowan's list of "what do you want to be when you grow up," biomedical research was at the top and law was at the bottom. He followed a systematic path toward bench science, majoring in chemistry at Williams College and working summers in labs, with his interests evolving from microbiology to immunology. He earned his PhD in immunology in 1983 from Washington University in St. Louis.

Elliot went on to NIH for a post-doc, where he was a Staff Fellow in the National Institute of Allergy and Infectious Diseases. While his work focused on the molecular basis of immune recognition, he took note of the NIH frenzy surrounding the search for the etiologic agent responsible for what was to be known as AIDS. HTLV-III/LMV was about to be discovered and a test soon followed. Little did he know what this would mean for his career several years in the future.

In 1986 Elliot joined the National Institute of Neurological Diseases and Stroke to explore an immuno-molecular basis for multiple sclerosis and disease mechanisms for a neurological disease with symptoms similar to MS and caused by HTLV-1. His work continued over the next seven years when an opportunity arose: the FDA was looking for someone with experience in HTLV to help with the regulation of HTLV blood donor screening tests. FDA's Division of Emerging and Transfusion Transmitted Diseases became his professional home.

Elliot was immersed in a regulatory workload of new tests that detected both HTLV-1 and HTLV-2 and accompanying policy issues. In 2000, momentum was building for the approval of rapid HIV tests that provided a result within 20 minutes from a fingerstick blood specimen. The lead reviewer for rapid HIV tests decided to leave the FDA and Elliot was asked to take over. The move landed him in the middle of policy and legal decisions on access to HIV testing, in close collaboration with CDC (Bernie Branson, et al.) and CMS, that had the attention of the media, the White House, and Congress. The approval of the first test was announced in 2002 by the Secretary of Health and Human Services, followed by President Bush announcing CLIA waiver for the test. There was a rapid succession of other product approvals, as well as the addition of an oral fluid claim. In 2005, Elliot was appointed the Chief of the Product Review Branch, overseeing the regulatory review staff in the Division and responsible for blood donor screening tests and retroviral diagnostics. His "final regulatory frontier" began in 2005 with what would be a seven year path toward the 2012 approval of the first over-the-counter HIV testing system.

As a result of his regulatory experience, Elliot was asked to look globally. He assisted WHO in developing its Prequalification of Diagnostics Programme and became a member of PEPFAR's Laboratory Technical Working Group, helping to address challenges to HIV testing in Africa. He also helped with the development of the current CDC/APHL-recommended HIV testing algorithm. Elliot retired from federal service to consult on the regulation of diagnostics through his firm, Partners in Diagnostics, intentionally named for his approach to regulation by working with people. His focus is on helping global health organizations, regional regulatory efforts in Africa, philanthropic foundations, and test manufacturers recognize and overcome regulatory barriers to get diagnostics to those who need them the most. Elliot will be quick to tell you he wouldn't be where he is today without the people he is proud to have as colleagues and friends he has met and made along the way. It was those people who showed him that merging his love of discovery with being immersed in law really isn't all that bad.



### **Barbara Werner, PhD**

Barbara began her work at the William A Hinton State Laboratory Institute, part of the Massachusetts Health Department starting in 1979 becoming the Director of the Clinical Investigations Division in 1982 then the Director of the Virology/Clinical Investigations Division in 1989. During her time in Massachusetts she led HIV testing efforts at the state as well as efforts around viral Hepatitis and other viruses. Following her partial retirement in 2003 she worked part-time as a consultant for the Massachusetts Department of Health to assist in the implementation of new HIV diagnostics and other laboratory developments. Under her advisement, Massachusetts was one of the first states to implement the new HIV Diagnostic Testing Algorithm, identifying 8 acute HIV infections in the first 12 months of testing.

Barbara has contributed greatly to the larger HIV and public health laboratory communities. She was a founding member of the APHL HIV Subcommittee, in 2006, serving as chair until 2008. In this role she was a key contributor to the CDC/APHL laboratory HIV algorithm guidance which recommends the use of HIV-1/HIV-2 antigen/antibody testing. Her contributions to the laboratory community were not limited to HIV diagnostics. Barbara served on the APHL Infectious Disease Committee from 2003-2008 serving as chair from 2006-2008. She is a contributing author on publications for a variety of infectious diseases including Hepatitis B, West Nile Virus, cytomegalovirus, and rabies.

Barbara is a recognized HIV diagnostics expert. She has educated colleagues, students and healthcare professionals about HIV testing, and has presented at many national teleconferences and conferences. Barbara is a contributing or first author on seminal publications on HIV diagnostics. She has presented her work at several HIV Diagnostics Conferences and has served on several planning committees.

Aside for her significant scientific knowledge and experience, Barbara's quick smile and contagious laugh make her a pleasure to work with. Her presence and contributions to the HIV Diagnostics community are appreciated and will be greatly missed.



# INDUSTRY REPRESENTATIVES

## **EDUCATIONAL GRANT**

Gilead Grants Program

## **CONFERENCE EXHIBITORS**

### SILVER LEVEL

Bio-Rad Laboratories

Hologic, Inc.

Roche Diagnostics

### BRONZE LEVEL

Oxford Diagnostic Laboratories

### GREEN LEVEL

Abbott Laboratories

BioLytical Laboratories

Chembio Diagnostic Systems

Ortho Clinical Diagnostics

Siemens Healthcare Diagnostics

### OTHER EXHIBITORS

Alere

Maxim Biomedical

Orasure Technologies

Trinity Biotech



# AGENDA

## MONDAY | MARCH 21, 2016

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<b>3:00 PM – 7:00 PM</b>	<b>On-site Registration</b>
<b>6:00 PM – 6:15 PM</b>	<b>The New Landscape of HIV Testing</b> <i>Monica M. Parker, PhD, Conference Co-Chair; New York State Department of Health</i>
<b>6:15 PM – 8:00 PM</b>	<b>HIV Testing 101 Workshop</b> <i>Moderator: Monica M. Parker, PhD, New York State Department of Health</i>
6:15 PM – 6:30 PM	<b>Update on HIV Testing Technology</b> <i>S. Michele Owen, PhD, Centers for Disease Control and Prevention</i>
6:30 PM – 6:45 PM	<b>Why HIV Tests are Regulated as They Are, and Understanding the Package Insert</b> <i>Pradip Akolkar, PhD, U.S. Food and Drug Administration</i>
6:45 PM – 7:00 PM	<b>Evaluating HIV Test Performance</b> <i>Bernard M. Branson, MD, Scientific Affairs</i>
7:00 PM – 7:15 PM	<b>Health Department HIV Testing Programs: Status and Opportunities</b> <i>Liisa M. Randall, PhD, National Alliance of State and Territorial AIDS Directors</i>
7:15 PM – 7:30 PM	<b>Uses of HIV Laboratory Data in Surveillance and Challenges with Reporting</b> <i>Albert Barksey, MPH, Centers for Disease Control and Prevention</i>
7:30 PM – 7:45 PM	<b>Use of Lab Data for Prevention</b> <i>AD McNaghten, PhD, MHSA, Centers for Disease Control and Prevention</i>
7:45 PM – 8:00 PM	Moderated Q & A



## TUESDAY | MARCH 22, 2016

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7:00 AM – 6:00 PM	<b>On-site Registration</b>
7:00 AM – 8:15 AM	<b>Satellite Breakfast Symposium Presented by ASHA and ASTDA</b> <b>HIV NAAT versus 4<sup>th</sup> Generation Antigen-Antibody Testing for Acute HIV Infection</b> <i>Joanne Stekler, MD, MPH, University of Washington</i> <b>Adding a Diagnostic Claim to HIV Prognostic Assays: Why not NAT?</b> <i>Elliot Cowan, PhD, Partners in Diagnostics, LLC</i> Sponsored by Hologic Inc.
8:15 AM – 8:20 AM	<b>Break</b>
8:20 AM – 8:30 AM	<b>Welcome</b> <i>Eugene McCray, MD, Director of the Division of HIV/AIDS Prevention in CDC's National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention</i>
8:30 AM – 9:30 AM	<b>Roundtable Discussion</b> <b>Overcoming the Challenges and Barriers to Implementing the HIV Diagnostic Testing Algorithm in your Laboratory</b> <i>Moderator: Monica M. Parker, PhD, New York State Department of Health</i> <i>Michael A. Pentella, PhD, D (ABMM), Massachusetts State Public Health Laboratory</i> <i>Anne M. Gaynor, PhD, Association of Public Health Laboratories</i>
9:30 AM – 10:45 AM	<b>Session A: Performance of HIV Screening Tests in the Laboratory</b> <i>Moderator: Barbara Body, PhD, D (ABMM), Laboratory Corporation of America</i>
9:30 AM – 9:45 AM	<b>A1. Performance Evaluation of Two Recently FDA-approved Antigen/antibody Combo Assays in Early HIV-1 Infections</b> <i>Silvina Masciotra, MS, Centers for Disease Control and Prevention</i>
9:45 AM – 10:00 AM	<b>A2. HIV Subtype and Acute Infection Sensitivity of Abbott Architect HIV Combo, Bio-Rad BioPlex 2200 HIV Ag-Ab and ADVIA Centaur HIV Ag/Ab Combo (CHIV)</b> <i>Teal Clocksin, MS, Tricore Reference Laboratories</i>
10:00 AM – 10:15 AM	<b>A3. Performance of the Abbott Architect HIV Ag/Ab 4th Gen Combo Assay in the US Army HIV Diagnostic Algorithm</b> <i>Sheila Peel, PhD, US Military HIV Research Program, WRAIR</i>
10:15 AM – 10:30 AM	<b>A4. Performance Evaluation of Determine™ HIV-1/2 Ag/Ab Combo in Plasma and Whole Blood from Early HIV-1 Infections</b> <i>Silvina Masciotra, MS, Centers for Disease Control and Prevention</i>
10:30 AM – 10:45 AM	Moderated Q & A



<b>10:45 AM – 11:00 AM</b>	<b>Morning Break</b>
<b>11:00 AM – 12:15 PM</b>	<b>Session B: Performance of Supplemental Tests and Nucleic Acid Tests</b> <b>Moderator: Richard L. Hodinka, PhD, University of South Carolina School of Medicine Greenville</b>
11:00 AM – 11:15 AM	<b>B1. Comparative Performance of the Geenius HIV-1/HIV-2 Supplemental Test in Florida's Public Health Testing Population</b> <b>S. Berry Bennett, MPH and Sally Fordan, BSMT, ASCP, Florida Bureau of Public Health Laboratories</b>
11:15 AM – 11:30 AM	<b>B2. Performance Evaluation of FDA-approved HIV Supplemental Assays</b> <b>Wei Luo, MS, Centers for Disease Control and Prevention</b>
11:30 AM – 11:45 AM	<b>B3. Diagnosis of Human Immunodeficiency Virus Type 2 (HIV-2) Infection by a HIV-2 Total Nucleic Acid Qualitative Assay Using Abbott m2000 platform</b> <b>Ming Chang, PhD, MB(ASCP), University of Washington</b>
11:45 AM – 12:00 PM	<b>B4. Validation of a Droplet Digital PCR Assay That Provides Sensitive Detection and Accurate Quantification of HIV-2 DNA in Whole Blood or Blood Cell Pellets</b> <b>Linda M. Styer, PhD, New York State Department of Health</b>
12:00 PM – 12:15 PM	Moderated Q & A
<b>12:15 PM – 1:30 PM</b>	<b>Lunch on your own</b>
<b>1:30 PM – 2:45 PM</b>	<b>Session C: CDC/APHL Laboratory Testing Algorithm</b> <b>Moderator: Laura G. Wesolowski, PhD, Centers for Disease Control and Prevention</b>
1:30 PM – 1:45 PM	<b>C1. Promoting the Recommended HIV Diagnostic Algorithm: Practical Information for Laboratories</b> <b>Laura D. Russell, MPH, New York State Department of Health</b>
1:45 PM – 2:00 PM	<b>C2. Evaluation of Newly Approved HIV Antigen-Antibody Tests Individually and When Used in the CDC/APHL HIV Diagnostic Algorithm</b> <b>Kevin P. Delaney, PhD, Centers for Disease Control and Prevention</b>
2:00 PM – 2:15 PM	<b>C3. Is It Always Necessary for the ARCHITECT 4th-Generation HIV-1/2 Ag/Ab Combo Assay to be Repeatedly Reactive before Moving Forward in the Centers for Disease Control and Prevention (CDC) HIV Screening Algorithm?</b> <b>Eric M. Ramos, MD, MS, University of Washington</b>

2:15 PM – 2:30 PM	<b>C4. APHL/CDC Project for Referral of HIV Nucleic Acid Amplification Testing (NAT) for US Public Health Laboratories (PHLs)</b> <i>Anne M. Gaynor, PhD, Association of Public Health Laboratories</i>
2:30 PM – 2:45 PM	Moderated Q & A
<b>2:45 PM – 3:00 PM</b>	<b>Afternoon Break</b>
<b>3:00 PM – 4:00 PM</b>	<b>Session D: CDC/APHL Laboratory Testing Algorithm (Part 2)</b> <i>Moderator: Kelly Wroblewski, MPH, MT(ASCP), Association of Public Health Laboratories</i>
3:00 PM – 3:15 PM	<b>D1. Efficacy of 4<sup>th</sup> Generation HIV Screening Algorithm in Detecting Acute HIV Infection and the Utility of Abbott Architect Signal-to-cutoff Ratio in that Regard</b> <i>Thomas P. Giordano, MD, MPH, Baylor College of Medicine</i>
3:15 PM – 3:30 PM	<b>D2. Real-world Performance of the New US HIV Testing Algorithm in Medical Settings</b> <i>Christopher D. Pilcher, MD, University of California, San Francisco</i>
3:30 PM – 3:45 PM	<b>D3. Comparison of Turn-around Time and Total Cost of HIV Testing Before and After Implementation of the 2014 CDC/APHL Laboratory Testing Algorithm for Diagnosis of HIV Infection</b> <i>Joseph D.C. Yao, MD, Mayo Clinic and Mayo Medical Laboratories</i>
3:45 PM – 4:00 PM	Moderated Q & A
<b>4:00 PM – 5:00 PM</b>	<b>Roundtable Discussion</b> <b>Challenges and Successes of Implementing the HIV Diagnostic Testing Algorithm: Reports from Four HIV Surveillance Programs</b> <i>Moderator: Irene Hall, PhD, Centers for Disease Prevention and Control</i> <i>Bridget J. Anderson, PhD, New York State Department of Health</i> <i>Marianne O'Connor, MPH, MT (ASCP), Michigan Department of Health and Human Services</i> <i>Joanne Gerber, MS, RN, New York State Department of Health</i> <i>Deepa T. Rajulu, MS, New York State Department of Health</i>
<b>5:00 PM – 6:30 PM</b>	<b>"Meet the exhibitors"</b> Use this opportunity to visit with the exhibitors and learn about the latest HIV tests. (Evening Reception Sponsored by Chembio Diagnostic Systems)

<b>7:00 AM – 5:00 PM</b>	<b>On-site Registration</b>
<b>7:00 AM – 8:15 AM</b>	<b>Satellite Breakfast Symposium Presented by ASHA and ASTDA</b> <b>HIV Testing: Evolution of the Species</b> <i>Thomas S. Alexander, PhD, D(ABMLI), Summa Health System</i> Sponsored by Bio-Rad Laboratories
<b>8:15 AM – 8:30 AM</b>	<b>Break</b>
<b>8:30 AM – 9:30 AM</b>	<b>Roundtable Discussion</b> <b>Improving the Impact of HIV Testing Through Better Linkage to Care and More Timely Viral Suppression</b> <i>Moderator: Kevin P. Delaney, PhD, Centers for Disease Control and Prevention</i> <i>Eugene G. Martin, PhD, Rutgers University - Robert Wood Johnson Medical School</i> <i>Joanne Stekler, MD, MPH, University of Washington</i> <i>Christopher D. Pilcher, MD, University of California, San Francisco</i>
<b>9:30 AM – 10:45 AM</b>	<b>Session E: Streamlining Test Result Turnaround Time and Linkage to Care</b> <i>Moderator: Liisa M. Randall, PhD, National Alliance of State and Territorial AIDS Directors</i>
9:30 AM – 9:45 AM	<b>E1. Rapid HIV Testing and Linkage to Medical Care, New Jersey, 2007-2011</b> <i>Debbie Mohammed, DrPH, Saint Michael's Medical Center</i>
9:45 AM – 10:00 AM	<b>E2. Using Reported HIV Diagnostic Testing Results to Identify Cases of Acute HIV Infection: Lessons Learned from New York State</b> <i>Bridget J. Anderson, PhD, New York State Department of Health</i>
10:00 AM – 10:15 AM	<b>E3. Implementation of 4<sup>th</sup> Generation HIV Antigen-Antibody Testing Algorithm at a Public Health STD Clinic for Real-time Screening and Confirmation</b> <i>Steve Gradus, PhD, City of Milwaukee Health Department Laboratory</i>
10:15 AM – 10:30 AM	<b>E4. Perceptions and Performance of Self-administered Rapid HIV Tests Conducted by Untrained Users in Real-World Settings</b> <i>Pollyanna R. Chavez, PhD, Centers for Disease Control and Prevention</i>
10:30 AM – 10:45 AM	Moderated Q & A
<b>10:45 AM – 11:00 AM</b>	<b>Morning Break</b>
<b>11:00AM – 12:15 AM</b>	<b>Session F: Performance of CLIA-Waived HIV Tests</b> <i>Moderator: Benjamin Tsoi, MD, MPH, New York City Department of Health and Mental Hygiene</i>



11:00 AM – 11:15 AM	<b>F1. Implementing HIV Testing in Nonclinical Settings: Updating CDC Guidance and Program Resources for HIV Testing</b> <i>Kristina L. Grabbe, MPH, Centers for Disease Control and Prevention</i>
11:15 AM – 11:30 AM	<b>F2. Performance Evaluation of the INSTI HIV-1/2 Antibody Point-of-Care Test in Early and Established Infections</b> <i>Sarah Adams, BS, Centers for Disease Control and Prevention</i>
11:30 AM – 11:45 AM	<b>F3. Performance of the NJ Rapid 4<sup>th</sup> Generation HIV POC Testing Algorithm</b> <i>Eugene G. Martin, PhD, Rutgers University - Robert Wood Johnson Medical School</i>
11:45 AM – 12:00 PM	<b>F4. Evaluation of New HIV Testing Technologies in a Clinical Setting with High Incidence: Rationale, Study Design and Preliminary Results from Project DETECT</b> <i>Kevin P. Delaney, PhD, Centers for Disease Control and Prevention</i>
12:00 PM – 12:15 PM	Moderated Q & A
<b>12:15 PM – 1:30 PM</b>	<b>Lunch on your own</b>
<b>1:30 PM – 2:45 PM</b>	<b>Session G: Special Testing Circumstances</b> <i>Moderator: S. Berry Bennett, MPH, Florida Bureau of Public Health Laboratories</i>
1:30 PM – 1:45 PM	<b>G1. Evolving State Laboratory Diagnostic Capacity During an HIV Outbreak</b> <i>Sarah J. Blosser, PhD, Indiana State Department of Health</i>
1:45 PM – 2:00 PM	<b>G2. Beyond Drug Resistance Testing: Using HIV-1 Sequence Data to Infer Transmission Networks and Inform Public Health Action</b> <i>M. Cheryl B. Ocfemia, MPH and Ellsworth M. Campbell III, MS, Centers for Disease Control and Prevention</i>
2:00 PM – 2:15 PM	<b>G3. Absence of Serological Response Following Early Treatment of Acute HIV Infection</b> <i>Mark M. Manak, PhD, Henry Jackson Foundation</i>
2:15 PM – 2:30 PM	<b>G4. HIV Antibodies as Markers of HIV Systemic Reservoir and Viral Suppression</b> <i>Michael P. Busch, MD, PhD, Blood Systems Research Institute</i>
2:30 PM – 2:45 PM	Moderated Q & A
<b>2:45 PM – 3:00 PM</b>	<b>Afternoon Break</b>
<b>3:00 PM – 4:15 PM</b>	<b>Session H: Testing Alternatives Using Dried Blood Specimens</b> <i>Moderator: Joanne Mei, PhD, Centers for Disease Control and Prevention</i>

3:00 PM – 3:15 PM	<b>H1. Evaluation of the Performance of the Bio-Rad GS HIV Combo Ag/Ab EIA and Bio-Rad Geenius™ HIV-1/2 Supplemental Assay Using Dried Blood Spots as an Alternative Specimen Type</b> <i>Silvina Masciotra, MS, Centers for Disease Control and Prevention</i>
3:15 PM – 4:15 PM	<b>Roundtable Discussion</b> <b>Dried Blood Spots (DBS) May Have High Utility Both in Resource Limited Settings and in Hard to Reach Populations for Diagnosis and Treatment Decisions</b> <i>Moderator: Joanne Mei, PhD, Centers for Disease Control and Prevention</i> <i>Silvina Masciotra, MS, Centers for Disease Control and Prevention</i> <i>Levinia Crooks, BA, Dep Ed, MBA, Australasian Society for HIV, Viral Hepatitis and Sexual Health Medicine</i> <i>Philip Cunningham, MSc Med, New South Wales State Reference Laboratory for HIV</i> <i>Bernard M. Branson, MD, Scientific Affairs</i>
4:15 PM – 5:45 PM	<b>Poster Session and "Meet the Exhibitors"</b>





**7:00 AM – 8:15 AM**

**Satellite Breakfast Symposium Presented by ASHA and ASTDA**

**Reducing Missed Opportunities: Reconnecting HIV & STI Screening**

**Barbara Van Der Pol, MD, PhD, University of Alabama at Birmingham School of Medicine**

**HIV Testing in the STD Clinic Setting**

**Cornelis A. Rietmeijer, MD, PhD, American Sexually Transmitted Diseases Association**

Sponsored by Roche Diagnostics

**8:15 AM - 8:30 AM**

**Break**

**8:30 AM - 9:30 AM**

**Session I: Integrated Testing for Multiple Pathogens**

**Moderator: Cornelis A. Rietmeijer, MD, PhD, American Sexually Transmitted Diseases Association**

8:30 AM - 8:45 AM

**I1. Evaluation of an Emergency Department HIV and Syphilis Screening Program Using Rapid Point of Care Diagnostics in Detroit, Michigan, 2015**

**David Cal Ham, MD, MPH, Centers for Disease Control and Prevention**

8:45 AM - 9:00 AM

**I2. Multiplex Screening Assays - Advancing Targeted Screening of Co-morbidity via DPP® HIV-Syphilis Multiplex Rapid Test**

**Tom Ippolito, BS, ChemBio Diagnostic Systems, Inc.**

9:00 AM - 9:15 AM

**I3. Performance of a Rapid, 60 second Multiplex Test for Simultaneous Detection of Antibodies to HIV-1, HIV-2 and *T. pallidum* in Serum, Plasma and Whole Blood**

**Richard A. Galli, BS, bioLytical Laboratories**

9:15 AM - 9:30 AM

Moderated Q & A

**9:30 AM - 9:45 AM**

**Morning Break**

**9:45 AM - 11:15 AM**

**Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance**

**Moderator: Eugene G. Martin, PhD, Rutgers University - Robert Wood Johnson Medical School**

9:45 AM - 10:00 AM

**J1. The Effects of MDRI Updates and Transition to a New Recency Assay on HIV incidence Estimates in a Selected Number of HIV Surveillance Areas, United States**

**Angela L. Hernandez, MD, MPH, Centers for Disease Control and Prevention**

10:00 AM - 10:15 AM

**J2. Development and Evaluation of a Bead-Based Multiplex Assay for HIV Detection, Serotyping and Estimation of Recent Infection**

**Ernest L. Yufenyuy, PhD, Centers for Disease Control and Prevention**

- 10:15 AM - 10:30 AM     **J3. Unmodified Diagnostic Assay Provides Similar Performance to Avidity Modification for Surveillance and Clinical Recency Staging Applications**  
*Eduard Grebe, PhD, Stellenbosch University*
- 10:30 AM - 10:45 AM     **J4. A Generalizable Method with Improved Accuracy for Estimation of HIV Infection Duration, Using Clinical HIV Testing Histories**  
*Christopher D. Pilcher, MD, University of California, San Francisco*
- 10:45 AM - 11:00 AM     **J5. Use of the Avioq VioOne Profile Assay for Detection of Recent HIV-1 Infection**  
*Don E. Lockwood, PhD, Avioq, Inc.*
- 11:00 AM - 11:15 AM     Moderated Q & A
- 11:15 AM - 12:15 PM     Feedback Session: New Technology and its Impact on the CDC/APHL Laboratory Testing Algorithm**  
*S. Michele Owen, PhD, Centers for Disease Control and Prevention*  
*Monica M. Parker, PhD, New York State Department of Health*  
*Laura G. Wesolowski, PhD, Centers for Disease Control and Prevention*
- 12:15 PM - 12:30 PM     Closing Statements**  
*S. Michele Owen, PhD, Conference Co-Chair, Centers for Disease Control and Prevention*



## Session A: Performance of HIV Screening Tests in the Laboratory

### A1. Performance Evaluation of Two Recently FDA-approved Antigen/antibody Combo Assays in Early HIV-1 Infections

S. Masciotra<sup>1</sup>, K. A. Price<sup>1</sup>, W. Fowler<sup>1</sup>, and S. M. Owen<sup>1</sup>

<sup>1</sup> DHAP HIV Laboratory branch, Centers for Disease Control and Prevention

**Objective:** The BioPlex<sup>®</sup> 2200 HIV Ag-Ab (Bplex; Bio-Rad Laboratories) and the ADVIA Centaur<sup>®</sup> HIV Ag/Ab (AdviaC; Siemens) Combo assays received approval by the Food and Drug Administration (FDA) in 2015. Bplex can differentiate reactivity against antigen, HIV-1 antibodies, and HIV-2 antibody while AdviaC gives non-differentiated results. We evaluated the performance of both assays in plasma specimens from individuals in early stages of HIV-1 infections.

**Methods:** Plasma specimens from 26 previously characterized commercial seroconverters were tested with Bplex and AdviaC. Assay performance was assessed by estimating the relative sensitivity of the assay before positive Western blot (WB) using a 50% cumulative frequency analysis (17 HIV-1 seroconverters) and by comparing to previously generated data with Abbott Architect (ARC), GS HIV Combo Ag/Ab (BRC), Alere Determine HIV-1/2 Ag/Ab combo (DC) and Roche HIV-1 RNA viral load assay (VL). Paired comparisons were done using the McNemar's test. Antigen detection was compared to VL results.

**Results:** Bplex and AdviaC became positive 21.5 and 18 days before the first positive Western-blot, respectively. From the paired comparison (n=229), Bplex performed significantly better than DC ( $p=0.0033$ ) and BRC ( $p=0.045$ ), whereas no significant difference was observed with ARC ( $p=0.72$ ). AdviaC performance (n=222) was similar when compared to DC ( $p=0.22$ ), BRC ( $p=0.83$ ) and ARC ( $p=0.33$ ). Only Bplex can distinguish early antigen reactivity and it was observed in specimens with VL ranging from 85.8 to  $10^7$  RNA copies/ml. With Bplex, three seroconverters showed a second negative phase during seroconversion. With AdviaC, no second negative phase was observed in the available results.

**Conclusions:** The recently FDA-approved Ag/Ab combo automated platforms perform well in early HIV-1 infections. Like the rapid test DC, Bplex allows identification of antigen-reactive specimens; however Bplex detected antigen sooner than DC in plasma specimens. Use of a screening Ag/Ab differentiation assay may lead to an alteration of the current recommended laboratory algorithm. However, additional studies are required to document the public health and individual benefit of antigen detection at the first step in the algorithm. With or without antigen differentiation, Ag/Ab combo assays have the ability to detect infection earlier in the course of disease.

## Session A: Performance of HIV Screening Tests in the Laboratory

**A2. HIV Subtype and Acute Infection Sensitivity of Abbott Architect HIV Combo, Bio-Rad BioPlex 2200 HIV Ag-Ab and ADVIA Centaur HIV Ag/Ab Combo (CHIV)**

T. Clocksin<sup>1</sup>, S. Young<sup>1</sup>, K. Culbreath<sup>1,2</sup>, and M. Crossey<sup>1</sup>

<sup>1</sup>TriCore Reference Laboratories

<sup>2</sup>University of New Mexico

**Objective:** Compare HIV subtype and acute infection sensitivities of HIV Ag/Ab assays on the Abbott Architect, Bio-Rad BioPlex and Siemens Centaur.

**Methods:** Our ten subtype panel included 13 antibody and 19 antigen positive samples. Antibody-positive members of this panel consisted of human plasma samples diluted with HIV-negative plasma to assay discriminating concentrations. Antigen-positive members were produced from viral isolates of tissue cultures and diluted in HIV-negative plasma. Three seroconversion panels consisted of human plasma with multiple antigen-positive bleed dates prior to seroconversion. An additional sensitivity panel was prepared from the World Health Organization HIV p24 antigen standard. Finally, 67 clinical samples included 36 seropositive and 31 seronegative patient samples. Samples were tested in single runs on all three assays.

**Results:** On the subtype panel the Architect, BioPlex, and Centaur assays detected 29/29, 25/29 and 8/29 reactive samples, respectively. The BioPlex detected all antibody positive samples, but missed four antigen positive samples. The Centaur detected 8/13 antibody positive samples and missed all 16 antigen positive samples. The Architect and Centaur showed equivalent performance on the seroconversion panels, while the BioPlex was able to detect one bleed date earlier on all three panels. The lowest p24 concentration detectable by the BioPlex, Architect and Centaur was 0.3 IU/mL, 1.25 IU/mL and 2.5 IU/mL, respectively. All platforms showed 100% concordance on the 67 clinical samples tested.

**Conclusion:** The Architect and the BioPlex performed similarly on the HIV subtype panel. The BioPlex failed to detect p-24 antigen in subtypes CRF01, G, and O. These subtypes are rarely seen in the US. The Centaur performed poorly on the subtype panel for both antigen and antibody detection. On the three seroconversion panels, the BioPlex detected reactive samples one bleed date (two, three or five days) earlier than the Centaur and Architect. All three assays performed equivalently using clinical samples. None of the clinical samples were from known acute HIV cases. The BioPlex is the most sensitive in detecting p24 antigen which is beneficial in early detection of acute HIV. However, laboratories should consider local population prevalence of HIV subtypes when selecting an assay for HIV Ab/Ag testing.

## Session A: Performance of HIV Screening Tests in the Laboratory

**A3. Performance of the Abbott Architect HIV Ag/Ab 4<sup>th</sup> Gen Combo Assay in the US Army HIV Diagnostic Algorithm**

M. Manak<sup>1</sup>, B. Danboise<sup>2</sup>, L. Jagodzinski<sup>2</sup>, A. Mott<sup>2</sup>, A. Shutt<sup>1</sup>, J. Ouellette<sup>1</sup>, Y. Beale<sup>2</sup>, J. Malia<sup>2</sup>, and S. Peel<sup>2</sup>

<sup>1</sup> US Military HIV Research Program, HJF

<sup>2</sup> US Military HIV Research Program, WRAIR

**Objectives:** The US Army HIV Surveillance Algorithm is designed to diagnose HIV infection with a single specimen, so that personnel may be rapidly routed into appropriate care and treatment programs. In March 2014, the US Army Contract Laboratory switched its primary HIV screening assay from the 3rd Gen HIV-1/2/O EIA (Bio-Rad, Redmond, WA) to the 4th Gen Architect HIV Ag/Ab Combo (Abbott, Chicago, IL), thus reducing the diagnostic window period by 7-8 days. The assay change resulted in increased cost for supplemental confirmatory testing. In this study, we examined the capacity of the Bio-Rad Ag/Ab Combo to improve algorithm specificity and Positive Predictive Value (PPV).

**Methods:** US Army Architect Combo assay repeat reactive (RR) samples are shipped to WRAIR for supplemental confirmatory testing by MultiSpot (MS) (Bio-Rad, Benicia, CA) and HIV-1 Western Blot (WB) (Bio-Rad, Benicia, CA), with WB positive (Pos) samples considered positive for HIV infection. WB Indeterminate or Negative (Neg) samples are reflexed to Aptima HIV-1 RNA qualitative assay (Hologic, La Jolla, CA); reactive Aptima is indicative of acute HIV-1 infection. Between January and August 2015 all RR Architect specimens submitted to WRAIR for confirmation were also retested by the Bio-Rad Ag/Ab Combo.

**Results:** Of 663,159 samples tested during the study period, 1,135 were RR by the Architect Combo of which 407 were positive for HIV (Table 1). Of the 407, 388 were WB Pos, and 19 were WB Neg/RNA Pos. The Architect Combo demonstrated high Sensitivity (100%), Specificity (99.89%), and Negative Predictive Value (100%), but low PPV (35.86%) relative to the confirmatory algorithm. Of 728 Architect RR specimens which were negative by WB and RNA, only 22 (3.0%) were reactive by the Bio-Rad Combo assay. All Architect RR, WB Neg/RNA Pos samples tested were reactive by the Bio-Rad Combo.

**Conclusions:** Reflex in duplicate of Architect initial reactive specimens to the Bio-Rad Combo assay would maintain sensitivity, significantly reduce the cost of supplemental confirmatory testing, and improve algorithm specificity (99.89% to 99.99%) and PPV (35.86% to 94.87%).

**Table 1.** Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) of the Architect Ag/Ab combo assay as used in the US Army HIV Surveillance Algorithm relative to confirmed HIV positive, and increase of Specificity and PPV with addition of Bio-Rad Combo prior to confirmatory testing.

		Confirmed Pos		
		+	-	
Architect	+	407	728	1,135
	-	0	662,024	662,024
		407	662,752	663,159

		Confirmed Pos		
		+	-	
Architect + Bio-Rad	+	407	22	429
	-	0	662,730	662,730
		407	662,752	663,159

	Value	95% CI	
Sensitivity	100%	99.10%	100%
Specificity	99.89%	99.88%	99.90%
PPV	35.86%	33.06%	38.73%
NPV	100%	100%	100%

	Value	95% CI	
Sensitivity	100%	99.10%	100%
Specificity	99.99%	99.99%	100%
PPV	94.87%	92.34%	96.76%
NPV	100%	100%	100%



# Session A: Performance of HIV Screening Tests in the Laboratory

## A4. Performance Evaluation of Determine™ HIV-1/2 Ag/Ab Combo in Plasma and Whole Blood from Early HIV-1 Infections

S. Masciotra<sup>1</sup>, W. Luo<sup>1</sup>, S. Cohen<sup>3</sup>, L. Hall<sup>4</sup>, P. J. Peters<sup>2</sup>, and S. M. Owen<sup>1</sup>

<sup>1</sup> DHAP HIV Laboratory branch

<sup>2</sup> DHAP, Centers for Disease Control and Prevention

<sup>3</sup> San Francisco Department of Public Health

<sup>4</sup> ICF International

**Objective:** The Determine™ HIV-1/2 Ag/Ab Combo (DC) rapid test detects early HIV-1 infections when used with plasma. Reported performance of DC on whole blood from individuals during early infection is inconsistent. We evaluated the performance of DC with plasma and whole blood in the context of screening for early HIV screening.

**Methods:** We tested two sets of samples with DC and compared results to previous data from the Abbott ARCHITECT (ARC), Multispot HIV-1/HIV-2 rapid test (MS), and APTIMA HIV-1 RNA assay (Aptima) or Abbott m2000 HIV-1 RNA viral load (VL). The sets included 329 plasma specimens collected in San Francisco in a prospective study (STOP), and mock whole blood created from 107 sequential plasma specimens from 20 seroconverters to which washed red blood cells were added at 40%. The McNemar's test was used for statistical comparisons.

**Results:** Of 288 ARC-positive specimens identified in the STOP study, DC detected 54.1% (46/85) of the early (MS- negative or –indeterminate) infections ( $p<0.0001$ ) and 100% (203/203) of the established infections (MS-positive). Of 85 early infections from the STOP study, DC detected 38 of 74 (51.4%) specimens that were ARC-positive/MS-negative with a median VL of  $1.65 \times 10^6$  cop/ml and 8 of 11 (72.7%) specimens that were ARC-positive/MS-indeterminate with a median VL of  $2.33 \times 10^6$  cop/ml. DC false-reactivity was not observed. The table shows the reactivity of DC in plasma and mock whole blood from seroconverters. Of 55 Aptima-positive/ARC-positive/MS-negative or –indeterminate specimens, DC was reactive in 51 (92.7%) of plasma ( $p=0.1336$ ) and 31 (56.4%) of whole blood ( $p<0.0001$ ). Eight seroconverters had a median delay in reactivity of six days in whole blood compared to plasma and one never became reactive. When all seroconverters were analyzed together, there was no difference in reactivity between whole blood and plasma.

**Conclusions:** DC used with plasma detected fewer specimens with early HIV-1 infection compared to an instrumented lab-based 4th generation. The delayed reactivity of DC with whole blood compared to plasma was mostly due to loss of antigen detection in whole blood. In settings where lab-based testing is not feasible DC might represent an advantage over other rapid tests in detecting infections earlier.

**Table.** DC reactivity in plasma and whole blood among HIV-1 seroconverters

	total	DC plasma				DC whole blood				invalid
		Ag-/	Ag+/ Ab-	Ag+/ Ab+	Ag-/	Ag-/	Ag+/ Ab-	Ag+/ Ab+	Ag-/	
		Ab-	Ab-	Ab+	Ab+	Ab-	Ab-	Ab+	Ab+	
<b>Results from previous testing</b>										
Aptima-neg/ARC-neg	8	8				8				
Aptima-pos/ARC-neg	14	14				12	1			1
Aptima-pos/ARC-pos/MS-neg	39	4	30	3	2	16	19	2	1	1
Aptima-pos/ARC-pos/MS-ind	16		1	5	10	7	1	4	4	
Aptima-pos/ARC-pos/MS-pos	30	1	1	5	23	1	1	3	25	

ARC: Architect; MS: Multispot; neg: negative; ind: indeterminate; pos: positive

## Session B: Performance of Supplemental Tests and Nucleic Acid Tests

**B1. Comparative Performance of the Geenius HIV-1/HIV-2 Supplemental Test in Florida's Public Health Testing Population**

S.B. Bennett<sup>1</sup>, S. Fordan<sup>1</sup>, S. Crowe<sup>1</sup>, O. Bajzik<sup>2</sup>, G. Stewart<sup>2</sup>, M. Ferret<sup>2</sup>, and M. Cardona<sup>2</sup>

<sup>1</sup> Retrovirology, FL Dept. of Health

<sup>2</sup> Infectious Disease Division, Bio-Rad Laboratories

**Objective:** The new HIV Diagnostic Algorithm (CDC, June 2014) recommends using an immunoassay (IA) that differentiates HIV-1 from HIV-2 after a reactive HIV-1/2 Ag/Ab (Combo) screening test. In October 2014, Bio-Rad Laboratories introduced the FDA approved Geenius HIV-1/HIV-2 Supplemental assay (Geenius) to eventually replace Multispot HIV-1/HIV-2 (MS) as the second test in the new algorithm. Geenius uses an automated cassette reader and proprietary software to interpret HIV-1 and HIV-2 results. The purpose of this investigation was to evaluate the performance of Geenius as well as the software/reader.

**Methods:** We conducted a comparative performance evaluation of the Geenius HIV-1/HIV-2 Supplemental testing system with 340 in-house frozen specimens previously tested with Abbott Combo IA, MS Differentiation IA and in some instances APTIMA HIV-1 RNA. The panel consisted of: 250 HIV-1 established infections, 60 false positive Combo specimens, 20 algorithm-defined HIV-1 acute infections, and 10 algorithm-defined HIV-1 early infections. In addition, 10 known HIV-2 Ab positive specimens, provided by Bio-Rad, were tested with Geenius.

**Results:**

- Of the 250 HIV-1 established infection specimens, the Geenius clinical interpretation of HIV-1 Positive (or HIV Positive) was 100% in agreement with MS HIV-1 reactivity. Only 1.6% (4/250) was Untypable (HIV-1 positive, HIV-2 positive).
- Of the 60 false positive Combo specimens with MS results of HIV-1/2 nonreactive (57) or HIV-1 indeterminate (3), 95% (57/60) had a Geenius clinical interpretation of HIV Negative, in addition 1.7% (1/60) was HIV-1 Indeterminate and 3.3% (2/60) HIV-2 Indeterminate after retesting four HIV-2 indeterminate initial results.
- Of the 20 HIV-1 algorithm-defined acute infection specimens (MS nonreactive), 85% (17/20) were Geenius HIV-1 Negative and 15% (3/20) HIV-1 Indeterminate.
- Similarly, of the 10 algorithm-defined early infection specimens (MS indeterminate), 30% (3/10) were Geenius HIV-1 Indeterminate, 60% (6/10) HIV-1 Positive and 10% (1/10) HIV Negative.
- Geenius was concordant with all HIV-2 Ab positive specimens.

**Conclusion:** The ability of Geenius to detect acute, early and established HIV infections was similar to MS. Fewer HIV-1 indeterminate results were observed with Geenius compared to MS on false positive Combo specimens, but overall more HIV-2 indeterminate results occurred with Geenius. Repeat testing may resolve approximately half as HIV-2 negative, resulting in similar performance between Geenius and MS.

## Session B: Performance of Supplemental Tests and Nucleic Acid Tests

**B2. Performance Evaluation of FDA-approved HIV Supplemental Assays**

W. Luo<sup>1</sup>, S. Adams<sup>3</sup>, V. Sullivan<sup>1</sup>, P. J. Peters<sup>2</sup>, E. Westheimer<sup>4</sup>, S. Cohen<sup>5</sup>, C. Gay<sup>6</sup>, L. Hightow-Weidman<sup>6</sup>, S. M. Owen<sup>1</sup>, and S. Masciotra<sup>1</sup>

<sup>1</sup> DHAP HIV Laboratory branch, Centers for Disease Control and Prevention

<sup>2</sup> Centers for Disease Control and Prevention

<sup>3</sup> Oak Ridge Institute for Science and Education

<sup>4</sup> New York City Department of Health & Mental Hygiene

<sup>5</sup> San Francisco Department of Public Health

<sup>6</sup> University of North Carolina

**Objective:** The CDC/APHL guidelines for HIV diagnosis in the laboratory recommends the use of a HIV-1/HIV-2 differential supplemental assay after a reactive result with an antigen/antibody combo screening test. The FDA-approved differentiation assays are Multispot HIV-1/HIV-2 test (MS) and Geenius HIV-1/HIV-2 Supplemental assay (Geenius). We compared the performance of these two FDA-approved supplemental tests using plasma specimens.

**Methods:** Plasma specimens were tested with Abbott Architect (ARC) and/or Bio-Rad Combo (BRC), MS, Geenius, HIV-1 RNA assays (NAT), and HIV-2 PCR. Early infections were ARC-positive/MS-negative or –indeterminate/NAT-positive, established infections were ARC- or BRC-positive/MS-positive or –undifferentiated, and HIV-false reactive were ARC- positive/ NAT-negative (HIV-negative). The specimens included 85 HIV-1 early infections, 82 established infections (41 HIV-1 and 41 HIV-2 -16 from US and 25 from Ivory Coast), and 92 ARC-false reactive. Eighty-seven ARC false-reactive plasma specimens were available for testing with BRC.

**Results:** Assay performance is described in the Table. Geenius confirmed five more early HIV-1 infections than MS, but 18 HIV infections (eight were MS-HIV-1 positive and ten MS-HIV-2 positive) required NAT for confirmation. With MS, seven HIV-1 and 16 HIV-2 specimens required further dilution for differentiation; one specimen each of HIV-1 and HIV-2 remained HIV-undifferentiated. Most Geenius HIV-untypable results were HIV-2 positive with MS after the dilution protocol. Geenius HIV-2 indeterminate (gp140 HIV-2 reactivity only) results were observed among HIV-1 and HIV-false reactive specimens. Overall, MS confirmed 40 HIV-1 and 40 HIV-2 infections, while Geenius confirmed 38 HIV-1 and 31 HIV-2 infections. Of ARC false-reactive specimens, 95.6% were MS HIV-negative and 93.5% were Geenius HIV-negative. Of 87 ARC false-reactive specimens, 6 (6.9%) were also BRC-positive, including one MS HIV-1 indeterminate/Geenius HIV-1 positive, and one MS HIV-1 indeterminate/Geenius HIV-1 indeterminate.

**Conclusions:** MS and Geenius had comparable performance in diagnosing HIV-1 in the recommended laboratory diagnostic algorithm. When compared to MS as a supplemental test, use of Geenius decreased the amount of testing required for HIV-1 antibody positive specimens by eliminating the need for dilutions and retesting. However, due to additional test interpretations available for Geenius and in particular the HIV-2 indeterminate interpretation, more NAT testing may be required

**Table.** Performance of HIV supplemental assays

		Geenius results						
	Total	HIV negative	HIV-1 indeter	HIV-1 positive	HIV-2 indeter	HIV-2 positive	HIV-2 pos (HIV-1 XR)	HIV untyp
HIV-1 infections								
ARC-positive/MS-negative	74	65	4	2	3			
ARC-positive/MS-indeter	11	5	3	3				
ARC-positive/MS-HIV-1 positive	40	3	5	32*				
ARC-positive/MS-undifferentiate	1			1				
HIV-2 infections								
BRC-positive/MS-HIV-2 positive	40	1			2**	15	15	7***
BRC-positive/MS-undifferentiate	1						1	
HIV-negative (false reactive)								
ARC-positive/MS-negative	86	82	1		3			
ARC-positive/MS-indeter	2		1	1				
ARC-positive/MS-HIV-2 positive	2	2						

indeter: indeterminate; HIV-1 XR: cross-reactivity with HIV-1; untyp: untypable

HIV infections were confirmed with nucleic acid testing

\* eight required 1:10 dilution with MS

\*\* one required 1:10 dilution with MS

\*\*\* four required 1:10 dilution and two 1:100 dilution with MS

## Session B: Performance of Supplemental Tests and Nucleic Acid Tests

**B3. Diagnosis of Human Immunodeficiency Virus Type 2 (HIV-2) Infection by a HIV-2 Total Nucleic Acid Qualitative Assay Using Abbott m2000 platform**

**M. Chang**<sup>1</sup>, A. J. Wong<sup>1</sup>, D. N. Raugi<sup>1</sup>, R. A. Smith<sup>1</sup>, A. M. Seilie<sup>1</sup>, J. P. Ortega<sup>1</sup>, K. Bogusz<sup>1</sup>, K. Faye<sup>2</sup>, F. Sall<sup>2</sup>, S. Ba<sup>2</sup>, I. Sall<sup>3</sup>, A. Niang<sup>3</sup>, M. Seydi<sup>2</sup>, G. S. Gottlieb<sup>1</sup>, and R. W. Coombs<sup>1</sup>

<sup>1</sup> University of Washington

<sup>2</sup> Universite Cheikh Anta Diop de Dakar

<sup>3</sup> Centre de Sante de Ziguinchor

**Objective:** The 2014 CDC fourth generation HIV diagnostic testing algorithm does not address acute HIV-2 infection and undifferentiated dual HIV-1/HIV-2 seropositivity. Detectable HIV-2 RNA in plasma can be used to confirm HIV-2 infection. However, undetectable HIV-2 plasma viral loads have been reported in a significant proportion of ART-naïve patients. A second-line confirmatory assay for detecting HIV-2 DNA and RNA (total nucleic acid, TNA) in peripheral blood mononuclear cells (PBMC) is essential for HIV-2 diagnosis. We developed and validated a qualitative TNA assay detecting HIV-2 in PBMC from patients with undetectable plasma HIV-2 RNA but tested positive for HIV-2 or undifferentiated HIV-1/-2 antibodies.

**Methods:** The qualitative HIV-1 and HIV-2 TNA assays used Abbott m2000 platform. External controls, an internal control, and a human endogenous gene control assessed nucleic acid extraction and assay inhibitors. Assay sensitivity was evaluated by spiking various copies of a HIV-2 full-genome plasmid to 1 million PBMC. Assay specificity was evaluated using PBMC from 25 HIV-1 seropositive, 25 HIV seronegative, and 30 HIV-2 seropositive individuals. Plasma HIV-1 antigen/antibody and HIV-2 antibody were detected using Abbott ARCHITECT HIV Ag/Ab Combo assay (Combo) and Bio-Rad Multispot HIV-1/-2 Rapid Test (Multispot).

**Results:** The assay limit of detection was 25 copies/million cells (95% CI, 13-37 copies/million cells). All 30 HIV-2 PBMC tested positive, notably including 21 samples containing undetectable plasma HIV-2 RNA (LOD=8 RNA copies/ml). Diagnostic performance was evaluated by comparing the outcome of PBMCs tested by the assay to results obtained with the Combo and Multispot assays using matching plasma samples from the same patients. Of 30 HIV-2 seropositive plasma specimens, one was HIV non-reactive by Multispot. Plasma samples from 50 non-HIV-2 individuals were confirmed non-reactive to HIV-2 Ab. Therefore, the agreement between the HIV-2 TNA assay and the combined results of the immunoassays was 98.8% (79 of 80). Furthermore, HIV-2 TNA was detected in 7 PBMC out of 8 HIV-1/2 dually- seropositive patients (Table).

**Conclusion:** The TNA assay can detect HIV-2 in PBMC from patients with either serologically-confirmed HIV-2 infection or indeterminate HIV status, and may be suitable for confirming HIV-2 infection in the CDC 4th generation HIV testing algorithm.



**Table.** Analysis of plasma and PBMC samples from HIV-1/2 dually-seropositive<sup>^</sup> patients.

Specimen ID	Plasma sample			PBMC	
	Multispot	HIV-1 RNA c/mL	HIV-2 RNA c/mL	HIV-1 TNA	HIV-2 TNA
<b>HD01</b>	HIV-1/2 at 1:100*	TND <sup>#</sup>	TND	Detected	1.38 DC <sup>§</sup>
<b>HD02</b>	HIV-1/2 at 1:100	85120	2592	Detected	11.60DC
<b>HD06</b>	HIV-1/2 at 1:100	510596	311	Detected	5.62 DC
<b>HD09</b>	HIV-1/2 at 1:100	TND	TND	Detected	8.08 DC
<b>HD12</b>	HIV-1/2 at 1:100	TND	TND	Detected	Detected <sup>~</sup>
<b>H2A036</b>	HIV-1/2 at 1:100	TND	136	Detected	7.96DC
<b>HD13</b>	HIV-1/2 at 1:100	Detected, <40c/mL	28726	Not detected	9.50 DC
<b>HD10</b>	HIV-1/2 at 1:100	13730	TND	Detected	Not detected

<sup>^</sup> HIV-1/HIV-2 dual seropositivity determined by Determine (Alere) and Immunocomb II (Organics).

\* All samples were tested at each of three concentrations: without dilution, at 1:10 and at 1:100 dilutions.

<sup>#</sup> Target Not Detected.

<sup>§</sup> The Delta Cycle (DC) value for each sample was calculated as the defined Cut Off (CD) cycle minus the target cycle number.

<sup>~</sup> Detected by a second assay using HIV2BHQplus probe.

## Session B: Performance of Supplemental Tests and Nucleic Acid Tests

**B4. Validation of a Droplet Digital PCR Assay That Provides Sensitive Detection and Accurate Quantification of HIV-2 DNA in Whole Blood or Blood Cell Pellets**

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<sup>1</sup> Bloodborne Viruses Laboratory, Wadsworth Center, New York State Department of Health

<sup>2</sup> Biomedical Sciences Department, School of Public Health, University at Albany

**Objective:** Human immunodeficiency virus, type 2 (HIV-2) is rare in the United States and has often been misclassified as HIV-1 because of antibody cross-reactivity on the Western blot. The HIV-1/HIV-2 differentiation assay, used as a supplemental test in the recommended algorithm, has improved HIV-2 detection. However, there are no FDA-approved HIV-2 nucleic acid assays to resolve indeterminate HIV-2 antibody results. HIV-2 RNA levels are naturally low; therefore, non-detectable RNA does not exclude HIV-2 infection. HIV-2 DNA is more abundant than RNA and exists in several forms (linear, LTR circles, provirus). Our objective was to develop a droplet digital PCR (ddPCR) assay to detect and quantify total HIV-2 DNA in easy-to-obtain specimens, blood and blood cell pellets (BCP).

**Methods:** BCP are the cells remaining after centrifuging blood and removing plasma. We tested frozen blood and BCP spiked with Group A and Group B HIV-2 plasmids or remnant frozen BCP from EDTA blood collected for HIV-2 viral load testing. DNA was extracted using the Biomereix EasyMAG on-board whole blood protocol. PCR targets included HIV-2 LTR and an internal control virus. The Bio-Rad QX100 ddPCR system partitioned each reaction into ~14,000 droplets, PCR amplified to endpoint, and recorded each droplet as positive or negative, providing a direct count of DNA copies.

**Results:** The HIV-2 DNA ddPCR assay is sensitive, with a limit of detection of 50 DNA copies/sample. Quantitative results are linear for samples with  $\geq 500$  copies/sample (expected vs. measured copies/sample: slope  $\sim 1.0$ ,  $R^2 > 0.99$ ) and are reproducible within and between runs (CV  $< 35\%$ ). Results are similar with Group A and Group B HIV-2 strains. HIV-2 DNA was detected in the remnant BCP of 43/44 clinical samples with detectable HIV-2 RNA. Importantly, HIV-2 DNA was also detected in 8/10 samples with undetectable HIV-2 RNA collected from individuals known to be infected with HIV-2.

**Conclusions:** The HIV-2 DNA ddPCR assay is sensitive, accurate and reproducible. The use of BCP will allow simultaneous quantification of HIV-2 DNA and RNA from the same specimen. HIV-2 DNA was detected in 80% of samples with undetectable levels of HIV-2 RNA, providing a valuable diagnostic tool.

## Session C: CDC/APHL Laboratory Testing Algorithm

**C1. Promoting the Recommended HIV Diagnostic Algorithm: Practical Information for Laboratories**

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<sup>1</sup>AIDS Institute, Office of the Medical Director

<sup>2</sup>Bloodborne Viruses Laboratory, Wadsworth Center, NYSDOH

**Project:** The goal of this project was to meet the informational needs of laboratory directors whose laboratories had not yet implemented the 4th generation HIV-1/2 Ag/Ab combo immunoassay and the recommended HIV diagnostic algorithm (algorithm). The New York State (NYS) Department of Health (DOH) AIDS Institute (AI) developed a video and electronic toolkit to provide this target audience with pertinent information for implementation.

**Issue:** Governor Cuomo's 2014 announcement of a three-point plan to end the AIDS epidemic in NYS includes the goal of "identify persons with HIV who remain undiagnosed and link them to health care". In response, the AI bolstered its efforts to facilitate statewide implementation of the algorithm for earlier and more accurate detection of HIV.

**Results:** Materials were developed to assist laboratories:

Toolkit:

Available at: <http://www.health.ny.gov/diseases/aids/providers/testing/toolkit.htm>

Compiles laboratory-focused fiscal, technical, and procedural information for planning and implementation.

Toolkit Summary Document:

Available at: [http://www.health.ny.gov/diseases/aids/providers/testing/docs/toolkit\\_highlights.pdf](http://www.health.ny.gov/diseases/aids/providers/testing/docs/toolkit_highlights.pdf)

Provides critical points for why implementing 4th generation HIV testing is needed.

Video - Recommended HIV Diagnostic Algorithm: Practical Information for Laboratories:

Available at: <http://www.nyhospitaltest4hiv.org/laboratory.cfm>

Includes rationale for the updated testing recommendations; explains the algorithm in detail with step-by-step laboratory footage; and an interview with two laboratory directors with different perspectives on implementation.

Input from NYS laboratories was solicited through three methods:

Advisory Committee:

Four laboratory directors participated in the 12-member Advisory Committee. Two represented laboratories who have implemented the algorithm and the other two represented laboratories currently working toward implementation.

Survey:

Results of a phone survey targeted at a sample of laboratory directors within NYS showed that challenges to implementing include:

- perception that the HIV testing volume is too low to upgrade equipment;
- lack of confidence in the HIV-1/HIV-2 antibody differentiation test;
- IT issues;
- the high cost of HIV testing.

Interview:

The video includes an interview with a director from a hospital laboratory and one from a public health laboratory.

**Lessons Learned:** Participation from laboratory directors in developing the materials was essential to delivering relevant, tailored content to the target audience.

## Session C: CDC/APHL Laboratory Testing Algorithm

**C2. Evaluation of Newly Approved HIV Antigen-Antibody Tests Individually and When Used in the CDC/APHL HIV Diagnostic Algorithm**

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<sup>1</sup> Division of HIV/AIDS Prevention, US Centers for Disease Control and Prevention

**Objective:** We evaluated five HIV Antigen/Antibody combination (Ag/Ab) assays: the GS HIV Combo Ag/AB, the Architect HIV Ag/Ab Combo (Architect), the ADVIA Centaur HIV Ag/Ab Combo, the BioPlex 2200 Ag/Ab, the Determine HIV-1/2 Ag/Ab Combo rapid test (Determine); the latter two differentiate between antigen and antibody reactivity. We assessed assay performance both individually and in the context of the CDC/APHL HIV diagnostic algorithm.

**Methods:** Specimens were collected from a high-risk population, stored at CDC and previously tested with all FDA-approved antibody only (Ab-only) laboratory tests and the Aptima HIV-1 nucleic acid test (Aptima). Fifteen had negative HIV-1 Western Blot and positive Aptima results (early infections); 274 were HIV-1 Western blot positive (HIV+) specimens from untreated persons; 370 were HIV+ specimens from treated persons; and 988 specimens were negative on both Western blot and Aptima (HIV-). Sensitivity of each test was calculated as the proportion of HIV+ and early infection specimens with reactive results. Specificity was calculated as the proportion of HIV- specimens with negative results. Based on individual test results we constructed algorithms, starting with either Ag/Ab or Ab-only assays, using 305 HIV+ and 207 HIV- specimens with reactive results on at least one test, and compared the number of Aptima tests performed and true infections identified by each algorithm.

**Results:** Sensitivity for the individual tests ranged from 98.5% to 99.1%, but confidence intervals overlapped for all assays (Table). Treatment did not affect assay sensitivity. All assays missed identifying the same six early infections; the Architect and Determine assays returned false-negative results on seven and nine specimens, respectively. Specificity ranged from 98.3% to 99.0% corresponding to between 10 and 17 false-positive results (Table). Screening with any Ag/Ab assay detected 2-4 more early infections and produced 3-6 more false-positive results than starting with any Ab- only assay. The differences were not statistically significant. No false-positive algorithm results occurred.

**Conclusions:** For this sample of specimens, the Ag/Ab assays had similar sensitivity and specificity. Beginning an HIV diagnostic algorithm with an Ag/Ab screening assay may increase the number of early HIV infections detected and require a few more Aptima tests than beginning with Ab-only assays.

**Table:** Sensitivity and Specificity of 5 FDA-approved HIV Antigen-Antibody Screening assays using well-characterized specimens of known HIV status

Test	Sensitivity												Specificity		
	Overall			Established Untreated <sup>1</sup>			Established Treated <sup>2</sup>			Early Infections <sup>3</sup>			TP	FN	% (95% CI)
	TP	FN	% (95% CI)	TP	FN	% (95% CI)	TP	FN	% (95% CI)	TP	FN	% (95% CI)			
<b>Determine HIV-1/2 Ag/Ab Combo</b>	649	10	98.5 (97.2, 99.3)	273	1	99.6 (98.0, 100)	370	0	100 (99.0, 100)	6	9	40 (16.3, 67.7)	978	10	99 (98.1, 99.5)
<b>GS HIV Combo Ag/Ab</b>	653	6	99.1 (98.0, 99.7)	274	0	100 (98.7, 100)	370	0	100 (99.0, 100)	9	6	60 (32.3, 83.7)	977	11 <sup>4</sup>	98.9 (98.0, 99.4)
<b>BioPlex 2200 Ag/Ab</b>	653	6	99.1 (98.0, 99.7)	274	0	100 (98.7, 100)	370	0	100 (99.0, 100)	9	6	60 (32.3, 83.7)	974	14	98.6 (97.6, 99.2)
<b>Architect HIV Ag/Ab Combo</b>	652	7	98.9 (97.8, 99.6)	274	0	100 (98.7, 100)	370	0	100 (99.0, 100)	8	7	53.3 (26.6, 78.7)	971	17 <sup>4</sup>	98.3 (97.3, 99.0)
<b>ADVIA Centaur HIV Ag/Ab Combo</b>	653	6	99.1 (98.0, 99.7)	274	0	100 (98.7, 100)	370	0	100 (99.0, 100)	9	6	60 (32.3, 83.7)	977	11 <sup>4</sup>	98.9 (98.0, 99.4)

<sup>1</sup> Includes specimens from persons known to be infected with HIV who reported not being on antiretroviral therapy and persons identified with previously undiagnosed HIV infection (N=171); all were HIV-1 Western blot positive

<sup>2</sup> Includes specimens from persons known to be infected with HIV who self-reported being on antiretroviral therapy; all were HIV-1 Western blot positive

<sup>3</sup> Includes specimens which were HIV-1 Western blot negative but reactive on the Aptima HIV-1 RNA qualitative assay

<sup>4</sup> Of the 17 specimens initially reactive on the Architect assay, 12 had enough volume to be repeated as required in the FDA-approved instructions for use (IFU). In the subset that underwent the full analysis per IFU, 977/983 were classified as HIV-negative; specificity = 99.4 (95% CI = 98.7-99.8). The false-reactive specimens identified by the GS Combo and ADVIA Centaur tests were also repeated per IFU but all remained reactive. No repeat testing was performed on specimens with initially reactive results on either the Determine or BioPlex assays.

## Session C: CDC/APHL Laboratory Testing Algorithm

**C3. Is It Always Necessary for the ARCHITECT 4th-Generation HIV-1/2 Ag/Ab Combo Assay to be Repeatedly Reactive before Moving Forward in the Centers for Disease Control and Prevention (CDC) HIV Screening Algorithm?**

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<sup>1</sup> University of Washington

**Objective:** For the screening ARCHITECT HIV Ag/Ab assay, an initially reactive specimen with a sample to cutoff ratio (S/CO)  $\geq 1.0$  is centrifuged and replicates retested before advancing to a discriminatory orthogonal test. We evaluated whether the ARCHITECT S/CO value could be used to modify this requirement for replicate testing.

**Methods:** A retrospective analysis of HIV-1/2 screening ARCHITECT test results obtained from a clinical research laboratory identified initially reactive (S/CO  $\geq 1.0$ ) samples with both replicate S/CO values  $< 1.0$  (non-reactive) and initially reactive (S/CO  $\geq 1.0$ ) samples with one or both of the replicates' S/CO value  $\geq 1.0$  (considered reactive and tested with the discriminatory Multispot test, and HIV-1 RNA when indicated).

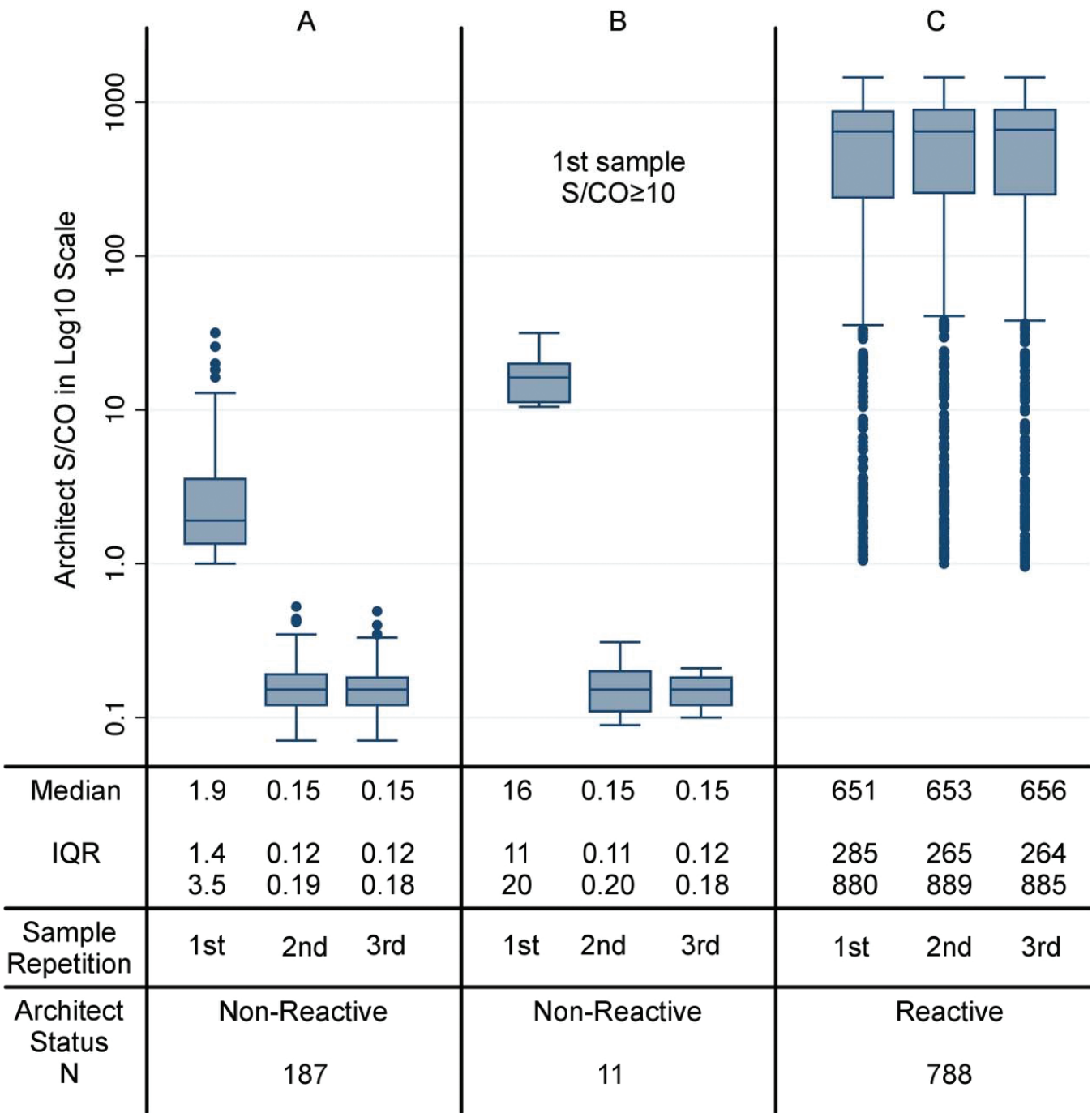
**Results:** One hundred and eighty-seven of 975 (19.2%) initially reactive samples were repeatedly non-reactive on replicate testing. The initial S/CO median and interquartile range [IQR; total range] was 1.9 [1.4-3.5; 1-31] and for the repeated aliquots, 0.15 [0.12-0.19; 0.07-0.53] (Wilcoxon Mann Whitney,  $p=0.44$ ). The Bland-Altman analysis for the first and second and for the second and third repeat aliquots had a bias  $\pm 2SD$  of  $3.0 \pm 8$  and  $0 \pm 0.1$ , respectively. Of the 788 repeatedly-reactive specimens, four specimens were discordant among replicates and 784 specimens were dually reactive. Among these repeatedly-reactive specimens, the S/CO medians [IQR; total range] for the first, second and third replicates were 651 [285-880; 1-1441], 653 [265-889; 0.9-1447] and 656 [264-885; 0.9-1454], respectively (Kruskal Wallis,  $p=0.97$ ). The Bland-Altman analysis of the S/CO values between the first and second replicates and between the second and third replicates had a bias  $\pm 2SD$  of  $-4.0 \pm 31$  and  $0.5 \pm 30$ , respectively. Of 713 samples with an initial S/CO  $\geq 10$ , only 11 (1.5%) had both replicate tests non-reactive for which the S/CO medians [IQR; total range] were 16 [11-20; 10-31] and 0.15 [0.11-0.20; 0.10-0.31], respectively (Figure 1).

**Conclusions:** For samples with an initial ARCHITECT S/CO  $\geq 10$ , the false-reactive rate was 1.5%; the threshold for no false-positives was S/CO  $\geq 31$ . To decrease turnaround time and total screening costs, all initially reactive research specimens with a S/CO  $\geq 10$  could reflex directly to Multispot discriminatory testing and HIV-1 RNA if indicated, while an initially reactive specimens with a S/CO between 1 and 10 could be rerun only in singleton after centrifugation.



ORAL ABSTRACTS

**Figure 1:** (A) ARCHITECT sample to cutoff ratio (S/CO) for initially reactive samples ( $S/CO \geq 1$ ) for which the second and third replicate aliquots were both non-reactive ( $S/CO < 1$ ); (B) for only those specimens with an initial  $S/CO \geq 10$  and non-reactive replicates; and (C) for all specimens with either one or both replicates reactive.





## Session C: CDC/APHL Laboratory Testing Algorithm

**C4. APHL/CDC Project for Referral of HIV Nucleic Acid Amplification Testing (NAT) for US Public Health Laboratories (PHLs)**

A. M. Gaynor<sup>1</sup>, K. Wroblewski<sup>1</sup>, L. G. Wesolowski<sup>2</sup>, S. F. Ethridge<sup>2</sup>, M. Parker<sup>3</sup>, T. J. Sullivan<sup>3</sup>, and S. B. Bennett<sup>4</sup>

<sup>1</sup> Infectious Disease Program, APHL

<sup>2</sup> CDC

<sup>3</sup> Wadsworth Center, NYSDOH

<sup>4</sup> Florida Bureau of Public Health Laboratories

**Objective:** HIV-1 NAT testing is necessary to resolve discordant screening and supplemental antibody results and identify acute HIV-1 infections. Because most US PHLs have very few specimens per year that require resolution with NAT, it is cost-prohibitive for most PHLs to maintain that testing in-house. A shared service approach was initiated in 2012 to address this need, providing an opportunity for earlier identification and linkage to care of individuals with acute HIV-1 infections.

**Methods:** APHL contracted with the New York State Department of Health's Wadsworth Center and the Florida Department of Health, Bureau of Public Health Laboratories to perform the APTIMA HIV-1 RNA qualitative assay (Hologic). Nine hundred ninety-seven (997) specimens were received from August 2012 through June 30, 2015 and 980 (98.3%) that met specimen criteria and had complete data were included in this analysis. Submitting labs were polled regarding strategies to improve testing turnaround times (TAT) and to describe the impact of results from the HIV-1 NAT Referral project on HIV Programs.

**Results:** APHL has enrolled 39 laboratories and 33 have submitted at least one specimen. Of the 980 specimens analyzed, 13% (n=130) were reactive by HIV-1 NAT (i.e., acute infections). While the number of submitted specimens has increased during the project, the TAT decreased (Table 1). The TAT from specimen collection to receipt at the submitting lab, from receipt at the submitting lab to shipment to the reference center, and from collection to HIV-1 NAT testing, have all decreased over the course of the project. One noticeable impact reported from a submitting laboratory is the reduction in the TAT to an HIV diagnosis and linkage to care because a single specimen can be used for all testing, including the HIV-1 NAT, as compared to when a secondary sample had to be obtained and tested to confirm a diagnosis.

**Conclusions:** The HIV NAT Referral project has demonstrated the feasibility of a shared services model for HIV NAT testing. It currently provides PHLs access to HIV-1 NAT referral testing ensuring timely reporting of results for persons with potentially acute HIV-1 infections.

**Table 1.** Summary Table of Specimens Received from 2012 to 2015 (TAT = Turnaround time in days, a) 2012-2015 includes analysis of all specimens submitted during the project. b) Only 33 labs submitted samples during the time frame, not every lab submitted specimens each year.)

Year	Labs Submitting Specimens (#)	Specimens submitted (#)	HIV-1 NAT Reactive (%)	Specimen Collection to Receipt at Submitting Lab (Mean TAT)	Receipt at Submitting Lab to Shipment to Reference Center (Mean TAT)	Receipt at Reference Center to Testing at Reference Center (Mean TAT)	Specimen collection to HIV-1 NAT test: ≤2 weeks (%)
2012-2013	22	141	9%	1.8	15.6	2.7	60%
2013-2014	28	415	15%	1.8	8.1	2.1	75%
2014-2015	26	424	13%	1.5	6.3	2.1	80%
2012-2015 <sup>a</sup>	33 <sup>b</sup>	980	13%	1.7	8.4	2.2	75%

## Session D: CDC/APHL Laboratory Testing Algorithm (Part 2)

**D1. Efficacy of 4<sup>th</sup> Generation HIV Screening Algorithm in Detecting Acute HIV Infection and the Utility of Abbott Architect Signal-to-Cutoff Ratio in That Regard**

S. Pasalar<sup>1</sup>, C. E. Stager<sup>2</sup>, M. Arya<sup>2</sup>, N. P. Miertschin<sup>1</sup>, S. Hoxhaj<sup>2</sup>, and T. P. Giordano<sup>2</sup>

<sup>1</sup> Harris Health System

<sup>2</sup> Baylor College of Medicine

**Objective:** To study the efficacy of the 4th generation HIV screening algorithm's ability to detect acute HIV infection and evaluate whether the Abbott Architect signal-to-cutoff ratio (SCR) can predict acute infections.

**Methods:** Harris Health System is the public safety net hospital system in the Houston area. Since 2008, a routine HIV screening program has been in place across Harris Health in which patients 16 and older may be tested for HIV unless they opt out. In February 2014, Harris Health implemented a revised CDC HIV Screening Algorithm. The initial HIV screen was the Abbott Architect HIV-1/2 4th generation assay and the confirmatory assay for HIV-1 was the HIV-1 Western blot. In October 2014, the confirmatory assay was changed to the BioRad Multispot. When the initial screen and the confirmatory assay were discordant, a Roche HIV-1 viral load (VL) was performed. We evaluated the efficacy of this algorithm in detecting acute infections. We also evaluated whether the signal-to-cutoff ratio reported by Abbott Architect could predict acute infections.

**Results:** A total of 198,726 HIV screening tests were performed. 3073 (1.5%) had a positive result, of which 43 (1.4% of positive tests; 0.02% of all tests) were confirmed acute infections after following through the algorithm (Table-1A). We were able to extract SCR for 976 of the positive screening tests and evaluated the SCR for the False Positive, Acute, and Chronic infection cases (Table-1B). In a recent study<sup>1</sup>, an SCR of ~151 was shown to have a 100% positive predictive value (PPV) and 67.4% sensitivity for detection of subsequently confirmed HIV infections. Our data confirms those findings for chronic cases (Figure-1); in fact in our data, an SCR of 37 had a 100% PPV and 97.7% sensitivity for chronic cases. However, either of those thresholds would miss all or most of acute infection cases.

**Conclusions:** The 4th generation HIV screening test with Multispot confirmatory testing and HIV VL for discordant results was successful in identifying acute HIV infections. A high SCR result (>37) for the Abbott Architect screening test predicts HIV infection but a low value does not rule-out acute HIV infection, and nucleic acid-based testing is required.

Reference:

1. A signal-to-cutoff ratio in the Abbott architect HIV Ag/Ab Combo assay that predicts subsequent confirmation of HIV-1 infection in a low-prevalence setting. J Clin Microbiol. 2015 May;53(5):1709-11.

**Table:** Summary of testing and signal-to-cutoff ratio (SCR) data

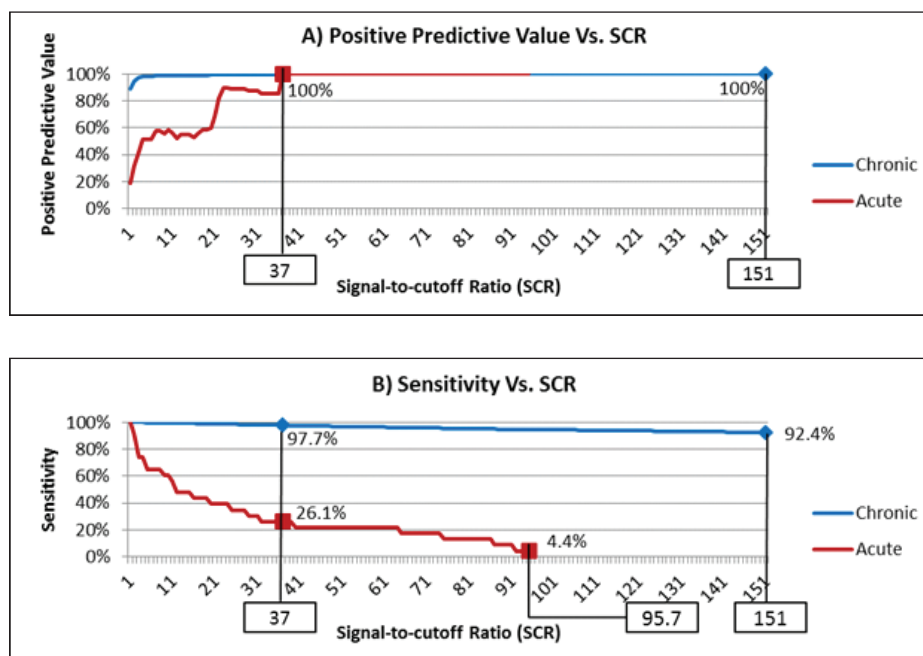
**A) Testing Data**

	#	Notes
<b>4<sup>th</sup> Generation Screening Tests</b>	198,726	Feb 2014 – Oct 2015
<b>Positive Screening Results</b>	3073	
<b>Followed by Western Blot</b>	812	Feb 2014 – Oct 2014
<b>Followed by Multispot</b>	1378	Oct 2014 – Oct 2015
<b>Confirmation test not performed</b>	883	Known positive/insufficient specimen
<b>Positive Confirmatory Results</b>	1869	
<b>Negative Confirmatory Results</b>	301	Indeterminate WB results (N=20) not evaluated
<b>Followed by Viral load</b>	199	to distinguish acute infection from false positive
<b>Undetectable VL</b>	155	False positive Screening
<b>VL &gt; 10,000 copies/mL</b>	43	Acute infection
<b>VL &lt; 10,000 but detectable</b>	1	Further tests needed

**B) Signal-to-cutoff ratio (SCR) data**

	Min	Max	Mean	Standard Deviation
<b>False Positive</b>	1.05	36.7	4	6.1
<b>Acute</b>	1.4	95.7	27.6	31.8
<b>Chronic</b>	4	1313	614.6	272.1

**Figure-1:** Signal-to-cutoff ratio Vs. positive predictive value and sensitivity



## Session D: CDC/APHL Laboratory Testing Algorithm (Part 2)

**D2. Real-world Performance of the New US HIV Testing Algorithm in Medical Settings**

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<sup>1</sup> Division of HIV, Infectious Diseases, and Global Medicine, Department of Medicine

<sup>2</sup> Department of Laboratory Medicine, University of California, San Francisco

<sup>3</sup> University of California, San Francisco

<sup>4</sup> David Geffen School of Medicine at UCLA

<sup>5</sup> San Francisco Department of Public Health

<sup>6</sup> Centers for Disease Control and Prevention

**Objective:** San Francisco General Hospital (SFGH) Clinical Laboratory has previously deployed round-the-clock rapid HIV testing. We evaluated implementation of the new US algorithm at SFGH.

**Methods:** SFGH performs HIV tests 2-hourly and VL 3X per week. In September 2015, SFGH switched from Unigold (RT) screening with immunofluorescence (IF) confirmation (RT-IF) to Architect (AR) screening with Multispot (MS) Ab confirmation-differentiation and viral load (VL) as needed for resolution of discrepant results (AR-MS-VL). We reviewed all consecutive HIV tests at SFGH during January-November 2015, before and after rollout of the new algorithm. Performance of AR-MS-VL tests at SFGH was compared with similar data on the same algorithm in the 2010-2013 CDC STOP study at MSM testing sites in San Francisco.

**Results:** 21,985 HIV tests were performed at SFGH, 16,467 by the RT-IF antibody algorithm and 5,518 by the AR-MS-VL algorithm. A total of 321 HIV infections were identified by diverse clinics and wards; however 271 were previously known to be HIV(+). Among 21,695 HIV(-/unknown) patients tested, there were 50 confirmed new HIV infections (0.23%). No antibody-negative acute HIV infections were identified. Median time to (+) results was slightly longer for AR (3.4 hrs) than RT screening (1.9 hrs); times to MS and VL were 20 hrs and 5 days respectively. Surprisingly, only 11/25 newly AR+ results with final status resolved were HIV infected ( $PPV_{AR+}=0.44[95CI\ 0.34,0.54]$ ) -- similar to the PPV associated with RT screening at SFGH ( $PPV_{RT+}=0.45[0.39,0.50]$ ). 14/16 AR+MS- results were confirmed to be VL-/HIV negative with 2 unresolved. By contrast, among 29,335 HIV(-/unknown) SF testers in STOP study sites with an HIV prevalence of 1.55%, most (422/453) AR+ results were HIV infected ( $PPV_{AR+}=0.93[0.91,0.94]$ ) and most (50/81) AR+/MS- discrepant results had VL+ acute HIV ( $PPV_{AR+/MS-}=0.62[0.56,0.67]$ ). AR assay specificity was high in both STOP (28880/28918=99.86%) and SFGH testing (5417/5431=99.74%).

**Conclusion:** Implementing the AR-MS-VL algorithm to return rapid results across a large hospital campus is feasible; however, the low prevalence of infection among HIV (-/unknown) testers in medical settings can lead to a high proportion of positive screening results being false positive. This has important implications for clinical decision making in the hospital.

## Session D: CDC/APHL Laboratory Testing Algorithm (Part 2)

### D3. Comparison of Turn-around Time and Total Cost of HIV Testing Before and After Implementation of the 2014 CDC/APHL Laboratory Testing Algorithm for Diagnosis of HIV Infection

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**Objective:** In June 2014 the U.S. Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL) issued updated recommendations on laboratory testing for the diagnosis of HIV infection, based on the use of 4<sup>th</sup> generation HIV immunoassays (4<sup>th</sup> Gen algorithm) that include the detection of HIV p24 antigen for early diagnosis of HIV infection prior to seroconversion. This study compared the turn-around time and cost of HIV testing before (3<sup>rd</sup> Gen algorithm) and after implementation of this new testing algorithm at a national reference testing laboratory.

**Methods:** The updated CDC/APHL HIV testing algorithm was implemented routine testing of clinical serum specimens at the Mayo Medical Laboratories in June 2014, and data were retrieved from the laboratory information system for all initial and subsequent supplemental HIV test results obtained over the 18-month period before and the same duration after this date. Turn-around time (duration from receipt of specimen in the laboratory to reporting of definitive test results) and cost (direct and indirect expenses) were determined for specimens with reactive initial test results.

**Results:** Of the 76,454 and 78,998 serum specimens tested during the 18-month periods before and after implementation of the new testing algorithm, respectively, 534 (0.7%) and 596 (0.8%) yielded reactive initial test results, respectively, with 108 (20%) and 159 (27%) of these reactive specimens eventually confirmed to be positive for HIV infection by reflex supplemental testing. Comparison of turn-around time and total cost for the various testing outcome is shown below:

Initial test result	Reflex supplemental test results	N (%)	Total cost	Turn-around time (hrs)		
				Median	Mean	Range
3 <sup>rd</sup> Gen - reactive	HIV-1 Ab Western blot-positive	107 (54)	\$75.04	27.1	32.1	6.9 - 89.3
	HIV-1 Ab Western blot-negative or indeterminate, HIV-2 Ab EIA-negative	44 (22)	\$103.91	52.4	60.2	27.4 - 125.2
4 <sup>th</sup> Gen - reactive	HIV Ab differentiation-positive	153 (77)	\$41.52	17.4	21.4	1.0 - 94.6
	HIV Ab differentiation-negative or indeterminate, HIV NAT-positive or negative	16 (9)	\$151.21	175.5	413.3	49.1 - 1,782.6

The overall mean turn-around time was 72.0 and 67.8 hours for the 3<sup>rd</sup> Gen and 4<sup>th</sup> Gen algorithms, respectively, with overall mean total cost of \$109.48 and \$53.95, respectively.

**Conclusion:** With similar total numbers of initial tests performed and initial reactive result rates for the two HIV testing algorithms each over an 18-month period, the 4<sup>th</sup> Gen algorithm had a shorter overall turn-around time, especially for reflex to negative supplemental test results, and was more cost-effective than the 3<sup>rd</sup> Gen algorithm in our reference testing laboratory.



## Session E: Streamlining Test Result Turnaround Time and Linkage to Care

## E1. Rapid HIV Testing and Linkage to Medical Care, New Jersey, 2007-2011

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**Background:** Efforts to identify and link HIV-infected persons to medical care are important to prevent transmission and reduce HIV-associated mortality and morbidity. The updated National HIV/AIDS Strategy (NHAS) goal is to link 85% of newly diagnosed persons to medical care in  $\leq 30$  days, by 2020. Among newly diagnosed HIV-infected persons in NJ from 2007-2011, we a) compare the percentage linked to medical care in  $\leq 30$  and  $\leq 90$  days b) identify predictors for linkage to medical care in  $\leq 90$  days from 2007-2011.

**Methods:** Data were obtained from New Jersey's (NJ) Enhanced HIV/AIDS Reporting System for 5,827 persons newly diagnosed at aged  $\geq 13$  years. We compared the percentages linked to medical care in  $\leq 30$  days and  $\leq 90$  days. We used survival analysis methods to test whether linkage to medical care depended upon testing-site-type (clinical vs. community) and test-type (Enzyme ImmunoAssay followed by Western Blot (EIA-WB) vs. RTA (rapid test followed by WB or second rapid)).

**Results:** In NJ, from 2007-2011, of 5,827 newly diagnosed persons, 3,936(67.6%) tested positive by EIA-WB while 1,891 (32.4%) tested positive by RTA. Overall 58.4% and 72.0% were linked to medical care in  $\leq 30$  days and  $\leq 90$  days respectively. In a competing risk model, stratified by year, by 2011, those who were tested by a RTA were at least 2 times more likely than those who underwent EIA-WB to link to care  $\leq 90$  days in community sites, similar to clinical sites, after controlling for race/ethnicity, age, transmission risk, IMPACT City and AIDS diagnosis. Females remained less likely to link to medical care in  $\leq 90$  days, regardless of test-type and test-site.

**Conclusion:** In NJ, from 2007-2011, linkage to medical care increased by at least 10%, when both  $< 30$  and  $< 90$ -day time-periods were evaluated. By 2011, linkage to medical care was equally likely from community and clinical sites among those tested by RTA compared to EIA-WB in community sites. Differences in linkage to care among population groups were eliminated except among females who remained slightly less likely to link to medical care.

**Table 1:** Cumulative Probabilities for Linkage to Medical Care among Newly Diagnosed Residents with HIV,  $\leq 30$  and  $\leq 90$  days and Overall, New Jersey-2007-2011

Variable	NUMBER OF DAYS TO LINKAGE TO MEDICAL CARE				
	Total	$\leq 30$ Days	$\leq 90$ Days	Overall	Median (IQR)
<b>Overall</b>	5,827	58.6	72.1	92.3	20 (3-127)
<b>Test-Type</b>					
EIA-WB	3,936	63.5	75.1	94.1	17 (2-90)
RTA	1,891	57	65.8	87.6	28 (6-246)
<b>Test-site</b>					
Clinical	4,152	62.6	76.1	93.8	16 (2-80)
Community	1,443	47.3	61.2	87	34 (9-454)
Unknown	242	54	69.1	97.6	25 (5-154)
<b>Location-by-Test-Type</b>					
Clinical-EIA-WB	3,554	63.5	76.6	94.2	15 (2-76)
Clinical-RTA	588	57	72.8	91	18 (2-130)
Community-EIA-WB	196	36.2	52	89	73 (13-482)
Community-RTA	1,247	49	62.7	85.8	32 (8-448)
Unknown-EIA-WB	186	54.8	70	97.2	24 (6-154)
Unknown-RTA	56	52	65	96.7	27 (2-149)
<b>Gender</b>					
Female	1,759	55.5	70.7	91.9	23 (4-141)
Male	4,068	59.7	72.6	92.5	18 (2-120)
<b>Race/Ethnicity</b>					
Non-Hispanic Black	3,057	55.3	68.3	90.7	23 (3-202)
Non-Hispanic White	1,026	64.5	78.2	94.1	14 (2-63)
Hispanic	1,501	60.1	74.7	93.4	19 (3-94)
Other	243	59.4	77	97	16 (1-76)
<b>Age</b>					
13-24	934	50.8	67.2	90.1	30 (6-248)
25-34	1,482	56.8	70.8	90.6	22 (4-140)
35-44	1,505	59.3	72.3	92.8	19 (2-122)
45-54	1,279	61.9	75.7	94.7	17 (2-85)
>55	627	64.3	74	93.4	14 (1-100)
<b>Transmission Risk</b>					
Male-to-Male Sex	1,786	58.3	72.7	93.5	20 (5-113)
Injection drug use	376	57.6	72.2	91.4	18 (2-140)
Heterosexual	792	59.1	73.6	94.1	21 (3-104)
Unknown	2,873	58.4	71.1	91.1	19 (2-141)

NUMBER OF DAYS TO LINKAGE TO MEDICAL CARE					
Variable	Total	≤30 Days	≤90 Days	Overall	Median (IQR)
Year of Diagnosis					
2007	1,275	49	64.8	91.9	30 (5-223)
2008	1,214	57	71.6	88.8	22 (3-135)
2009	1,244	60.3	73.4	91.8	18 (3-106)
2010	1,138	64.8	76.6	90.7	15 (2-76)
2011	956	62.8	75.3	89.4	14 (2-84)
IMPACT City					
Yes	2,892	61.4	67.9	91.2	22 (3-196)
No	2,935	55.4	76.2	93.4	18 (3-81)
AIDS					
Yes	2,142		76.1	99.7	16 (2-84)
No	2,534		80	99.9	18 (5-59)
Unknown	1,151		29.2	46.8	384 (56-1834)

**Abbreviations:** HIV: Human Immunodeficiency Virus, CI: Confidence Interval, IQR: Interquartile Range, EIA-WB: Enzyme Immunoassay HIV test for antibody followed by Western Blot for confirmation, RTA: Rapid HIV antibody for screening followed by either a second Rapid test for presumptive confirmation or a Western Blot for confirmation of HIV status, IMPACT: Refers to ten cities with the highest prevalence of HIV in New Jersey, AIDS: Acquired Immuno Deficiency Syndrome.

**Table 2:** Adjusted Hazard Ratios for Linkage to Medical Care ≤ 90 days, Stratified by Year of HIV Diagnosis, New Jersey, 2007-2011

Variable	2007 aHR (95%CI)	2008 aHR (95%CI)	2009 aHR (95%CI)	2010 aHR (95%CI)	2011 aHR (95%CI)
<b>Location-by-Test-Type</b>					
<b>Clinical-EIA-WB</b>	1.46 (1.18-1.81)	0.85 (0.61-1.18)	2.01 (1.20-3.36)	1.49 (0.55-4.01)	2.52 (1.18-5.34)
<b>Clinical-RTA</b>	1.43 (1.07-1.92)	0.70 (0.48-1.03)	1.90 (1.11-3.27)	1.50 (0.55-4.07)	2.20 (1.02-4.77)
<b>Community-EIA-WB</b>	1	1	1	1	1
<b>Community-RTA</b>	1.20 (0.93-1.56)	0.64 (0.45-0.91)	1.40 (0.83-2.36)	1.25 (0.46-3.38)	2.34 (1.10-5.00)
<b>Gender</b>					
<b>Female</b>	0.93 (0.81-1.07)	0.94 (0.82-1.09)	0.92 (0.79-1.06)	0.99 (0.85-1.16)	0.83 (0.70-0.98)
<b>Male</b>	1	1	1	1	1

Model was adjusted for Age, gender, race/ethnicity, transmission risk, IMPACT City, AIDS-diagnosis

**Abbreviations:** HIV: Human Immunodeficiency Virus, aHR: adjusted Hazard Ratio, CI: Confidence Interval, EIA-WB: Enzyme Immunoassay HIV test for antibody followed by Western Blot for confirmation, RTA: RTA HIV antibody for screening followed by either a second RTA test for presumptive confirmation or a Western Blot for confirmation of HIV status, IMPACT: Refers to ten cities with the highest prevalence of HIV in New Jersey, AIDS: Acquired Immune Deficiency Syndrome

## Session E: Streamlining Test Result Turnaround Time and Linkage to Care

## E2. Using Reported HIV Diagnostic Testing Results to Identify Cases of Acute HIV Infection: Lessons Learned from New York State

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**Project:** One of the most appealing features of the Center for Disease Control and Prevention and Association of Public Health Laboratories recommended HIV Diagnostic Testing Algorithm (algorithm) is the ability to detect HIV infection earlier compared to conventional testing strategies. The first test of the algorithm, the HIV-1/HIV-2 immunoassay, can detect HIV-1 antigen (Ag) in the very early stages of infection when antibody (Ab) is not yet present. Reported algorithm results were reviewed to identify possible acute or early HIV infection (AHI).

**Issue:** In June 2015, 41 laboratories were permitted and certified by the New York State Department of Health to submit results of the algorithm for public health reporting. Several labs use alternate algorithms that include the HIV Western blot (WB). Reported algorithm/WB results with specimen collection May 2013-June 2015 were assessed for scenarios that were indicative of AHI -- defined as negative or indeterminate Ab result in conjunction with a detectable HIV-1 Nucleic Acid Test result.

**Results:** 43,187 algorithm components were reported electronically. About 67% of confirmed algorithm/WB results are for persons with established infection. Incomplete reporting is common. Only 13,746 complete algorithm result sets were received. 951 negative or indeterminate WB results were reported; 45% without the required additional testing. 8,511 reported diagnostic test result sets were incomplete and therefore represented unresolved HIV-infection status. 169 potential cases of AHI were identified from reported lab data (101 algorithm and 68 WB based). Based on the supporting evidence of high viral loads proximate to the algorithm/WB or refuting evidence of concurrent/late AIDS diagnosis, only 71 (42%) may be probable AHI. Of these, only 21 (30%) had AHI or acute retroviral syndrome diagnosis documented in the medical record and captured by the public health investigation.

**Lessons Learned:** Partial execution of the algorithm by laboratories and incomplete reporting of test results hinder the detection of AHI by surveillance programs. Improvements in execution and reporting are needed to achieve the public health goals of recognition and timely confirmation of AHI, rapid linkage to care, and prompt partner services, all of which are critical to control of HIV transmission.

## Session E: Streamlining Test Result Turnaround Time and Linkage to Care

### E3. Implementation of 4th Generation HIV Antigen-Antibody Testing Algorithm at a Public Health STD Clinic for *Real-time* Screening and Confirmation

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<sup>4</sup>University of Wisconsin School of Medicine and Public Health

**Project:** The City of Milwaukee Health Department and Laboratory (MHDL) in collaboration with the State of Wisconsin Department of Health Services HIV Program (WDPH), implemented 4th generation HIV Ag/Ab combo testing using the Architect instrument at the satellite STD Clinic/Lab with MultiSpot HIV 1 & 2 differentiation at the main MHDL within 24 hours. Over a two-year period, MHDL worked with WDPH to justify state funding and supplies from manual HIV rapid screening to the new method.

**Issue:** Turn-around-time (TAT) during previous practices for manual rapid screening, followed by 3rd or 4th Gen HIV testing and confirmation of positives at the Wisconsin State Laboratory of Hygiene (WSLH), was 1-2 weeks. Additional challenges included: i) remodeling the STD lab to accommodate the Architect instrument; ii) temporarily relocating the clinic lab during renovation; and iii) coordinating efforts to improve the patient interview and testing workflow using LEAN tools.

**Results:** From February through December 2015, 3,436 patients were screened and 13 HIV-positive patients confirmed and counseled, with no extended wait time. Manual rapid screening was eliminated upon introduction of random access 4th Gen HIV screening. Point-of-care HIV-1/2 Ab and HIV-1 p24 antigen combo testing is available as a back-up. LEAN workflow analysis eliminated 15 minutes from each patient's clinic wait time, which typically does not exceed one hour.

**Lessons Learned:** Replacing manual 3rd Gen HIV rapid screening with CDC's 4th Gen HIV Ag/Ab combo testing algorithm and in-house confirmation improved TAT from 1-2 weeks to 24 hours, enhanced early detection, and improved follow-up and treatment of HIV cases, including potential acute cases. This improved clinician case management and can decrease morbidity and mortality locally and statewide.

**Next Steps:** Geenius HIV 1 & 2 confirmatory differentiation assay will soon be implemented onsite at the satellite STD clinic lab, eliminating transport of positive screened specimens to the MHD main lab. Patient confirmatory results and counseling will be achieved within hours and prior to patient departure.

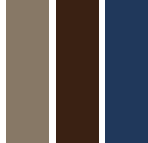
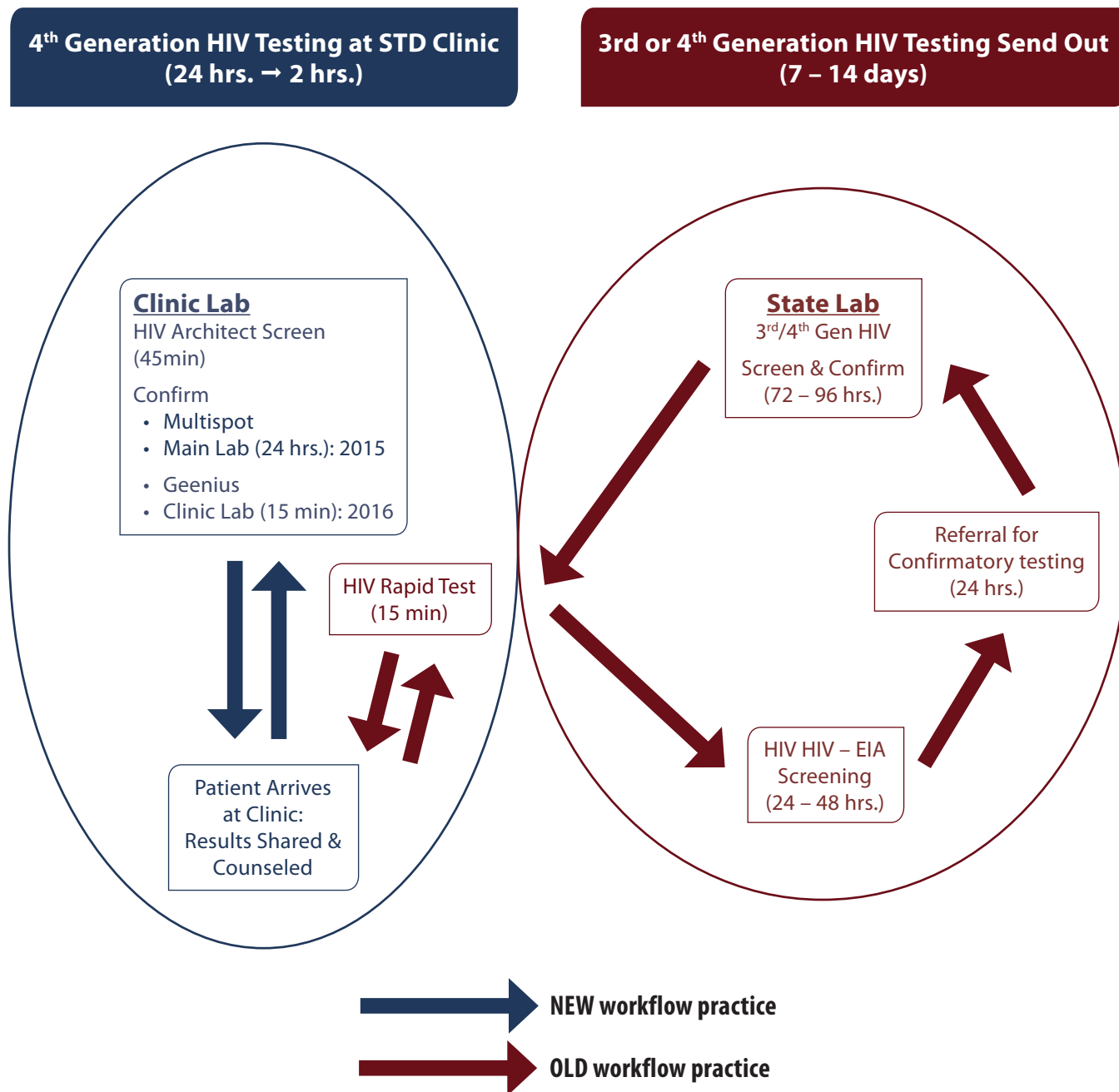


Figure 1

## CONFIRMATION *turn-around-time* of HIV Positive Results



## Session E: Streamlining Test Result Turnaround Time and Linkage to Care

## E4. Perceptions and Performance of Self-administered Rapid HIV Tests Conducted by Untrained Users in Real-World Settings

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**Objectives:** We characterized perceptions of self-administered rapid HIV tests, and evaluated how well the OraQuick In-Home HIV Test (OQ) and Sure Check HIV 1/ 2 Assay (SC) performed when administered by untrained men who have sex with men (MSM).

**Methods:** During May-October 2014, MSM reporting HIV-negative or unknown status were recruited online. Participants were mailed 1 OQ, 1 SC, and 1 dried blood spot (DBS) collection kit. Participants provided results online, matched their result to a stock test result image, completed a survey, and mailed back the DBS card which was analyzed in the CDC lab with GS HIV Combo Ag/Ab EIA, Avioq HIV-1 Microelisa System, and Western blot. The DBS result was the standard used in the performance analyses which were limited to 515 persons with both self-test results.

**Results:** Knowledge of HIV self-tests was high among 818 participants: 80% had heard about them, and 12% had used one in the past year. Online response rates were as follows: 76% reported their OQ result, 70% reported their SC result, 67% mailed back their DBS card and 70% completed the survey. Among respondents, 85% reported OQ as very easy to use and 68% reported the same for SC. Over 90% were very confident interpreting both rapid test results. Complete trust in the OQ and SC test results was reported by 52% and 71% of participants, respectively. The image selected was 100% concordant with results reported among participants reporting positive and invalid results. Among participants reporting OQ and SC negative results, 98% and 99% respectively, chose a negative image. Of 16 participants with at least one positive rapid test, 56% were linked to care. Performance results are shown in Table 1. The proportion of invalid results among SC results was 4.5% and among OQ results was 0.97%.

**Conclusion:** Without prior in-person training, internet-recruited MSM who reported their results online successfully conducted 3 self-testing activities. Participants had less trust in OQ than in SC despite its ease of use. Specificity was high for both. Sensitivity had large confidence intervals due to the small number of infected participants recruited. Participants correctly interpreted the large number of invalid SC results.



**Table 1.** Performance <sup>a, b</sup> of OraQuick® In-Home HIV Test (OQ) and Sure Check® HIV 1/2 Assay (SC) performed as self-administered rapid HIV tests relative to dried blood spot testing in 515 untrained men who have sex with men

OQ Result (n=514)	DBS result <sup>c</sup>		Sensitivity (95% CI)	Specificity (95% CI)
	DBS positive (n=8)	DBS negative (n=506)		
Positive	6	0		
Negative	2	501		
Invalid	0	5		
<b>Performance</b>			81.8% (48.2, 97.7)	100% (99.3, 100)
Corrected <sup>**†</sup> OQ Result (n=515)	DBS positive (n=9) <sup>†</sup>	DBS negative (n=506)	Corrected Sensitivity (95% CI)	Corrected Specificity (95% CI)
Positive	8	0		
Negative	1	501		
Invalid	0	5		
<b>Performance</b>			88.9% (51.8, 99.7)	100% (99.3, 100.0)
SC Result (n=514)	DBS result <sup>c</sup>		Sensitivity (95% CI)	Specificity (95% CI)
	DBS positive (n=8)	DBS negative (n=506)		
Positive	4	1		
Negative	1	485		
Invalid	3	20		
<b>Performance</b>			80% (28.4, 99.5)	99.8% (98.9, 99.9)
Corrected <sup>**†</sup> SC result (n=515)	DBS positive (n=9) <sup>†</sup>	DBS negative (n=506)	Corrected Sensitivity (95% CI)	Corrected Specificity (95% CI)
Positive	6	0		
Negative	0	486		
Invalid	3	20		
<b>Performance</b>			100% (54.1, 100.0)	100% (99.2, 100.0)

<sup>a</sup> We also present corrected performance measures that include information provided verbally by participants

<sup>b</sup> Sensitivity and specificity were calculated using as a standard the result of the analysis of the DBS card with Avioq HIV-1 Microelisa System, followed by Western blot, when repeatedly reactive. Results with GS HIV Combo Ag/Ab EIA were concordant with the results obtained with Avioq.

<sup>c</sup> The quality of the DBS cards received was scored visually by CDC staff who concluded they were all of high enough quality to perform all the assays necessary for assessing performance.

<sup>\*\*</sup> The OQ results and the SC result reported online by one participant was changed from negative to positive after he communicated by phone he had reported erroneous results into the online system. A second participant reported online a negative OQ and a positive SC result. He communicated by phone his SC result was negative and we updated the dataset with this information.

<sup>†</sup> Another participant had a positive DBS result and reported online a negative OQ result but not his SC result. He communicated by phone both rapid test results were positive. Once his SC result was added this changed the overall sample size in the corrected performance analysis from 514 to 515.

## Session F: Performance of CLIA-Waived HIV Tests

### F1. Implementing HIV Testing in Nonclinical Settings: Updating CDC Guidance and Program Resources for HIV Testing

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**Project:** Recommendations for HIV counseling, testing, and referral in nonclinical settings were last released by CDC in 2001. However, recent scientific and programmatic advances in HIV prevention, care, and treatment warranted updating this previous guidance. This presentation will review CDC's newly released guide: *Implementing HIV Testing in Nonclinical Settings: A Guide for HIV Testing Providers* (Implementation Guide). The session will highlight key programmatic updates and implications for nonclinical HIV testing programs.

**Issue:** The nation's HIV prevention efforts are guided by the recognition that if everyone with HIV was aware of their infection and receiving the treatment they need, HIV infections in the U.S. would be greatly reduced. Significant advances in HIV testing make it now easier than ever before to get tested for HIV. HIV testing providers need updated tools and information in order to provide high-quality HIV testing services to populations at greatest risk for acquiring HIV.

**Results:** The Implementation Guide includes 8 chapters including topics such as: program principles and standards; targeting and recruitment; HIV tests and testing strategies; new protocols for HIV testing with individuals, couples, and partners; and referral, linkage, and navigation. The guide is designed to orient HIV testing providers working in nonclinical settings to the key programmatic issues they need to be aware of to provide high-quality HIV testing services to their clients.

**Lessons Learned:** This Implementation Guide provides several updates to current HIV testing processes. These updates include de-linking HIV prevention counseling from the testing event, advances in HIV testing technologies, couples and partner testing protocols, and an increased focus linkage to HIV medical care and pre-exposure prophylaxis (PrEP). This session will review these updates and capacity building assistance (CBA) opportunities for implementing the guidance.

## Session F: Performance of CLIA-Waived HIV Tests

**F2. Performance Evaluation of the INSTI HIV-1/2 Antibody Point-of-Care Test in Early and Established Infections**

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<sup>3</sup> DHAP, Centers for Disease Control and Prevention

<sup>4</sup> New York City Department of Health & Mental Hygiene

<sup>5</sup> San Francisco Department of Public Health

<sup>6</sup> University of North Carolina

**Objective:** The availability of improved point-of-care technology could increase the number of people diagnosed with HIV. The flow-through INSTI™ HIV-1/HIV-2 Rapid Antibody (INSTI) test has been approved in the U.S. for fingerstick and venous whole blood and plasma, and is Clinical Laboratory Improvement Amendments (CLIA) waived for fingerstick whole blood. We evaluated the performance of INSTI in a laboratory using plasma and/or whole blood specimens from early and established HIV-1 infections.

**Methods:** Assay performance was assessed by: a) estimating the relative sensitivity of INSTI before a positive Western blot (WB) using a 50% cumulative frequency analysis (17 HIV-1 seroconverters); b) comparing the performance with other FDA-approved rapid tests (RTs) using a McNemar's analysis (26 HIV-1 seroconverters); c) comparing results of 85 plasma specimens from early HIV-1 infections (Architect-positive/Mustispot (MS)-negative or -indeterminate/Aptima-positive); d) comparing results from 55 plasma and simulated whole blood specimens (40 plasma specimens from 8 HIV-1 seroconverters and 15 HIV-negative individuals); e) calculating sensitivity from 716 HIV-1 groups M (B and non-B subtypes) and O and HIV-2 (groups A and B) specimens and specificity from 499 HIV-negative specimens.

**Results:** In early HIV-1 infections, INSTI was positive 9 days before a positive WB. In the paired comparison, INSTI performed similarly to MS as screening assay, but detected significantly more infections than the antibody-based lateral flow RTs approved in the US using plasma from seroconversion panels (Table). In plasma from recently infected individuals with HIV-1, INSTI detected 27% (23/85) of early HIV-1 infections. Using simulated whole blood there was no delay detecting early infections compared to plasma, but four additional false-reactive results were observed. The sensitivity in plasma for established infection was 99.84% for HIV-1 and 100% for HIV-2 and the specificity was 99.80%.

**Conclusions:** INSTI performed significantly better than antibody-based lateral flow RTs at detecting HIV-1 early infections. Sensitivity and specificity were within the manufacturer's reported ranges. Further evaluation with fingerstick/venipuncture whole blood is needed to evaluate point of care performance. Considering the observed test performance and the availability of almost immediate results, indicates INSTI offers an advantage for detecting HIV-1/HIV-2 antibodies at the point-of-care.

**Table.** Summary of the paired comparison analysis using the McNemar's test

Test 1	Results comparison test 1/INSTI				<i>p value</i>
	neg/neg	neg/pos	pos/neg	pos/pos	
<b>Determine Combo</b>	102	2	34	92	<i>&lt;0.0001*</i>
<b>Multispot<sup>a</sup></b>	133	6	2	88	<i>0.2888</i>
<b>Reveal G2/G3<sup>a</sup></b>	134	14	1	80	<i>0.0019*</i>
<b>DPP HIV-1/2</b>	134	15	2	79	<i>0.0036*</i>
<b>Statpak</b>	134	20	1	74	<i>&lt;0.0001*</i>
<b>Complete</b>	135	22	1	74	<i>&lt;0.0001*</i>
<b>Unigold</b>	136	23	0	70	<i>&lt;0.0001*</i>
<b>Oraquick Adv</b>	134	34	2	60	<i>&lt;0.0001*</i>

<sup>a</sup> 229 total samples available for analysis; pos: positive, neg: negative

\* statistically significant

## Session F: Performance of CLIA-Waived HIV Tests

**F3. Performance of the NJ Rapid 4th Generation HIV POC Testing Algorithm**

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**Objective:** Falsely positive rapid HIV test results can occur for many reasons including: manufacturing, operator performance and/or other issues (transportation anomalies, handling and storage conditions, etc.). In 2009, NJ introduced a two-test rapid HIV testing algorithm (RTA) to reduce false positives results, and improve rapid screening and linkage to care. While the introduction of a 4th generation, rapid point-of-care (POC) test offers the potential for earlier detection, enhanced screening performance and rapid linkage into care; the addition of a p24Ag biomarker complicates orthogonal confirmation. The NJ DOH manages HIV rapid testing at more than 160 sites across NJ with a seroprevalence of 0.84%. In 2015, we introduced the Alere Determine Combo (DC) a new, CLIA-waived 4<sup>th</sup> generation rapid test and a modified RTA to expedite linkage to care.

**Methods:** When initial rapid HIV1/2 screening results are positive and a second manufacturer's HIV1/2 rapid test indicates a negative result, it is called a discordant result (DR). Because of the absence of a second, approved rapid assay able to identify p24Ag an RTA becomes more complicated with a 4<sup>th</sup> gen. assay. As a result, we rely upon immediate linkage for all p24Ag positive screens, and orthogonal confirmation only of antibody positive screens. We continue to perform additional testing for those with p24Ag only and to resolve DRs.

**Results:** As of September, 2015, 16,520 had been screened using DC in NJ with 139 (.84%) identified as preliminary positive. Of these, 25 failed to confirm on a second rapid (Trinity Unigold). Additional laboratory-based testing identified three (3) as truly positive, early infections, while 22 (88%) represented false positive initial DC screens. The distribution of discordant results among the 160 sites did suggest that operator inexperience has relevance and that training and assistance play important roles in reducing the frequency.

**Conclusions:** Discordant results are rare and are usually due to initial false positive screening tests. As testing modalities grow more sensitive, discordant results create additional demands for rapid analysis and resolution of ambiguous results. Even with the addition of p24Ag, RTA remains an effective tool for discriminating falsely positive results efficiently and at the POC.

## Session F: Performance of CLIA-Waived HIV Tests

**F4. Evaluation of New HIV Testing Technologies in a Clinical Setting with High Incidence: Rationale, Study Design and Preliminary Results from Project DETECT.**

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<sup>2</sup> University of Washington

<sup>3</sup> Centers for Disease Control and Prevention

<sup>4</sup> Public Health Seattle & King County Laboratory

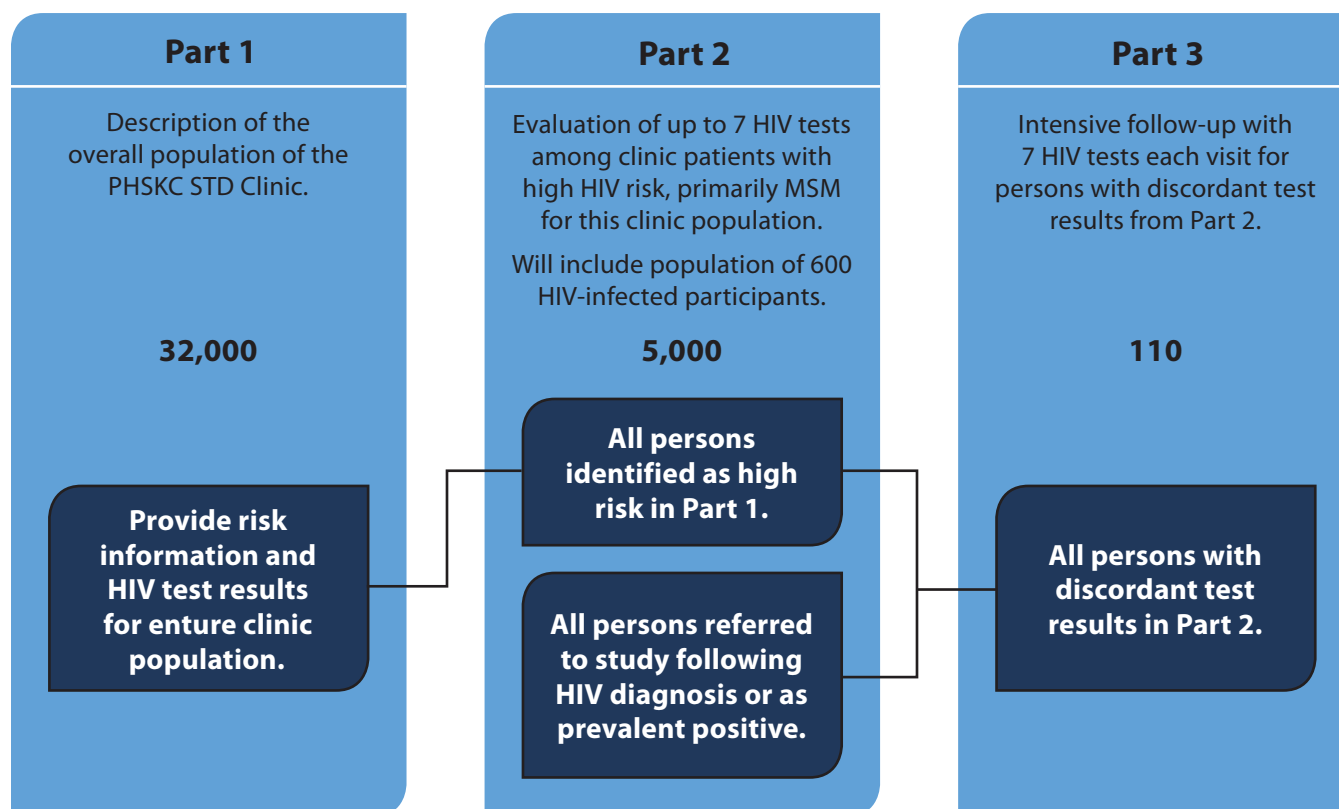
**Objective:** Project DETECT is being conducted to evaluate the performance of the newest point-of-care (POC) HIV tests using fresh whole blood and oral fluid specimens. We are particularly interested in the sensitivity of the tests early in infection, when the antibody response is developing.

**Methods:** CDC and the University of Washington are conducting the study in 3 parts (Figure 1). In Part 1, HIV risk is assessed among clients seeking care. In Part 2, men who have sex with men (MSM) undergo a panel of HIV tests (Figure 1). Participants with discordant results on POC HIV tests or laboratory assays are offered enrollment in Part 3, during which they are followed for up to 9 visits (70 days).

**Results:** Through 11/30/2015, 59 MSM have enrolled in Part 2; 1 participant tested HIV-positive on all POC tests, 5 participants had discordant results, and 3 of these enrolled in Part 3. One participant with a false-reactive INSTI result has remained reactive on only this test through 7 visits (39 days of follow-up). The other two Part 3 participants have results indicative of early HIV infection. Both reported symptoms of seroconversion illness and had initiated antiretroviral therapy after diagnosis and within 2 weeks prior to enrollment in Project DETECT. The first was referred after testing pooled NAT positive. He was reactive on all blood tests and oral fluid OraQuick at enrollment, has lost reactivity to the latter over time, and was never reactive on DPP with oral fluid. The second was referred after a reactive ARCHITECT test and negative Multispot, was reactive on only Determine(AB) at enrollment, remains negative on both oral fluid tests, and has shown slightly better sensitivity with venous blood than fingerstick on several tests (e.g., a 1 visit delay in INSTI reactivity), through 27 days of follow-up.

**Conclusions:** To date, the study protocol has efficiently identified recently infected individuals and has provided novel findings in early serial follow-up. A panel of test results is being compiled to compare whole blood and oral fluid sensitivity and can be expanded in the future to evaluate new tests such as POC NAT.

**Figure 1:** Flow diagram of study participants and eligibility criteria for each part of Project DETECT



The objective of Part 1 is to identify HIV-negative MSM (who are at high-risk for early infection) and to characterize the overall population of clients attending the Public Health Seattle and King County STD clinic over the 5-year study period.

The objective of Part 2 is to evaluate the tests under study using fresh specimens collected from no more than 5,000 participants, including a minimum of 600 HIV-infected participants, with at least 50 identified with early infection (defined as a reactive result on at least one but not all tests with documented seroconversion in Part 3). Tests performed in this part of the study currently include: OraQuick and DPP performed on blood and oral fluid, Determine Combo and INSTI performed on blood, and Geenius performed whenever at least one of the other tests is reactive. Laboratory testing includes screening with the Architect Ag/AB Combo, followed by Multispot if the Architect is reactive and pooled NAT testing (Abbott Realtime in 25 member pools) if Architect is non-reactive. Specimens with reactive Architect results undergo individual testing with Abbott realtime to confirm infection and establish a baseline viral load value.

The objective of Part 3 is to evaluate the seroconversion sensitivity of the new HIV tests through serial follow-up and describe characteristics of persons in the process of seroconversion compared to those of persons with established infection. Part 3 involves serial testing 3, 7, 10, 14, 21, 28, 42, 56, and 70 days after the Part 2 visit or until these discordant results are resolved. The tests listed for Part 2 will be performed at each time point; in Part 3, tests are performed using both fingerstick and anticoagulated (K3-EDTA) whole blood. It is expected that a minimum of 50 individuals with documented seroconversion during follow-up will be included in the total sample of specimen panels delivered to CDC and that the remaining panels would include partial panels from persons who don't complete follow-up and panels from persons enrolled in Part 3 who initially tested false-positive in Part 2.



## Session G: Special Testing Circumstances

### G1. Evolving State Laboratory Diagnostic Capacity During an HIV Outbreak

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<sup>4</sup>Laboratories, Indiana State Department of Health

<sup>5</sup>Division of HIV/AIDS Prevention

<sup>6</sup>Epidemiology Branch, Centers for Disease Control and Prevention

<sup>7</sup>Centers for Disease Control and Prevention

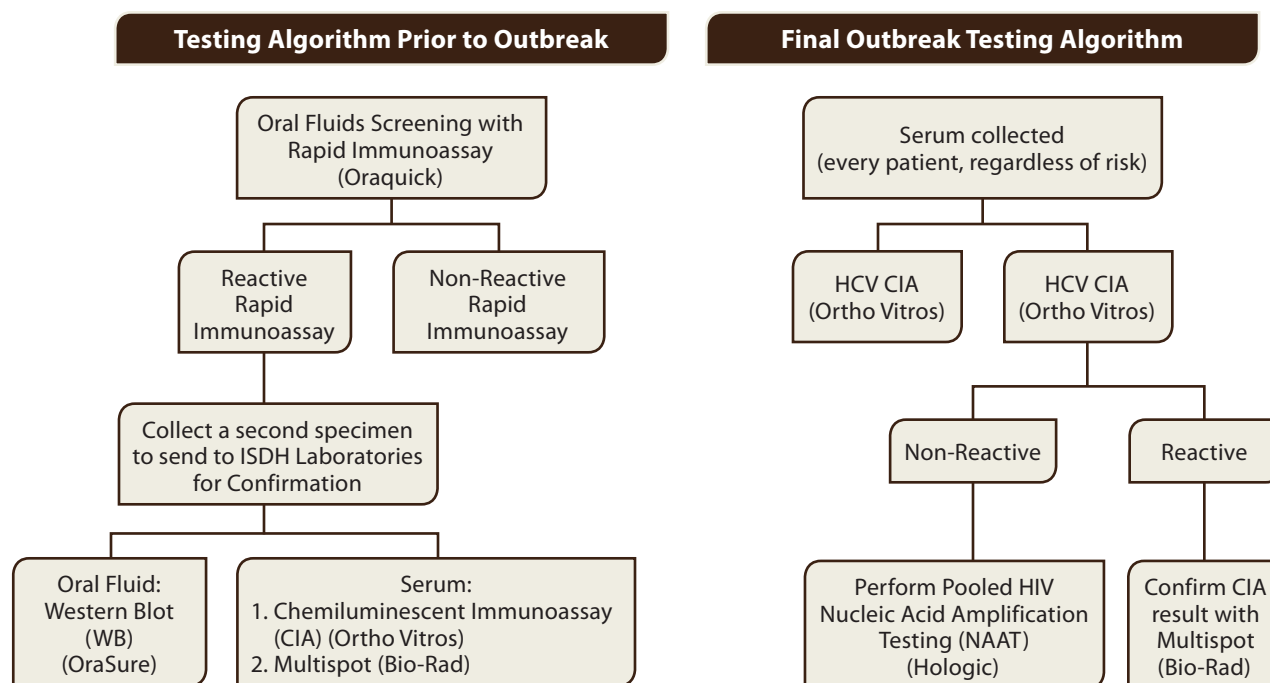
**Project:** In 2015, an outbreak involving 184 new cases of HIV-1 infection were identified in southeastern Indiana, in an area that reports <5 new cases of HIV infection annually.

**Issue:** Prior to this outbreak, all individuals receiving HIV testing through the Indiana State Department of Health (ISDH) were screened with an oral fluid rapid test (Oraquick). Blood or oral fluid specimens with positive screening results were then sent to the ISDH Laboratories (ISDHL) for confirmation by 3<sup>rd</sup> generation chemiluminescent immunoassay (CIA, Ortho Vitros) and Multispot HIV-1/HIV-2 differentiation assays (Bio-Rad) (FIGURE). The HIV testing algorithm of ISDHL was adapted four times during the 2015 outbreak to meet investigational needs, and included modifications in both the HIV and Hepatitis C Virus (HCV) testing menus.

**Results:** First, to decrease the detection window for acute HIV infection, state-wide pooled HIV nucleic acid amplification testing (NAAT, Hologic) was implemented for all HIV-antibody (HIV-Ab) negative specimens. HIV-Ab negative specimens were pooled into intermediate pools of 16 specimens, and 16 intermediate pools were combined into a master pool of 256 specimens. Master pools were tested weekly by NAAT and led to early detection for three outbreak-related cases. Second, HCV testing (Ortho Vitros) was performed on all serum specimens submitted for outbreak-related HIV testing, due to the high preponderance of injection drug use in this cohort (Ortho Vitros). Third, all individuals receiving HIV testing were asked to submit a blood specimen, regardless of their risk factors, in order to maximize HIV and HCV case detection (FIGURE). Finally, in December 2015, 4<sup>th</sup> generation HIV antigen/antibody combination testing (Abbott Architect) replaced the previous algorithm of 3<sup>rd</sup> generation testing followed by pooled NAAT on HIV Ab negatives. As of December 2015, 1557 outbreak-related serum specimens have been submitted to ISDHL for both HIV and HCV testing. Within this cohort, HIV positivity was 8.09%, with an HCV co-infection rate of 92.9%.

**Lessons Learned:** Overall, this dynamic shift from a traditional diagnostic algorithm to one tailored for outbreak management demonstrated the flexibility required of this state public health laboratory in an emerging HIV outbreak investigation.

**Figure.** Comparison of prior and final outbreak HIV and HCV testing algorithms –Indiana State Department of Health, 2015-2016.



## Session G: Special Testing Circumstances

**G2. Beyond Drug Resistance Testing: Using HIV-1 Sequence Data to Infer Transmission Networks and Inform Public Health Action**

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<sup>1</sup> Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention

Recent years have brought an expansion in the use of molecular data to understand the spread of infectious diseases. When combined with epidemiologic data, HIV genetic sequences obtained from routine drug resistance testing can enhance understanding of the spread of HIV among and between populations, identify growing clusters of genetically linked infections, and direct prevention efforts. This roundtable will discuss CDC's system for molecular HIV surveillance, describe current successes and challenges, and highlight the development of new tools to analyze large datasets. Our first presentation will describe CDC's Molecular HIV Surveillance (MHS) system. The 27 state and local HIV surveillance programs that participate in MHS collaborate with commercial/private, public, and hospital-based laboratories to electronically collect sequence data from resistance testing performed for HIV care; >100,000 genetic HIV sequences have been reported to date. We will explain how these data have been used to infer transmission networks and understand transmission between subpopulations. We will also describe recent analyses to identify growing clusters and prioritize investigation and prevention efforts. Analysis of clusters and transmission networks requires specific software, and our second presentation will describe a new Microbial Transmission Networks Analytic Platform that is being developed to analyze and visualize transmission networks and identify growing clusters of concern. We will also discuss approaches to making these results and analytic tools available to state and local health departments. By the end of the session, participants will gain appreciation of the importance of molecular surveillance and how sequence data generated for clinical purposes can be harnessed for public health action.

## Session G: Special Testing Circumstances

### G3. Absence of Serological Response Following Early Treatment of Acute HIV Infection

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<sup>2</sup>DLDM, WRAIR

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One approach to HIV cure is to initiate highly active antiretroviral therapy (HAART) at very early times in acute HIV infection (AHI) to rapidly reduce viral load to levels below those required for establishment of stable infection. The reduction of plasma viremia to below the threshold levels required to trigger HIV-1 immune response, may also prevent emergence of HIV diagnostic markers in blood. HIV infected infants who initiated treatment before 12 weeks of age frequently become HIV seronegative by 2 years of age, but have not cleared virus from latent reservoirs. In the absence of therapy, typical HIV infection dynamics in adults present as detectable HIV RNA (Fiebig I); followed shortly by HIV-1 p24 Antigen (Fiebig II); emergence of anti HIV EIA (Fiebig III); and finally HIV Western blot signal by approximately 2-3 weeks detection of RNA. In a IRB approved study in Bangkok, Thailand, HIV-1 viremic volunteers who initiated HAART prior to establishment of confirmed HIV-1 antibody responses were followed subsequently for evolution of serological markers of infection. Plasma samples collected at Week (Wk) 0, 2, 12, and 24 were tested by EIA 1/2 Plus O (3<sup>rd</sup> Gen), HIV-1 Western blot (WB), and MultiSpot (MS) assays (Bio-Rad Laboratories, Inc; Redmond, WA). Of 22 volunteers initiating HAART at Fiebig I, 12 (54.5%) remained EIA Neg and 16 (72.7%) failed to seroconvert to WB reactivity (R) by Wk 24. Two of 41 (4.8%) volunteers treated at Fiebig II, failed to seroconvert to EIA R by Wk 24 and an additional 12 (29.3%) individuals remained WB NEG or IND at Wk 24. One of 17 (5.9%) individuals treated at Fiebig IV, became EIA NEG by Wk 12, and 8 (52.9%) others remained WB IND by Wk 24. Of the 80 individuals initiating ART at Fiebig I to IV in our study, 37 (46.3%) tested WB NEG and 54 (67.5%) were MS NEG at Wk 24. Caution is urged in interpretation of negative serological signal in individuals on ART as the absence of infection.

**Table 1.** WB Negative rates following initiation of therapy at early times in infection.

	N	Number WB Neg (%)							
		Wk 0		Wk 2		Wk 12		Wk 24	
<b>Untreated</b>	<b>27</b>	<b>27</b>	<b>100%</b>	<b>24</b>	<b>88.9%</b>	<b>0</b>	<b>0.0%</b>	<b>0</b>	<b>0.0%</b>
<b>Stage at Treatment Initiation</b>									
Fiebig I	22	22	100%	22	100%	17	77.3%	16	72.7%
Fiebig II	41	41	100%	32	78.0%	14	34.1%	12	29.3%
Fiebig IV	17	17	100%	10	58.8%	6	35.3%	9	52.9%
Total Treat	80	80	100%	64	80.0%	37	46.3%	37	46.3%

## Session G: Special Testing Circumstances

**G4. HIV Antibodies as Markers of HIV Systemic Reservoir and Viral Suppression**

S. M. Keating<sup>1</sup>, C. D. Pilcher<sup>2</sup>, V. Jain<sup>2</sup>, M. Lebedeva<sup>3</sup>, D. Hampton<sup>3</sup>, X. Deng<sup>1</sup>, S. G. Deeks<sup>2</sup>, and **M. P. Busch**<sup>1</sup>

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<sup>2</sup>Department of Medicine, UCSF

<sup>3</sup>Blood Systems Research Institute

**Objective:** Assay sensitivity is a major limitation in measuring the HIV reservoir in anti-retroviral (ART) suppressed individuals; there is a need for inexpensive, high-throughput assays for monitoring continued viral suppression or quantifying the latent viral reservoir to support cure research. HIV antibody (Ab) “Recency Assays” (RA) are used to identify recently infected individuals to project population incidence from cross-sectional serosurveys. In these studies ART-treated or spontaneous (elite) control elicit reductions in HIV Ab that correlates with duration and level of viral-suppression (ART<elite<chronic). We hypothesized that application of RAs to longitudinal specimens from ART-suppressed individuals would demonstrate progressive Ab decline as a consequence of reduction of antigenic stimulation from viral reservoirs, and that the concentration and avidity of the Ab responses after long-term viral control would correlate with viral reservoir measurements.

**Methods:** Three RAs were used to measure quantity and avidity of Ab over time: Less-Sensitive (LS: 1:400 dilution in buffer; increased cutoff) and avidity modifications (AI: guanidine incubation) for the VITROS® Anti-HIV1+2 assay and the Limiting Antigen (LAg) assay. We investigated 31 early-treated (ET) and 35 late-treated (LT) individuals at five timepoints before and after treatment initiation. We also measured the dynamic changes of antibodies over time in long-term treated individuals; we had antibody and viral measurements from all timepoints, and cell-associated RNA (CA-R) and proviral DNA (PV-D) measurements at the final 2 timepoints.

**Results:** Ab from pre-treatment timepoints from chronically-infected individuals correlate with viral loads (LS- and AI VITROS  $p<0.005$ ; LAg  $p<0.05$ ). The decline in Ab reactivity by RAs are faster in the LT compared to the ET group ( $p<0.001$ ) and for the LT, Ab concentrations continue to decline with viral suppression. The PV-D and CA-R measurements correlate with LAg and LS-VITROS reactivity (both  $p=0.01$ ).

**Conclusions:** There is progressive and consistent reduction in quantity and avidity of HIV Abs with time on treatment. This corresponds with reduction in circulating virus and active and latently infected lymphocytes. The Ab measurements correlate with pre-ART viral loads and post-ART viral reservoirs. Measuring the quantity and quality of HIV Ab may be a useful indirect marker of reservoir size/activity for monitoring viral suppression and measuring the systemic viral reservoir.

## Session H: Testing Alternatives using Dried Blood Specimens

# H1. Evaluation of the Performance of the Bio-Rad GS HIV Combo Ag/Ab EIA and Bio-Rad Geenius™ HIV-1/2 Supplemental Assay Using Dried Blood Spots as an Alternative Specimen Type

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<sup>2</sup> Oak Ridge Institute for Science and Education

<sup>3</sup> Bio-Rad Laboratories

**Objective:** FDA-approved antigen/antibody combo and HIV1/2 differentiation supplemental tests used in the CDC/APHL recommended diagnostic algorithm are not approved for use with dried blood spot (DBS). We evaluated DBS specimen suitability for use with the Bio-Rad GS HIV Combo Ag/Ab (BRC) and Geenius™ HIV-1/2 (Geenius) Supplemental Assay.

**Methods:** DBS specimens included 60 prepared from simulated whole blood from 11 HIV-1 seroconversion panels, 105 from persons with established HIV-1 infections stored long-term at -20° C, and 348 from persons who inject drugs screened with a rapid test during HIV surveillance. The DBS eluate for both assays was obtained from one 6 mm punch in 150 µL of working strength GS HIV-1 Western blot (WB) specimen diluent/wash buffer incubated overnight at 2-8°C. For BRC, 75 µL of the eluate, 60 min sample incubation at RT (625 rpm), and a different cutoff assay were used. For Geenius, 40 µL of the eluate followed by 1 drop of assay buffer (well #1) was used. Geenius was tested in BRC-reactive specimens. DBS results were compared to results from matched plasma tested with Bio-Rad GS HIV-1/HIV-2 PLUS O EIA (BR+O) and Geenius, or to HIV diagnosis reached at each site during surveillance.

**Results:** Of 60 DBS from seroconversion panels, 47 were BRC-plasma reactive, 32 BR+O-plasma reactive and 39 BRC-DBS reactive. BRC-DBS detected more infections than BR+O-plasma ( $p=0.0133$ ), but less infections than BRC-plasma ( $p=0.0133$ ). Of 47 BRC-plasma reactive specimens from seroconverters, 22 were Geenius-HIV-1 positive (plasma algorithm). The DBS algorithm detected fewer HIV-1 infections than plasma (15 vs. 22  $p=0.0455$ ). All HIV-1 established infections were correctly classified using long-term stored DBS. Of 348 DBS collected for HIV surveillance (Table), without retesting and nucleic acid results, the DBS algorithm sensitivity was 99.0% and the specificity was 99.6%.

**Conclusions:** The DBS algorithm was less sensitive than plasma in early infections, but the BRC-DBS protocol was more sensitive than an IgG/IgM test (BR+O-plasma). Nucleic acid testing with DBS will be required; however, the results were promising when applied in a high-risk population. Implementation of a DBS diagnostic testing algorithm would benefit individuals reluctant to have blood draws and HIV surveillance.

**Table.** Performance of the HIV diagnostic algorithm using dried blood spots during HIV surveillance

Reported HIV status/rapid test result/final result	n	First DBS eluate						Second DBS eluate	
		BRC		Geenius				BRC	
		NR	R	negative	HIV-1 positive	invalid	not done	NR	RR
unaware/negative/HIV-negative	245	242	3	2			1	2 <sup>a</sup>	1 <sup>a</sup>
unaware/preliminary positive/HIV-negative	1		1	1				1	
unaware/preliminary positive/HIV-1 positive	35		35		35				
self-reported positive/not done/HIV-1 positive	67		67		66	1			

n: number of specimens; NR: non-reactive; R: reactive; a: HIV-1 viral load (DBS)= Target not detect

## Session I: Integrated Testing for Multiple Pathogens

# I1. Evaluation of an Emergency Department HIV and Syphilis Screening Program Using Rapid Point of Care Diagnostics in Detroit, Michigan 2015

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<sup>1</sup> DHAP, CDC

<sup>2</sup> CDC

<sup>3</sup> Henry Ford Hospital

**Objective:** The number of primary and secondary syphilis cases in Detroit, MI increased from 73 in 2010 to 199 in 2013, with 56% of cases in young black men who have sex with men, and 52% HIV coinfection rate. To respond to a need for HIV and syphilis testing services, we implemented a health services model in an emergency department (ED) using recently CLIA-waived rapid point-of-care (POC) tests for HIV and syphilis.

**Methods:** We offered HIV and syphilis screening to men aged 18-34 years who sought care at the ED starting in July 2015. We used two rapid POC tests: the Alere Determine HIV-1/2 Ag/Ab Combo test (Determine) and the Syphilis Health Check (SHC) treponemal test. All patients were also tested with the Biorad 4<sup>th</sup> generation HIV test, with reactive specimens undergoing confirmatory testing with the Multispot HIV-1/HIV-2 rapid test (Multispot) and Roche COBAS TaqMan HIV-1 Test, v2.0 (VL) testing for discordant specimens. All patients were also tested with the rapid plasma reagin (RPR) and *Treponema pallidum* particle agglutination (TPPA) tests. Dedicated testing staff conducted counseling and testing to reduce ED staff burden.

**Results:** Of 392 participants (87% black, median age: 25 years), HIV (n=2) or syphilis (n=2) infection was identified in 1.0% of participants by rapid testing. Overall, HIV prevalence was 0.8%. Three patients screened reactive with Determine, two were confirmed to have HIV infection and one result was a false positive (Table). A fourth patient had a nonreactive Determine test but was diagnosed with acute HIV by laboratory testing. Four patients had reactive SHC tests, with two confirmed syphilis infections, one false positive, and one awaiting further testing (Table). All three HIV-infected patients were linked to care, and one of the two confirmed syphilis cases was treated during their ED visit.

**Conclusions:** A targeted HIV and syphilis screening program is feasible to implement in an ED using dedicated, non-ED staff. A similar high frequency of HIV and syphilis infections have been identified and treated highlighting a potential role for dual HIV and syphilis rapid testing in settings with patients at risk for these infections.

**Table 1:** Test results for HIV and syphilis rapid point-of-care (POC) and laboratory tests

Case Number	Determine Rapid HIV POC	Biorad Ag/Ab Generation	Multispot	HIV-1 RNA Viral Load	Linked to HIV Care	SHC Rapid Syphilis POC	RPR	RPR Titer	TPPA	Treated in ED
1	Non-reactive	Non-reactive	n/a	n/a	n/a	Reactive	Non-reactive	n/a	Non-reactive	Yes
2	Non-reactive	Non-reactive	n/a	n/a	n/a	Reactive	Reactive	1:04	Reactive	No
3	Reactive	Reactive	Reactive	n/a	Yes	Reactive	Non-reactive	n/a	Pending	Yes
4	Non-reactive	Non-reactive	n/a	n/a	n/a	Reactive	Reactive	1:16	Reactive	Yes
5	Reactive	Reactive	Reactive	n/a	Yes	Non-reactive	Non-reactive	n/a	Pending	n/a
6	Non-reactive	Reactive	Non-reactive	1 million copies/mL	Yes	Non-reactive	Non-reactive	n/a	Pending	n/a
7	Reactive	Non-reactive	n/a	n/a	n/a	Non-reactive	Non-reactive	n/a	Pending	n/a

RPR – rapid plasma reagin; TPPA – *Treponema pallidum* particle agglutination; ED – emergency department; POC – point of care

## Session I: Integrated Testing for Multiple Pathogens

## 12. Multiplex Screening Assays - Advancing Targeted Screening of Co-Morbidity via DPP® HIV-Syphilis Multiplex Rapid Test

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**Objective:** Brothers Health Collective (BHC), Chicago, IL, serves a population with a high prevalence ( $\geq 5\%$ ) and incidence of Syphilis and HIV infection. BHC evaluated a new rapid test, DPP® HIV-Syphilis Assay (DPP Test) developed by ChemBio Diagnostics. This new assay offers the advantage of sensitive, simultaneous screening of HIV and Syphilis which allows for individuals to immediately receive results at the Point-of-Care (POC).

**Methods:** Subjects of varying combinations of HIV and Syphilis status were recruited by BHC from the City of East Moline, Chicago and Suburban Cook County between January and May 2015 (Table 1).

Serum specimens were collected from each subject and tested on the DPP Test (Figure 1). Results were interpreted using the DPP reader.

Patient statuses (PS) were confirmed at reference laboratories.

**Results:** When compared to reference results available, the DPP Test resulted in:

HIV sensitivity and specificity of 100% ( $101/101 = 100\%$  with 95% CI = 96.3% - 100%) and 100% ( $55/55 = 100\%$  with 95% CI = 93.5% - 100%), respectively.

Syphilis sensitivity and specificity of 100% ( $63/63 = 100\%$  with 95% CI = 94.3% - 100%) and 93.4% ( $127/136 = 93.4\%$  with 95% CI = 87.9% - 96.5%), respectively.

Interestingly, the DPP Test identified new syphilis infections in subjects from the HIV Known Positive (18%, 17/96) and in the High Risk (6%, 3/50) groups. Eight new identified syphilis cases (ages 19-36) had RPR titer of  $\geq 1:32$ , indicative of active infection, of these 7 were self-identified as MSM. One subject from the MSM population, who was a transgendered individual with a history of prior diagnosis and treatment of HIV and Syphilis, yielded an RPR titer of 1:8192, suggesting re-infection with syphilis.

**Conclusions:** This study confirms that the multiplex DPP Test performs equivalently to lab based tests. The use of a sensitive rapid test for the detection of both Syphilis and HIV provides the benefit of increased cost savings due to the simultaneous detection of two co-morbidities using one specimen. The DPP Test is easy to use and the DPP Reader mitigates risks associated with the subjectivity of visual interpretation.

**Figure 1** DPP HIV Syphilis Assay System





**Table 1** Summary of Study Population and Reference Laboratory Test Results

Population Description	HIV Status Unknown	HIV Positive	HIV Status Unknown	HIV Positive
	Syphilis Unknown n = 50	Syphilis Unknown n = 96	Syphilis Positive n = 13	Syphilis Positive n = 40
Median Age (Range)	42.5 (18-66)	47.5 (19-78)	48 (22-57)	41.5 (21-67)
Male	66% (33/50)	77.1% (74/96)	69.2% (9/13)	80% (32/40)
Female	30% (15/50)	20.8% (20/96)	30.8% (4/13)	15% (6/40)
Transgender	4% (2/50)	2.1% (2/96)	0% (0/13)	5% (2/40)
<b>Race</b>				
White	6% (3/50)	10.4% (10/96)	0% (0/13)	5% (2/40)
Black	92% (46/50)	83.3% (80/96)	92.3% (12/13)	95% (38/40)
Other	2% (1/50)	6.3% (6/96)	7.7% (1/13)	0% (0/40)
<b>Risk Factors</b>				
MSM	25% (13/50)	55.2% (53/96)	15.4% (2/13)	75% (30/40)
Multiple Sex Partners	32% (16/50)	15.6% (15/96)	38.5% (5/13)	7.5% (3/40)
Other <sup>1</sup>	42% (21/50)	29.2% (28/96)	46.2% (6/13)	17.5% (7/40)
HIV Positive: (4 <sup>th</sup> Generation EIA) <sup>2</sup>	6% (3/48 <sup>4</sup> )	98.6% (70/71 <sup>5</sup> )	10% (1/10 <sup>6</sup> )	100% (27/27 <sup>7</sup> )
Syphilis positive: (EIA +/ RPR +) <sup>3</sup>	2% (1/50)	13.5% (13/96)	7.7% (1/13)	62.5% (25/40)
Syphilis positive: (EIA +/ RPR -) <sup>3</sup>	4% (2/50)	4.2% (4/96)	30.8% (4/13)	32.5% (13/40)

<sup>1</sup> "Other" encompasses the five (5) remaining risk factor categories: (1) Born to an HIV or syphilis positive mother, (2), Injected illegal drugs, (3) History of unprotected sex with an injection drug user, (4) History of sex with a partner with any STD, and (5) History of any sexually transmitted disease (STD). Each category represents < 5% of each population.

<sup>2</sup> Confirmation of results was conducted according to the current recognized algorithm, the "4<sup>th</sup> generation" algorithm, for the detection of HIV (CDC Laboratory Testing for the Diagnosis of HIV Infection: Updated Recommendations, 2014). The following tests were used in the 4<sup>th</sup> generation algorithm at the reference laboratory: Abbot Architect<sup>®</sup> HIV Ag/Ab Combo Assay, Bio-Rad Multispot HIV-1/HIV-2 Rapid Test, and the Gen-Probe<sup>®</sup> APTIMA<sup>®</sup> HIV-1 RNA Qualitative Assay.

<sup>3</sup> Confirmation of results was conducted according to the alternate algorithm for the detection of Syphilis infection (EIA/RPR/TPPA). The following tests were used in the reverse algorithm at the reference laboratory: Bio-Rad Bioplex<sup>®</sup> 2200 Syphilis IgG EIA Screen for treponemal antibodies, BD Macro-Vue<sup>™</sup> RPR Confirmation with titer, and the Fujirebio Diagnostics, Inc. SERODIA<sup>®</sup>-TPPA.

<sup>4</sup> Two (2) specimens were excluded from calculations as the time between specimen collection and reference testing exceeded the reference laboratory's stability requirements (3 days), and thus, these specimens were determined to be unacceptable for HIV testing. In total, 48 specimens were included in HIV calculations for the High Risk population (HIV Status and Syphilis status unknown).

<sup>5</sup> One (1) specimen was negative via 4<sup>th</sup> Generation EIA at the reference laboratory. Additionally, twenty-five (25) specimens were excluded from calculations as the time between specimen collection and reference testing exceeded the reference laboratory's stability requirements (3 days), and thus, these specimens were determined to be unacceptable for HIV testing. In total, 71 specimens were included in HIV calculations for the HIV Known Positive only population.

<sup>6</sup> Three (3) specimens were excluded from calculations as the time between specimen collection and reference testing exceeded the reference laboratory's stability requirements (3 days), and thus, these specimens were determined to be unacceptable for HIV testing. In total, 10 specimens were included in HIV calculations for the Syphilis Known Positive only population.

<sup>7</sup> Thirteen (13) specimens were excluded from calculations as the time between specimen collection and reference testing exceeded the reference laboratory's stability requirements (3 days), and thus, these specimens were determined to be unacceptable for HIV testing. In total, 27 specimens were included in HIV calculations for the HIV Known Positive/Syphilis Known Positive ("Co-infected") population.

## Session I: Integrated Testing for Multiple Pathogens

**I3. Performance of a Rapid, 60 Second Multiplex Test for Simultaneous Detection of Antibodies to HIV-1, HIV-2 and *T. pallidum* in Serum, Plasma and Whole Blood**

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**Objective:** To determine the performance of the INSTI Multiplex HIV-1/HIV-2/Syphilis Antibody Test compared to reference methods for detection of HIV-1, HIV-2 and *T. pallidum* antibodies.

**Methods:** Laboratory and field studies were conducted to assess performance of the INSTI Multiplex relative to Comparator Methods (CM) for detection of antibodies to HIV-1, HIV-2, and *T. pallidum* in serum, plasma and contrived whole blood. One in-house non-clinical laboratory study compared INSTI Multiplex *T. pallidum* antibody results to a *T. pallidum* Particle Agglutination Assay (Serodia-TPPA,) for 524 frozen, commercially sourced serum and plasma samples. A study conducted in, Paris, France investigated the *T. pallidum* sensitivity of INSTI Multiplex on 103 serum samples from patients in primary, secondary or early latent clinical stages of syphilis infection. In a field study in Bangalore India on a population at risk for HIV and STI (n=1010 plasma samples), the performance of the INSTI Multiplex was assessed against syphilis and HIV status as determined by a multiple test algorithm of syphilis HIV antibody tests. Finally, performance of the INSTI Multiplex for *T. pallidum* antibody was compared to TPPA for 169 contrived EDTA whole blood specimens.

**Results:** From the 524 commercially sourced serum/plasma samples, the positive and negative percent agreement with TPPA for *T. pallidum* antibodies was 95.2% (138/145) and 98.7% (374/379) respectively. From the 103 clinically staged syphilis samples, *T. pallidum* sensitivity of INSTI Multiplex was 100% for secondary syphilis (41/41), 95.5% for early latent syphilis (21/22), and 72.5% for primary syphilis (29/40). From the 1010 samples in the India field study, positive and negative percent agreement of INSTI Multiplex for *T. pallidum* antibody status was 81.2% (13/16) and 99.9% (993/994) respectively; for HIV-1/HIV-2 antibody, positive and negative percent agreement were each 100% (136/136 positive; 874/874 negative). For the 169 contrived whole blood samples the positive and negative percent agreement with TPPA for *T. pallidum* antibodies was 96.9% (62/64) and 100% (105/105) respectively.

**Conclusions:** Performance of the INSTI Multiplex HIV-1/HIV-2/Syphilis Antibody Test for *T. pallidum* was substantially equivalent to other *T. pallidum* antibody methods; performance for HIV was equivalent to the FDA approved INSTI HIV-1/HIV-2 Antibody Test.

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

# J1. The Effects of MDRI Updates and Transition to a New Recency Assay on HIV Incidence Estimates in a Selected Number of HIV Surveillance Areas, United States

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**Objective:** Monitoring trends in HIV incidence is critical as the National HIV Surveillance System (NHSS) shifts from using the BED HIV-1 Incidence EIA (Sedia Corp., Calypte Corp.) (BED) to the avidity-based, modified Bio-Rad HIV-1/HIV-2 plus O EIA (Bio-Rad avidity) for HIV recency determination. We explored the effects of transitioning to Bio-Rad avidity and updated BED mean duration of recent infection (MDRI) on HIV incidence estimates.

**Methods:** Data from persons  $\geq 13$  years with HIV diagnosed in 2010 and reported to the NHHS were used to estimate HIV incidence in selected surveillance areas using the stratified extrapolation approach. MDRI for BED and Bio-Rad avidity were estimated using a revised survival method and subtype B U.S. specimens. Incidence estimates were calculated using BED (current MDRI=162 days and new MDRI=198 days) and Bio-Rad avidity (MDRI=239 days) at developer-recommended cutoffs for recent result (Bio-Rad avidity, index threshold=30; BED, normalized OD=0.8). Of the 12,893 persons diagnosed in 2010 with BED results, 5,423 (42%) were also tested with Bio-Rad avidity at the CDC DHAP laboratory. Multiple imputation was used to account for missing data. Simple z-score tests were used to compare incidence estimates.

**Results:** Overall HIV incidence was estimated at 24,921 infections (95% CI: 21,931–27,910) using BED with MDRI=162, 21,999 infections (95% CI: 18,889–25,109) using BED with MDRI=198 and 22,457 infections (95% CI: 19,669–25,245) using Bio-Rad avidity. Estimates based on BED with MDRI=198 were significantly lower when compared to those derived using BED with MDRI=162. There was no significant difference between the overall estimate based on BED with MDRI=198 and Bio-Rad avidity. However, Bio-Rad based estimates were higher than BED (MDRI=198) based estimates among whites and persons with infection attributed to injection drug use.

**Conclusion:** HIV incidence estimates depend on the accuracy of the MDRI and variations have an effect; a longer MDRI results in lower incidence estimates. A similar statistical approach was used to calculate MDRI estimates for BED and Bio-Rad avidity; the new BED MDRI was longer than previous estimates. HIV incidence estimates based on the new BED MDRI and the Bio-Rad avidity assay were comparable.

**Table.** Estimated HIV incidence in a selected number of surveillance areas using the stratified extrapolation approach based on BED and Bio-Rad avidity

Assay	Cutoff BED ODn/Bio-Rad Avidity Index	MDRI* (days)	Estimated HIV Incidence	95% Confidence Interval	p-value
BED (Updated MDRI)	0.8	198	21,999	18,889–25,109	Ref
BED (Current MDRI)	0.8	162	24,921	21,931–27,910	0.005
Bio-Rad Avidity	30	239	22,457	19,669–25,245	0.6

\* Mean duration of recent infection

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

**J2. Development and Evaluation of a Bead-Based Multiplex Assay for HIV Detection, Serotyping and Estimation of Recent Infection**E. Yufenyuy<sup>1</sup> and B. Parekh<sup>1</sup><sup>1</sup> International Laboratory Branch, Division of Global HIV/AIDS, Centers for Disease Control and Prevention, Atlanta, GA 30333 USA

**Objective:** Initially a death sentence, HIV-1 infection has now become a manageable disease, but one that requires lifelong treatment with antiretroviral drugs. While the quest for an HIV-1/AIDS cure continues, measures are being taken to know areas that are heaviest hit by the disease and to curb the emergence of new HIV-1 infections. For these measures to be successful, accurate determination of HIV-1 incidence is critical in tracking the leading edge of the epidemic and targeting of limited resources. Hence, reliable incidence assays are crucial. Our study describes the development of a multiplex assay that simultaneously performs diagnosis, serotyping and the estimation of recent infection of HIV in a single well.

**Methods:** Two recombinant proteins; p24-gp4 and rIDR-M, and HIV-2 IDR peptide were coupled on three different microspheres. The coupled antigens were serologically assessed using several, well-characterized panel of specimens for development, optimization and assay evaluation. HIV diagnosis and serotyping is achieved with the binding of specific antibodies to p24-gp41 and HIV-2 IDR respectively. The HIV-2 IDR differentially binds to antibodies from HIV-2 specimens or dual infections. Only high avidity antibodies from HIV-1 or HIV-1/2 bind effectively to the rIDR-M protein to separate recent from long term infections.

**Results:** After initial development and optimization, the assay showed great inter and intra assay, and inter coupling reproducibility with %CV < 10% for positive samples. A panel of 1500 specimens was blindly tested on the multiplex platform and the results compared to results from EIA, western blot, multispot and the LAg assay. The diagnostic component of the assay performed with high sensitivity and specificity (99.7% and 99.6% respectively), while the specificity of the serotyping was 99.9% and the sensitivity 96.3%. There was a very strong agreement between the detection of new infections using the LAg assay and that from the multiplex assay. With very strong inter and intra assay concordance, the multiplex assay has the ability to diagnose, perform serotyping and detect new HIV infections.

**Conclusions:** This assay has the potential to revolutionize HIV prevalence and incidence studies especially in low income settings: making them more accurate, rapid and less expensive.

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

### J3. Unmodified Diagnostic Assay Provides Similar Performance to Avidity Modification for Surveillance and Clinical Recency Staging Applications

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**Objective:** Recent Infection Testing Algorithms (RITAs) are of sustained interest for cross-sectional estimation of HIV incidence, and there is strong demand for clinical applications. This study seeks to characterise and evaluate the performance, for recency determination, of an unmodified high dynamic range fourth-generation chemiluminescent microparticle immunoassay (Abbott ARCHITECT HIV Ag/Ab Combo Assay) and an avidity modification of the assay, designed to increase dynamic range (ARCHITECT Avidity Assay).

**Methods:** Performance of the assays was investigated by application to a well characterised, previously described, panel of 2500 specimens established for the evaluation of RITAs by the CEPHIA collaboration. In line with previous findings that viral suppression is the main predictor of spurious 'low' (i.e. 'recent') immunoassay signal, supplementary viral load testing was performed. The critical indicators of recency test performance – Mean Duration of Recent Infection (MDRI) and False Recent Rate (FRR) – were estimated using previously described binomial regressions. Reproducibility was investigated by means of repeat testing of blinded control specimens.

**Results:** The estimated MDRI and FRRs for a range of recent/non-recent discrimination thresholds are summarised in the table, indicating that MDRI is tuneable from several tens to a few hundred days. MDRI and FRRs are similar for the unmodified and avidity assays. In virally suppressed subjects, the introduction of a viral load threshold largely eliminates false recency. Reproducibility of avidity index readings from 25 repeat tests of three control specimens with the avidity assay (CoV 3.5%, 3.3% and 7.4%) is slightly better than that in signal-to-cutoff ratio readings from the unmodified assay (CoV 4.5%, 5.5% and 9.5%), probably as a result of normalization.

**Conclusions:** The performance, for recency determination, of an unmodified high-throughput, highly sensitive and specific, diagnostic assay is comparable to that of the avidity modification and other customised recency assays. This opens up the transformative possibility of handling diagnosis and staging on a single platform within routine clinical use and epidemiological studies. The ARCHITECT Avidity assay provides modestly improved recency determination, but the use of a customised assay implies greater logistical complexity and cost.

**Table:** Comparison of assay performance

UNMODIFIED ARCHITECT ASSAY				
S/CO Threshold	MDRI <sup>1</sup>	MDRI (VL>1000) <sup>1</sup>	FRR (%) ART-naïve <sup>2</sup>	FRR (%) ART-suppressed <sup>3</sup>
100	89 (73-107)	69 (55-86)	1.0 (0.2-2.8)	34.1 (25.4-43.6)
150	130 (111-151)	110 (92-129)	1.3 (0.3-3.2)	40.7 (31.6-50.4)
200	170 (147-196)	141 (119-165)	3.2 (1.5-5.8)	46.0 (36.6-55.6)
250	215 (188-244)	180 (154-207)	5.4 (3.2-8.6)	53.5 (43.9-63.0)
300	270 (240-303)	225 (196-256)	7.8 (5.1-11.4)	57.1 (47.4-66.4)
350	331 (298-364)	278 (246-311)	11.2 (7.9-15.2)	62.8 (53.2-71.7)
400	388 (353-422)	334 (300-367)	15.3 (11.5-19.8)	67.3 (57.8-75.8)
ARCHITECT AVIDITY ASSAY				
AI Threshold	MDRI <sup>1</sup>	MDRI (VL>1000) <sup>1</sup>	FRR (%) ART-naïve <sup>2</sup>	FRR (%) ART-suppressed <sup>3</sup>
70	88 (69-109)	75 (57-96)	0.0 (0.0-1.9)	27.9 (19.9-37.1)
75	122 (100-146)	104 (84-127)	1.0 (0.1-3.6)	33.2 (24.6-42.7)
80	128 (105-153)	109 (88-133)	1.5 (0.3-4.4)	33.6 (25.0-43.1)
85	146 (121-173)	123 (99-148)	2.5 (0.8-5.8)	35.4 (26.6-45.0)
90	205 (176-235)	173 (146-202)	7.6 (4.3-12.2)	43.8 (34.5-53.5)
95	288 (256-321)	244 (214-276)	15.4 (10.7-21.2)	55.3 (45.7-64.7)
100	389 (354-423)	328 (295-361)	33.3 (26.8-40.4)	66.4 (56.9-75.0)

<sup>1</sup> Restricted to untreated subjects and excluding elite controllers. MDRI expressed in days.

<sup>2</sup> Excluding elite controllers.

<sup>3</sup> Restricted to subjects on first treatment and on treatment for at least three months.

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

**J4. A Generalizable Method with Improved Accuracy for Estimation of HIV Infection Duration, Using Clinical HIV Testing Histories**

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**Objective:** Attempts by clinical/public health and research to date HIV infection duration using “Fiebig staging” are limited by unavailability of assays, incomplete data and logistics. We sought a more generalizable method for estimating HIV infection duration that could use data typically available in histories of HIV seroconversion.

**Method:** This was secondary data analysis involving HIV test results previously obtained on specimen panels from seroconverting blood plasma donors. We included only data from individuals who converted from RNA<100 to >100 cp/mL on successive bleeds<7 days apart, allowing precise imputation of a “date of detectable infection (DDI)” at the 100 cp/mL level for each subject and time since this DDI for each specimen. Alternative estimates of a predicted DDI were then made from the data, using several candidate predictive models, and results directly compared. Models included: 1) a conventional Fiebig-derived rule; 2) a novel VL ramp-up model (mean of slopes obtained from linear regression of logVL vs. time in training data); and 3) a generalizable seroconversion history formula placing the EDDI at the middle of a plausible interval defined by the testing history, accounting for known differences in assay conversion timing.

**Results:** Analyses included 468 specimens (174 in stages F1-3), from 70 subjects that met stringent criteria; agreement of model estimates with time since DDI was greatest for the VL ramp-up model (intra-class correlation ICC=0.78, R<sup>2</sup>=0.62). Compared with Fiebig-derived method (ICC 0.33, R<sup>2</sup>=0.35), the seroconversion formula agreed somewhat better with DDI when it was applied to results that changed between test dates (ICC 0.47, R<sup>2</sup>=0.49); this same formula applied to discrepant results from the same-day (in the manner of Fiebig staging) gave agreement similar to the Fiebig method (ICC 0.30-0.37) and these models correlated strongly with Fiebig estimates (ICC=0.93).

**Conclusions:** We propose a two step model for estimating HIV infection duration from HIV test results, which can be applied to any case of HIV seroconversion. If an acute specimen viral load result is available, this will provide the most precise estimate. If not, the detailed seroconversion history may give similar or better estimation of time since detectable infection than Fiebig stage-based estimation.

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

**J5. Use of the Avioq VioOne Profile Assay for Detection of Recent HIV-1 Infection**

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**Objective:** The Avioq VioOne™ HIV Profile™ assay is an ELISA for confirmation and differentiation of individual antibodies directed to various gene products of HIV-1 and HIV-2. It may also be used as an aid to determine recent HIV-1 infections. A study was performed to determine if the assay can correctly identify samples from patients with recent and longstanding infections contained in the HIV Recency Biomarker Screening Panel (HRBS) provided by the Consortium for Evaluation and Performance of HIV Incidence Assays (CEPHIA).

**Methods:** Profile utilizes HIV-1 *env*, *pol*, and *gag* recombinant gene products and HIV-2 peptide coated microwells (solid phase) to capture HIV-1 and HIV-2 antibodies. Detection and differentiation is accomplished with either individual antigen-HRP or biotin/streptavidin-HRP conjugates with TMB substrate. For detection of recent infections, HIV-1 *env* (gp160) is coated at normal and reduced concentrations in separate wells. A Recency Index (RI) is calculated to differentiate between recent and longstanding HIV-1 infections. The RI is the multiple of sample signal to cutoff (S/CO) values produced in normal and reduced gp160 concentration wells. To evaluate the utility to predict recent infections, the assay was tested with well characterized specimens provided by CEPHIA designed for biomarker discovery and incidence assay model development. The panel includes 124 plasma samples from patients with chronic HIV infection (n=42), early HIV infection (n=24), on antiretroviral therapy (ART, n=22), elite controllers (n=11), and HIV negative patients (n=25).

**Results:** Average RI on samples from Recent Infections is much smaller compared to Longstanding Infection and Challenge samples. Using a RI cutoff of 19.00, samples correctly identified by Avioq's Profile assay are compared to a Limited Antigen Avidity assay in the Table below.

**Conclusions:** Results indicate Avioq's RI calculation has the potential to distinguish between recent and longstanding HIV-1 infections with improved accuracy over the LAg Avidity assay.

Specimen Populations	n	Average Profile RI	HIV Profile Correct ID	LAg-Avidity Assay Correct ID
Recent Infection (<12 mo)	24	10.19	22	20
Longstanding Infection (>12 mo)	42	121.92	42	40
Challenge: Elite	11	91.16	10	7
Challenge: ART-Treated (initiated early)	10	22.97	3	2
Challenge: ART-Treated (initiated late)	11	78.94	10	10



## Session A: Performance of HIV Screening Tests in the Laboratory

2	Performance of the Abbott ARCHITECT HIV Ag/Ab Combo Assay In a Low Incidence Population <b>Michael A. Pentella</b> , PhD, D(ABMM), Massachusetts Department of Public Health
3	Detecting Acute HIV in a High Incidence, Low Screen Setting with ARCHITECT 4th Generation HIV Ag/Ab Testing <b>Kimia Sobhani</b> , PhD, Cedars Sinai Medical Center
4	Evaluation of Antigen and Antibody Sensitivity in 4th Generation HIV Combo Assays Using a Genetically Diverse HIV Panel: ARCHITECT® HIV Ag/Ab Combo vs ADVIA Centaur HIV Ag/Ab Combo (CHIV) <b>Xiaoxing Qiu</b> , PhD, Abbott Laboratories

## Session B: Performance of Supplemental Tests and Nucleic Acid Tests

6	Successful Identification of Acute HIV Infections through Pooled Nucleic Acid Amplification Testing in New York City <b>Anthony Tran</b> , DrPH, MPH, D(ABMM), New York City Department of Health and Mental Hygiene
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## Session C: CDC/APHL Laboratory Testing Algorithm

7	Experience with the Fourth Generation HIV Testing Algorithm in Saint Louis, Missouri <b>Neil W. Anderson</b> , MD, Washington University School of Medicine
8	Increase in the Use of 4th generation HIV-1/2 Immunoassays in the HIV Diagnostic Testing Algorithm Over Time - New York State's Experience <b>Joanne Gerber</b> , MS, RN, New York State Department of Health
9	Distribution of the ARCHITECT Sample to Cutoff Ratio (S/CO) by Fiebig Stage of HIV-1 Infection <b>Eric M. Ramos</b> , MD, University of Washington
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## Session A: Performance of HIV Screening Tests in the Laboratory

### 2. Performance of the Abbott ARCHITECT HIV Ag/Ab Combo Assay in a Low Incidence Population

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**Background:** In March 2015, the Massachusetts State Public Health Laboratory (MA SPHL) implemented the automated Abbott Architect i2000 system for HIV Ag/Ab combo (CMIA), to handle increasing HIV testing volume and to test all submissions for HCV antibody. The performance characteristics for 12,998 specimens, through August 2015, are reported.

**Methods:** Serum specimens were collected and shipped to the laboratory within 72 hours for testing using the CDC recommended algorithm of screening with a 4<sup>th</sup> generation antigen/antibody combination immunoassay and testing repeatedly reactive specimens with the BioRad MultiSpot HIV-1/HIV-2 antibody differentiation immunoassay (ADI). If results were discordant, an HIV-1 RNA NAT was performed.

**Results:** Over six months, MA SPHL reported results for 12,998 specimens. Of those, 126 (0.97%) were reactive by both CMIA and ADI. Twenty-nine (0.22%) were CMIA reactive, ADI negative or indeterminate, and NAT negative. Two discordant specimens were NAT positive. The signal-to-cut off (s/c) value of the true positives ranged from 5.45 to 977.13 with a mean of 500.24. The s/c value of the combo immunoassay false positives ranged from 1.01 to 42.15 with a mean of 5.08. The s/c of true positives varied on repeat testing by 10%, while s/c varied by 22% for the false positives. There were 12,841 true negative tests. The positive predictive value (PVP) was 81.5% and the negative predictive value (PVN) was 100%. During the same time period in 2014, 7,240 specimens were tested with BioRad HIV antigen/antibody combo EIA. Of those, 103 (1.4%) were reactive by both EIA and ADI. Seven (0.01%) were BioRad combo reactive and ADI negative and NAT negative. There were 7,129 true negative tests. The PVP was 93.64%. The EIA NPV was 100%

**Conclusions:** By changing to the Abbott Architect automated platform, the laboratory gained efficiencies e.g, handling increased specimen volume and decreasing TAT and allowing for simultaneous testing for HCV antibody; however, the increased percentage of false positives required additional testing. With the CMIA, significant variance at low s/c values was observed, supporting the need for supplemental testing.

## Session A: Performance of HIV Screening Tests in the Laboratory

### 3. Detecting Acute HIV in a High Incidence, Low Screen Setting with ARCHITECT 4<sup>th</sup> Generation HIV Ag/Ab Testing

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<sup>2</sup> Abbott Laboratories

**Project:** Historically, ~37% of individuals who are diagnosed with HIV progress to AIDS within 6 months, indicating that many are not caught before acute symptoms fade and are not re-tested until symptoms return in late stages. Furthermore, in September 2015, the WHO released guidelines stating that newly diagnosed HIV patients should receive antiretroviral therapy immediately after diagnosis, rather than waiting for symptoms to develop; this further highlights the need for detecting HIV infection as early as possible. This study assesses the ability of 4<sup>th</sup> generation HIV screening in detecting acute cases in a high incidence setting (Los Angeles, CA).

**Issue:** During the acute stage, patients do not develop measurable antibodies to HIV. Consequently, testing these patients with 3rd generation tests, which only detect antibodies, will yield negative results. We studied the ability of 4th generation antigen-antibody (Ag/Ab) testing in detecting acute HIV infection in a high transmission setting with selective screening.

**Results:** Over a 19-month period at Cedars-Sinai Medical Center, 8 acute HIV-1 positive cases (7 males, 1 female) were detected by Abbott ARCHITECT 4th generation HIV Ag/Ab Combo screening (Table 1). This high number was detected with physician-directed screening on 0.3% of our ED population. An acute diagnosis constituted Combo positive, Western blot negative results, which were confirmed positive by PCR. Of the 8 cases, 7 presented to the ED with acute symptoms. Additionally, data from previous opt-out screening studies predicts that, if we had a blanket opt-out in place vs. physician-directed testing, potentially 16 acute HIV cases could have been detected within this timeframe. The main barriers to implementing opt-out screening are the added testing and staff costs (i.e., follow-up).

**Lessons Learned:** These cases demonstrate the importance of HIV screening in detecting both acute and established infections with accuracy, particularly in high transmission areas. By preventing new transmissions through early and accurate diagnosis, we can approach a future where rampant transmission becomes a thing of the past. Lastly, the 8 acute cases detected on 0.3% of our ED population via selective screening helps demonstrate the significant potential yield of blanket opt-out testing. Ultimately the healthcare benefits (endorsed by CDC and WHO) outweigh the added costs.

**Table 1:** Acute cases detected. All presented to the ED

Case	Patient	Presentation/Symptoms	Abbott ARCHITECT HIV Combo (4th Gen)	Western Blot	PCR Viral Load (copies/ml)
1	34 y/o Male	Presented to ED with fever, headache, chills	Positive	Negative	156,000
2	34 y/o Male	Presented to ED w/ fever, rash, enlarged tonsils	Positive	Negative	3,510,000
3	27 y/o Male	Presented to ED w/ fever/chills	Positive	IND	5,600,000
4	49 y/o Male	Outpatient specimen (no further information)	Positive	Negative	>10,000,000
5	37 y/o Female	Presented to ED with abdominal pain, diarrhea	Positive	NT	>10,000,000
6	25 y/o Male	Presented to ED with fever, muscle aches, and diarrhea	Positive	Negative	1,760,000
7	52 y/o Male	Presented to ED with abdominal pain	Positive	Negative	3,050,000
8	24 y/o Male	Presented to ED with myalgia, fever, and emesis	Positive	Negative	>10,000,000

NT=Not Tested, IND=Indeterminate, y/o=year old

## Session A: Performance of HIV Screening Tests in the Laboratory

### 4. Evaluation of Antigen and Antibody Sensitivity in 4<sup>th</sup> Generation HIV Combo Assays Using a Genetically Diverse HIV Panel: ARCHITECT® HIV Ag/Ab Combo vs ADVIA Centaur HIV Ag/Ab Combo (CHIV)

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<sup>1</sup>Abbott Laboratories

<sup>2</sup>ARUP Laboratories

**Objective:** The use of 4<sup>th</sup> generation HIV antigen/antibody (Ag/Ab) combination assays has decreased the window between HIV exposure and detection. These assays are designed to detect acute and chronic infections by simultaneously measuring HIV p24 antigen and antibody. Early detection of acute infection is dependent upon antigen sensitivity of the assay, and genetic variation of HIV strains may also impact assay performance. In this study, a genetically diverse panel of HIV virus isolates and HIV-infected plasma was used to compare performance of two 4<sup>th</sup> generation Ag/Ab combo assays: Abbott ARCHITECT HIV Ag/Ab Combo and Siemens ADVIA Centaur HIV Ag/Ab Combo (CHIV).

**Methods:** A panel of 100 unique members representing diluted HIV antigen (n=51) or antibody (n=49) samples including divergent HIV-1 and HIV-2 subtypes and groups as well as 7 seroconversion panels were tested with the FDA approved Siemens ADVIA Centaur HIV Ag/Ab Combo (Centaur CHIV) and Abbott ARCHITECT HIV Ag/Ab Combo (ARCHITECT HIV Combo) assays according to each manufacturer's protocol. Analytic sensitivity of both assays was determined using the WHO International HIV-1 p24 antigen standard.

**Results:** ARCHITECT HIV Combo detected all 50 HIV-1 and HIV-2 virus isolate dilutions and 1 diluted antigen only plasma sample, while Centaur CHIV only detected 10 strains, missing 28/35 group M, 9/11 HIV group O, 2 group N and both HIV-2 virus dilutions. In addition, analytic sensitivity of ARCHITECT HIV Combo (0.74 IU/mL) was 2.4-fold better than Centaur CHIV (1.8 IU/mL) based on WHO p24 standard. Of the 49 diluted antibody samples, 47 were ARCHITECT HIV Combo reactive whereas 34 were detected by Centaur CHIV. Two of 34 Centaur CHIV reactive antibody dilutions were not detected by ARCHITECT HIV Combo. Notably, ARCHITECT HIV Combo showed better seroconversion sensitivity than Centaur CHIV, detecting one bleed earlier in 3 of 7 seroconversion panels.

**Conclusions:** In comparison with the recently FDA-approved Centaur HIV Combo assay, ARCHITECT HIV Combo demonstrated more sensitive detection of p24 antigen across divergent HIV-1 and HIV-2 strains as well as superior antibody sensitivity for group O and HIV-2 infections.

## Session B: Performance of Supplemental Tests and Nucleic Acid Tests

### 6. Successful Identification of Acute HIV Infections through Pooled Nucleic Acid Amplification Testing in New York City

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**Objective:** Acute HIV infection (AHI), characterized by high viral loads in blood and genital secretions along with non-specific clinical symptoms, leads to increased transmission of HIV. Until recently, rapid HIV tests were unable to detect AHI, leaving a critical gap in the early detection and prevention of HIV transmission. Pooled HIV nucleic acid amplification testing (NAAT) can help identify AHI from non-reactive rapid HIV tests. This study describes the utility of pooled NAAT after initial screening on a 3<sup>rd</sup> generation rapid HIV test.

**Methods:** Specimens screened for HIV at NYC STD clinics from May 1, 2012–October 28, 2015 were included in the study. Plasma samples from individuals with non-reactive rapid tests (OraQuick ADVANCE HIV-1/2) who agreed to AHI testing were sent to the PHL for pooled HIV NAAT on the Aptima HIV-1 RNA qualitative assay. Mini-pools of 16 plasma specimens are batched and tested twice weekly. If any pool was positive, it was deconstructed and the individual sample was tested to determine positivity. In total, 35,607 rapid test non-reactive specimens were evaluated in the laboratory.

**Results:** Pooled testing of rapid test negative samples by NAAT identified AHI in 156 specimens during the study period. This equates to a diagnostic yield of 0.44%. Individuals testing positive by pooled NAAT are subsequently referred into treatment and care.

**Conclusion:** We continue to detect a high number of acute HIV infections from our pooled NAAT testing algorithm in New York City. On average one acutely HIV infected individual was identified weekly during the study period. The study shows the continued utility of pooled HIV NAAT testing in high prevalence settings for the identification of AHI that would not have been identified through rapid testing alone. Further evaluation of this algorithm with a 4<sup>th</sup> generation antigen/antibody combination rapid HIV test will be conducted in the near future.

## Session C: CDC/APHL Laboratory Testing Algorithm

### 7. Experience with the Fourth Generation HIV Testing Algorithm in Saint Louis, Missouri

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**Objective:** In 2014 the Centers for Disease Control (CDC) recommended transitioning to the new fourth generation testing algorithm to screen for HIV. The purpose of this study was to retrospectively examine our experience at Barnes Jewish Hospital (Saint Louis, MO) with the new testing algorithm.

**Methods:** We retrospectively reviewed total test volumes and results for each test included in the fourth generation algorithm. Results from the antigen/antibody screen were classified as either “false positive” or “true positive” according to the remaining tests in the algorithm. A detailed chart review was performed on all patients with either “false positive” or “true positive” antigen/antibody screens.

**Results:** Of the 10,536 patient specimens tested by the fourth generation algorithm, 1% (n=82) were positive by the antigen/antibody screen. Following Multispot testing, 72% (n=62) of screen positive specimens were positive for HIV-1. No specimens were positive for HIV-2 and only 2% (n=2) of screen positive specimens were classified as “undifferentiated” (reactive for both HIV-1 and HIV-2 targets). Negative Multispot results were obtained for 22% (n=18) of the screen positive specimens. Only 17 were tested by NAAT, of which only 1 specimen was positive.

Chart review of patients with “true positive” screens (n=60) revealed the diagnosis of HIV-1 was already known in 24 of the tested patients (testing performed to re-establish care). Of the 36 patients with newly diagnosed HIV-1, 78% (n=28) had documented risk factors, 14% (n=5) had a lack of risk factors, and 8% (n=3) had no history available in the patient chart. None were pregnant or had autoimmune disease. In contrast, of the 14 patients with false positive screens, only 14% (n=2) had documented HIV-1 risk factors (Figure 3). Pregnancy and autoimmune disease was observed in 50% (n=7) of these patients

**Conclusion:** Testing specimens from our patient population by the antigen/antibody HIV screen yields a positivity rate of 1%. However, approximately 20% of positive screens are determined to be false positives. The presence of HIV-1 risk factors may be a useful predictor of a true positive screen, whereas conditions such as autoimmune disease or pregnancy may be useful predictors of false positive screens.



## Session C: CDC/APHL Laboratory Testing Algorithm

### 8. Increase in the Use of 4th generation HIV-1/2 Immunoassays in the HIV Diagnostic Testing Algorithm Over Time - New York State's Experience

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<sup>1</sup> Bureau of HIV/AIDS Epidemiology, AIDS Institute

<sup>2</sup> Wadsworth Center

<sup>3</sup> Division of Epidemiology, Evaluation and Research, AIDS Institute, New York State Department of Health

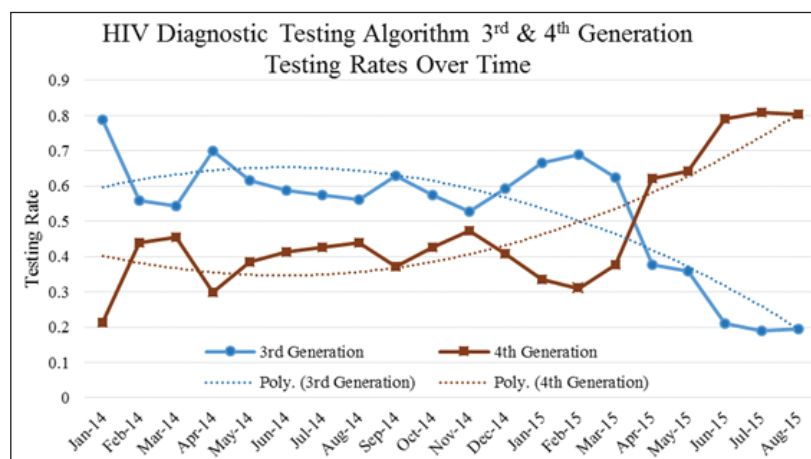
<sup>4</sup> University of Albany, School of Public Health

**Objective:** The Centers for Disease Control and Prevention and Association of Public Health Laboratories recommended HIV Diagnostic Testing Algorithm (DTA) provides several advantages over the conventional Western blot strategy including earlier and more accurate detection of HIV-1 and improved detection of HIV-2. The recommended first test (step one) of the DTA is a HIV-1/2 antigen (Ag) antibody (Ab) combo immunoassay (4<sup>th</sup> generation). Laboratories have been urged to replace less-sensitive 3<sup>rd</sup> generation HIV-1/2 immunoassays with a recommended 4<sup>th</sup> generation immunoassay. The objective of this study was to use electronic laboratory reporting data submitted to New York State Department of Health (NYSDOH) to assess implementation of the recommended 4<sup>th</sup> generation immunoassay.

**Methods:** As of August 2015, 46 laboratories were permitted by NYSDOH Clinical Laboratory Evaluation Program and certified to electronically report step one immunoassay results to NYSDOH via the Electronic Clinical Laboratory Reporting System. Over 22,000 step one results from these laboratories for specimens collected between January 1, 2014 and August 31, 2015, were assessed. Each laboratory report contained a LOINC code to identify test type and testing methodology (i.e., 3<sup>rd</sup> or 4<sup>th</sup> generation). Reports were unduplicated and monthly rates were compared by testing methodology. The Mantel-Haenszel test for trend was applied to determine change over time.

**Results:** In January 2014, 15% (7/46) of labs used a 4<sup>th</sup> generation testing methodology, reporting 21% of the step 1 results from the recommended immunoassay. By August 2015, 52% (24/46) of labs used 4<sup>th</sup> generation testing methodology and 80% of results were from the recommended immunoassay. Although the rates are variable over time, there was a clear transition from 3<sup>rd</sup> to 4<sup>th</sup> generation assays ( $p < 0.0001$ ). In March 2015, the 4<sup>th</sup> generation test became the dominant method employed by laboratories reporting step one DTA results to NYSDOH.

**Conclusion:** After nearly two years, the majority of laboratories reporting to the NYSDOH have transitioned to the 4<sup>th</sup> generation HIV Ag/Ab combo immunoassay. Though substantial progress has occurred, several labs are still using inferior testing technologies in the DTA. Health departments should consider monitoring adoption of the recommended test to improve early detection of infection.



## Session C: CDC/APHL Laboratory Testing Algorithm

### 9. Distribution of the ARCHITECT Sample to Cutoff Ratio (S/CO) by Fiebig Stage of HIV-1 Infection

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<sup>1</sup> University of Washington

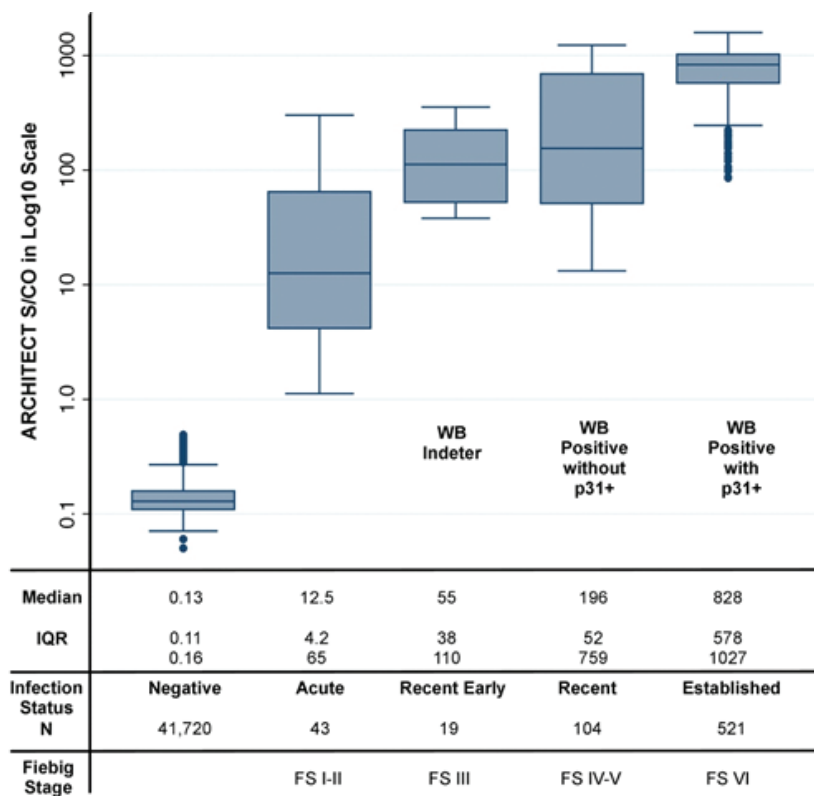
**Objective:** The ARCHITECT HIV Ag/Ab assay detects both HIV-1 p24 antigen and HIV-1/2 specific antibodies; a test result is reactive at a sample to cutoff ratio (S/CO)  $\geq 1$  and non-reactive at S/CO  $< 1$ . Since the S/CO increases initially with viral replication (HIV-1 p24 antigen) and then with the rise in HIV specific antibodies, we sought to correlate the S/CO signal with Fiebig stage (FS) of infection to determine the recency of HIV-1 infection.

**Methods:** A retrospective analysis was done using our primary screening HIV diagnostic algorithm (ARCHITECT) using samples from an academic clinical HIV diagnostic laboratory. The testing interpretation algorithm was: Negative (S/CO  $< 1.0$ ); Acute infection (AHI) FS I-II (S/CO  $\geq 1$ , Bio-Rad Multispot HIV-1/2 rapid test (MS) non-reactive and a positive NAT); Recent early infection FS III (S/CO  $\geq 1$  with MS reactive and indeterminate Western blot (WB)); Recent and established infection (positive WB without p31 band [FS IV or V] or with p31 band present [FS VI], respectively).

**Results:** From 42,407 specimens tested, 41,720 were considered negative with a S/CO median and interquartile range [IQR] of 0.13 [0.11-0.16]. A total of 687 (1.6%) specimens were reactive of which 43 (6.1%) were confirmed as AHI with a S/CO median [IQR] of 12.5 [4.2-65] and a viral load median [IQR] of  $1.45 \times 10^6$  RNA copies/mL [ $4.48 \times 10^5 - 10.0 \times 10^6$ ]. Of the 644 MS reactive, 19 were WB indeterminate with a S/CO median [IQR] of 55 [38-110] and considered as a recent early infection. The rest were divided in two groups; 104 were WB positive without p31 (recent HIV infection) and 521 were p31 positive (established HIV infection) with a S/CO median [IQR] of 196 [52-759] and 828 [578-1027], respectively. The S/CO medians were significantly different among the FS stages (Kruskal-Wallis,  $p < 0.0001$ ) as show the Figure 1. Also were significantly different between acute, recent early and recent HIV infection against established HIV infection (Wilcoxon Mann-Whitney,  $p < 0.0001$ ) and between recent early and early HIV infection (Wilcoxon Mann-Whitney,  $p = 0.004$ ).

**Conclusions:** The ARCHITECT S/CO range of values may be used to presumptively differentiate between AHI, recent and established HIV infection.

**Figure 1:** Association between ARCHITECT sample to cutoff ratio (S/CO) and Fiebig stage of HIV-1 infection.



## Session C: CDC/APHL Laboratory Testing Algorithm

### 10. Rapid HIV Diagnosis in the Hospital Emergency Room and Clinic Settings: Successful Experience and Challenges

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<sup>2</sup> Emergency Medicine, Emory University School of Medicine

<sup>3</sup> Grady Memorial Hospital

Routine HIV testing & diagnosis in the hospital emergency department (ED) and primary care clinics (PCC) began in July 2013 for identification and linkage to care for newly diagnosed HIV-positive patients.

Relevant issues include (1) implementation of rapid testing and reporting of HIV testing in the ED and PCC; (2) follow up for newly diagnosed patients manage the linkage to care after discharged from the ED and PCC.

Relevant efforts include (1) manage the rapid testing of HIV for the FOCUS program using the updated HIV testing algorithm; (2) identify newly diagnosed patients and link them to HIV-related medical care and support services.

The routine testing program began on July 9, 2013, and HIV Ag/Ab testing replaced HIV EIA screening on February 16, 2015; data presented here are for tests completed through November 30, 2015 (3<sup>rd</sup> generation: 19 months; 4<sup>th</sup> generation: 9.5 months) . During this period, 62,002 total tests were completed, belonging to 53,113 unique patients and 465 patients were identified with a new HIV diagnosis (0.9% of unique tested). A higher frequency of patients were identified with acute HIV via 4<sup>th</sup> generation testing compared to 3<sup>rd</sup> generation testing (7.7% vs. 3.7% of new HIV diagnoses,  $p = 0.06$ ). 62.3% of newly diagnosed patients with at least 90 days to be linked to care attended a first appointment with an HIV-care provider (223 out of 413). 70.0% of patients with acute HIV and at least 90 days to be linked to care attended a first medical appointment (14 of 21 patients). For linkage to care, the denominator is adjusted for patients who were unable to be linked because they were deceased, incarcerated, declined linkage, or moved out of the area.

**Supporting Table.** Unique patients tested from July 9, 2013 – November 30, 2015

	3 <sup>rd</sup> Gen (EIA) 7/9/13 - 2/15/15 N=28,825	4 <sup>th</sup> Gen (Ag/Ab) 2/16/15 - 11/30/15 N=24,288	Total N=53,113
Patients newly diagnosed with HIV	297 (1.0% of unique tested)	168 (0.7% of unique tested)	465 (0.9% of unique tested)
Patients with an acute HIV diagnosis	11 (3.7% of new HIV+)	13 (7.7% of new HIV+)	24 (5.2% of new HIV+)

## Session E: Streamlining Test Result Turnaround Time and Linkage to Care

### 11. Impact of In-house HIV Confirmatory Testing on Linkage to Care in Alaska

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<sup>1</sup> HIV/STD Program, <sup>2</sup>Alaska State Virology Laboratory, Alaska Dept of Health & Social Services

**Project:** This project examined the timeliness of human immunodeficiency virus (HIV) test reporting and linkage to care with a new in-house serodiagnosis and confirmation algorithm adopted by the Alaska State Virology Laboratory (ASVL), and determined if transitioning to the new algorithm impacted the turnaround time of test reporting and linkage to care.

**Issue:** Prior to 2012, all confirmatory HIV Western Blot (WB) for Alaska patients were sent to out-of-state reference laboratories. In 2012, ASVL began using the BioRad Multispot HIV-1/HIV-2 antibody differentiation immunoassay for in-house confirmation of HIV. Laboratory data from January 2010 through October 2015 were analyzed to determine the average number of days from the specimen collection date to the date of laboratory report, as well as the date of initial CD4 and viral load (VL), which are used as a proxy to determine if an HIV patient has been linked to medical care. The average number of days from the date of report to the date of initial CD4 and VL testing were also analyzed to determine if the Alaska Section of Epidemiology's new Linkage to Care (L2C) Program, which was implemented during the same period, might have also affected the linkage to care turnaround time.

**Results:** The laboratory data showed that transitioning from WB to Multispot reduced the average turnaround time from the collection date to the report date from 11.3 days [range 9–19] to 6.2 days [range 3–9], and reduced the time from the date of specimen collection to the date of the initial CD4 and VL tests from an average of 17.8 days [range 11–29] to 13.1 days [range 4–28]. The average number of days from the date of report to the date of initial CD4 and VL did not change, indicating that the L2C program efforts did not impact turnaround times (Table 1).

**Lessons Learned:** Offering in-house confirmatory testing for HIV reduced the turnaround time of test reporting and linkage to care. This reduction can result in direct health benefits to the patient as well as benefits to the wider public through preventing further HIV transmission.

**Table 1:** Alaska State Virology Lab HIV Confirmatory Test Turn Around Times by Test Type 1/2010 – 10/2015 (n=41)

	Average number of days from specimen collection date until receipt date [range]	Average number of days from specimen collection date until report date [range]	Average number of days from specimen collection date until date of initial CD4/VL [range]	Average number of days from report date until initial CD4/VL [range]
Western Blot (n=16)	4.3 [1 - 7]	11.3 [9 - 19]	17.8 [11 - 29]	7.6 [1 - 18]
Multi Spot (n=25)	3.3 [2 - 6]	6.2 [3 - 9]	13.1 [4 - 28]	7.8 [0 - 25]

## Session E: Streamlining Test Result Turnaround Time and Linkage to Care

### 12. Do Point-of-Care HIV Testing Technologies Affect Linkage to Care? Results from a Large-Scale HIV Testing Initiative

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<sup>1</sup> Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention

<sup>2</sup> ICF Macro International

**Objective:** The role of point-of-care (POC) rapid testing technologies –tests that deliver results in 60-seconds, or those tests that return results in approximately 15-20 minutes – in successfully linking persons to medical care is unknown. Some have suggested that the 60-second test could decrease counselors' rapport with clients, who then may not adequately access medical services. We investigated the impact of 60-second vs. 15-20 minute rapid testing technologies on linkage to care.

**Methods:** The MSM Testing Initiative (MTI), conducted in 25 cities across the US during 2013-2015, tested and identified men who have sex with men (MSM) with previously undiagnosed HIV infection and linked them to medical care (confirmed doctor's visit within 90 days post-diagnosis). Staff initiated linkage to care activities immediately upon receipt of a reactive rapid test result. Participants were recruited in a variety of settings, including clinical and non-clinical; this analysis excluded MSM recruited in clinical settings to focus on venues where POC rapid tests are commonly used. Risk ratios and 95% confidence intervals (95%CI) calculated from multivariable logistic regression models adjusted for age, race/ethnicity, receiving the rapid test result, and venue type were used to estimate the association between testing technology and linkage to care for those with reactive rapid test results in non-clinical venues.

**Results:** Of 1,843 MSM testing preliminary positive in non-clinical settings, those tested in public areas, bars, or large events had lower linkage to care rates (48.7%) than those testing positive in community-based organization locales (72.4%; aRR=0.67, 95%CI= 0.62-0.73). Test type was related to linkage to care, and varied depending on where testing events took place. In public areas/bars/large events, 60-second tests were associated with higher linkage (51.6%; aRR=1.74, 95%CI=1.29-2.33) compared to 15-20-minute tests (28.2%); but in community-based organization locales, linkage to care was lower for those tested with 60-second tests (70.2%; aRR=0.87, 95%CI=0.79-0.97) compared with 15-20-minute tests (80.7%).

**Conclusions:** In settings such as public areas/bars and events where MSM with HIV infection may risk being lost to medical care, a 60-second POC test could be beneficial for providing immediate linkage to medical care. Additional research should investigate how test type and settings affect linkage to care.

## POSTER ABSTRACTS

**Table 1.** Results of multivariate logistic regression models of the association of linkage to medical care within 90 days among participants testing preliminary HIV-positive identified during venue-based recruitment events in non-clinical settings\*\*

	Linkage to Care		Risk Ratio (95% CI)	Adjusted Risk Ratio (95% CI)
	Yes N (%)	No N (%)		
<b>TOTAL</b>	1076 (58.4)	767 (41.6)		
<b>Age</b>				
Less than 18	13 (43.3)	17 (56.7)	0.75 (0.49 - 1.13)	0.73 (0.48 - 1.12)
18-24	295 (55.6)	236 (44.4)	0.96 (0.86 - 1.07)	1.01 (0.90 - 1.12)
25-34	471 (61.3)	298 (38.8)	1.06 (0.96 - 1.16)	1.08 (0.99 - 1.19)
35+	297 (57.9)	216 (42.1)	Ref	Ref
<b>Race</b>				
Hispanic	384 (60.8)	248 (39.2)	1.01 (0.90 - 1.12)	1.04 (0.93 - 1.17)
Non-Hispanic White	189 (60.4)	124 (39.6)	Ref	Ref
Non-Hispanic Black	434 (55.2)	352 (44.8)	0.91 (0.82 - 1.02)	1.03 (0.91 - 1.16)
Other	57 (62.6)	34 (37.4)	1.04 (0.86 - 1.24)	1.11 (0.93 - 1.33)
<b>Received Test Result</b>				
Yes	1072 (58.8)	752 (41.2)	2.35 (1.01 - 5.50)	1.76 (0.67 - 4.58)
No	4 (25.0)	12 (75.0)	Ref	Ref
<b>HIV Rapid Test Type</b>				
60-second Test	888 (58.9)	620 (41.1)	1.08 (0.95 - 1.22)	1.17 (1.04 - 1.33)
Other Rapid Tests (15-20 minutes)	129 (54.7)	107 (45.3)	Ref	Ref
<b>Venue Category</b>				
Community-based Organizations	546 (72.4)	208 (27.6)	Ref	Ref
Bars, Public Areas, and Large-scaled Events	530 (48.7)	559 (51.3)	<b>0.67 (0.62 - 0.72)</b>	<b>0.67 (0.62 - 0.73)</b>
<b>Community-based Organizations*</b>				
60-second Test	416 (70.2)	177 (29.9)	<b>0.87 (0.78 - 0.96)</b>	<b>0.87 (0.79 - 0.97)</b>
Other Rapid Tests (15-20 minutes)	96 (80.7)	23 (19.3)	Ref	Ref
<b>Bars, Public Areas, and Large-scaled Events*</b>				
60-second Test	472 (51.6)	443 (48.4)	<b>1.83 (1.36 - 2.46)</b>	<b>1.74 (1.29 - 2.33)</b>
Other Rapid Tests (15-20 minutes)	33 (28.2)	84 (71.8)	Ref	Ref

\* Interaction term

\*\* predicted marginal risk ratios estimated from a logistic regression controlling for all variables

## Session E: Streamlining Test Result Turnaround Time and Linkage to Care

### 13. Use of a Point of Care Rapid-Rapid HIV Testing Algorithm for Partners/Contacts in a Ryan White Clinic Will Facilitate Linkage to Care

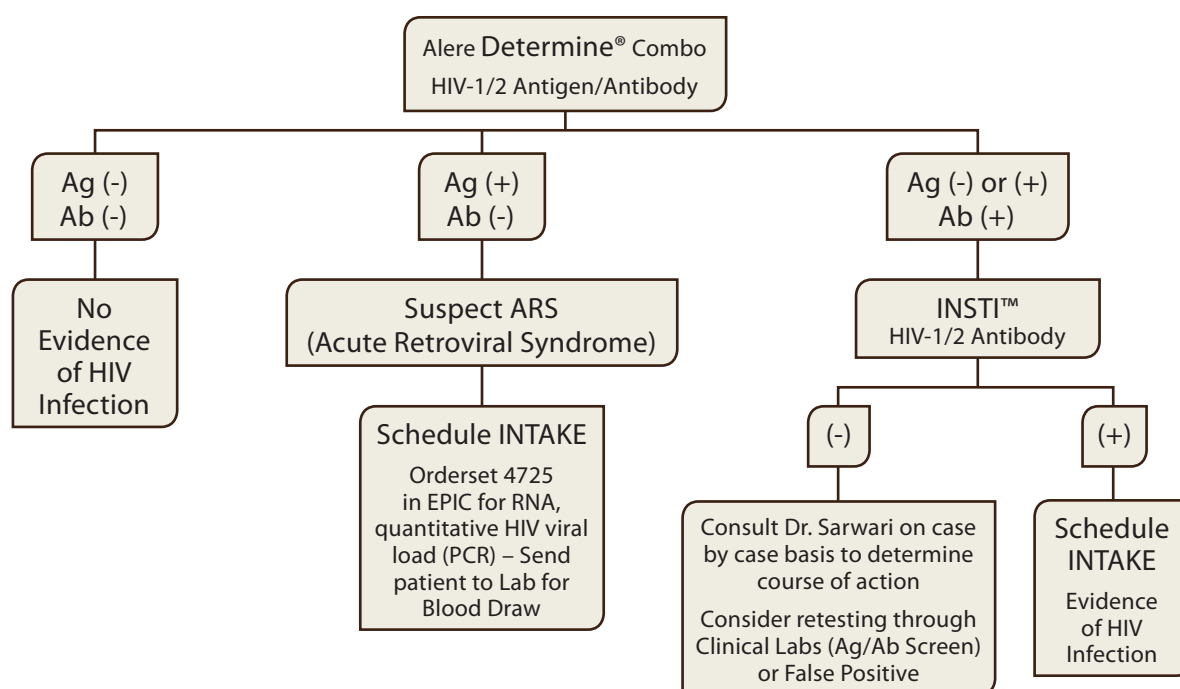
A. R. Sarwari<sup>1</sup> and A. L. Rogers<sup>1</sup>

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**Background:** The CDC currently recommends an HIV testing algorithm utilizing a fourth generation test followed by an HIV differentiation assay/RNA testing for diagnosis of HIV infection. This process increases sensitivity in identifying those individuals with acute retroviral infection. The recommended algorithm can be implemented in traditional HIV testing sites where individuals seek care or request an HIV test, however, those individuals that test positive must then be referred to an HIV care provider (typically outside the testing site) where they must keep their medical appointment to access antiretrovirals and eventually achieve viral suppression. According to CDC's National HIV Care Continuum data (*MMWR* 63:1113-17, 2014) the greatest impact on the ultimate goal of viral suppression is at the point of diagnosis and linkage to care.

**Description:** In 2006 we established a non-traditional HIV testing model by offering free, confidential, rapid HIV testing to partners of our HIV infected patients in the Ryan White Clinic. We have established a modified algorithm when testing these high risk individuals to facilitate diagnosis of HIV infection and linkage to care at the time of testing (point of care). Current HIV positive patients and their partners are asked to participate during regularly scheduled appointments in the Ryan White Clinic using a single finger stick whole blood sample. Testing is performed using two CLIA-waived rapid HIV tests: Alere Determine™ HIV 1/2 Ag/Ab Combo (4<sup>th</sup> generation) and Insti™ HIV-1/2 Ab. An algorithm was developed using the 4<sup>th</sup> generation combination assay as the primary test with reflex testing using a 2<sup>nd</sup> generation test for Ab only or Ag/Ab reactive specimens and RNA testing for Ag only reactive specimens. See figure below.

**Implications:** Since HIV Care Clinics and Disease Intervention Specialists are uniquely positioned to offer HIV testing to partners and contacts of HIV positive patients, we can expedite the linkage to care of new positives using the same team of healthcare professionals who have established a rapport during testing. Having the ability to identify a new HIV infection in a single testing visit and offering immediate support and entry to care in the same location should not be underestimated.





## Session F: Performance of CLIA-Waived HIV Tests

### 14. The Optimization and Evaluation of HIV Screening Algorithm Used in Men Who Have Sex with Men in Metropolitan Bangkok, Thailand

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<sup>4</sup>Chulalongkorn University

<sup>5</sup>SEARCH

**Objective:** HIV diagnosis in Thailand is usually performed at the clinic or hospital. Serum or plasma used for testing requires laboratory equipment to process. A positive result must be followed by two more confirming tests. Sites lacking equipment for confirmation by serum or plasma tests cannot report results in the same day. The mobile clinic is a limited-resource setting. HIV algorithms based on testing whole blood can report results on the same day as testing.

**Methods:** HIV algorithm for the mobile clinic used three different tests: Alere Determine™ HIV 1/2, DoubleCheckGold™ Ultra HIV 1/2, and SD Bioline HIV 1/2 3.0 as first and second confirmatory tests respectively. We compared as first screening test, the mobile algorithm clinic with the standard procedure at the Anonymous Clinic of the Thai Red Cross AIDS Research Centre. At the anonymous Clinic Architect HIV Ag/Ab was used as screening test followed by Alere Determine™ HIV 1/2 and Serodia HIV 1/2 as the confirmatory test. Then we evaluated performance of this algorithm for HIV testing of MSM clients at six venues (4 saunas and 2 spas) in Bangkok, Thailand and compared the result with Architect HIV Ag/Ab. Discordant results were confirmed with nucleic acid amplification test (NAAT) by Aptima assay.

**Results:** The evaluated HIV algorithm demonstrated sensitivity of 100% (95% CI: 96.41, 100) and specificity of 99.65% (95% CI: 98.09, 99.99). The algorithm was applied to participants at six venues. Two hundred thirty-three MSM participants were tested using this algorithm. 38 (16.3%) MSM were found HIV positive by TRC Anonymous Clinic testing algorithm. With the mobile clinic algorithm, we found 36 (15.5%) positive results. We found a sensitivity of 94.9% (95% CI: 82.7, 99.4) and specificity of 100% (95% CI: 98.1, 100) due to 2 cases of acute HIV infection detected in the sauna (1 with 4<sup>th</sup> generation assay positive only and 1 with NAAT positive only).

**Conclusion:** The reported HIV screening algorithm appears satisfactory for mobile clinic setting with same day results. However, for high risk population, a more sensitive 4<sup>th</sup> generation rapid test is highly needed.

## Session F: Performance of CLIA-Waived HIV Tests

### 15. From 2<sup>nd</sup> to 4<sup>th</sup> Generation Rapid HIV Screening — ‘Rolling-Out’ an Enhanced HIV Screening & Linkage Algorithm in New Jersey (NJ)

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<sup>3</sup> Department of Health, Division of HIV, STD & TB Services, State of New Jersey

**Project:** It's not just a question of how sensitive a test is... it's also a question of how often we test, how effectively we link those infected into care, and how well we retain clients in care.

Following CLIA-waiver in December, 2014, NJ began statewide implementation of 4<sup>th</sup> generation, Alere Determine™ HIV-1/2 Ag/Ab Combo (DC), screening at 162 state-funded rapid HIV screening sites. A rapid testing & linkage strategy was implemented at many of these sites to expedite linkage into care and to follow-up on possible discordant results.

**Issue:** In use since 2011, the NJ rapid testing algorithm (NJ - RTA) utilizes orthogonal testing i.e., independent verification of an initial antibody result using a second, but different HIV rapid test to confirm initial HIV screening results. FDA-approval of a 4<sup>th</sup> generation rapid point-of-care test (DC) that detects both HIV-1/2 antibodies and the HIV-1 p24 antigen, offers the potential of earlier detection that could improve screening performance and linkage into rapid HIV care. What remains unclear is the effectiveness of the revised linkage strategy and the overall test performance.

**Results:** Of 162 sites in NJ scheduled to implement DC testing in 2015, 142 (88%) were operational as of October 1, 2015. A rapid linkage to care algorithm was implemented utilizing alternative, second generation rapid tests to provide presumptive confirmation of HIV antibody positives and link individuals into care immediately. The average time to link an identified positive to additional laboratory testing and link them to care was 1.7 days. As of September, 16,520 had been screened using DC with 139 (.84%) identified as preliminary positive. Of those, 25 were subsequently determined to be negative on a second rapid (Trinity Unigold). Three (3) were subsequently identified by laboratory testing as truly HIV rapid positives, 22 (88%) were resolved as false positive initial DC screens.

**Lessons Learned:** A strategic implementation plan is necessary. Beginning with local, pilot sites will identify problems and avoid perpetuating resolvable issues. Performance of the screen will improve as operator issues are resolved and shared in training. Insuring credible clinical referrals is essential.

**Table 1:** Implementation of 4<sup>th</sup> Gen. Rapid HIV Testing

NEW JERSEY DOH – DHSTS SITES			
As of 10/1/2015	<i>New Jersey Clinical Lab License Holder</i>		ALL
	RWJMS (BLD)*	NON-RWJMS (BLD)	
Not Yet Trained	0	20	20
Testing via 4 <sup>th</sup> Generation Rapid	101	41	142
<b>Total - NJ Rapid HIV Screening Sites</b>	<b>101</b>	<b>61</b>	<b>162</b>

\* - RWJMS BLD = The NJ Clinical Lab License is provided by: Rutgers University - Robert W. Johnson Medical School including NJ Bioanalytical Laboratory Directorship (BLD)

## Session F: Performance of CLIA-Waived HIV Tests

### 16. Performance of Determine Combo and Other Point-of-Care HIV Tests Among Seattle MSM

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<sup>3</sup> Public Health - Seattle & King County

<sup>4</sup> Gay City Health Project

**Objective:** The Rapid Test Study was a real-time comparison of point-of-care (POC) HIV tests designed to determine their relative abilities to detect early HIV infection.

**Methods:** HIV-negative MSM and transgender persons were recruited at the Public Health - Seattle & King County STD Clinic, Gay City Health Project, and University of Washington Primary Infection Clinic. Study procedures included one POC test performed on oral fluids (OraQuick) and POC tests performed on fingerstick whole blood specimens: OraQuick, Uni-Gold Recombigen HIV Test, Determine HIV-1/2 Ag/Ab Combo, and INSTI HIV-1/HIV-2 Rapid Antibody Test. Serum specimens from subjects with negative POC results were sent for EIA and pooled NAAT. McNemar's exact tests were used to compare the numbers of HIV-infected subjects detected by the different tests.

**Results:** Between February 2010 and August 2014, 3438 subjects were enrolled (Table). Twenty-four subjects had discordant POC results with at least one reactive and one non-reactive POC test, including one subject with a reactive Determine p24 antigen and an HIV RNA level of 5.8 million copies/mL. This subject represented 9% of the 11 cases of acute (RNA+) and early (EIA+) HIV infection diagnosed at the three sites who were screened prospectively by Determine. OraQuick performed on oral fluids identified fewer men with discordant results compared to all fingerstick tests. OraQuick performed on fingerstick also identified significantly fewer men with discordant results compared to the Determine antibody test component ( $p=.008$ ) and the overall Combo ( $p=.004$ ), and there was a trend when compared to INSTI ( $p=.06$ ).

There were 21 (1.0%) false-positive test results in 2121 visits among HIV-negative persons screened at the STD Clinic. False-positive results were obtained for three participants tested by OraQuick performed on oral fluids (specificity 99.9%), six participants on the Determine Combo antigen and nine on the antibody (combined specificity 99.0%), and four by EIA (specificity 99.8%).

**Conclusion:** As reported by others, Determine underperforms compared to laboratory-based testing for acute HIV infection, but it detected more persons with early HIV infection compared to other one commonly used fingerstick test. The lower specificity of Determine may limit its usefulness in populations with lower HIV incidence.

**Table:** Distribution of point-of-care and laboratory HIV test results among study participants, Seattle, 2010-2014

	STD Clinic n=2189	Gay City n = 1215	PIC n=34 <sup>1</sup>	Total n=3438 <sup>2</sup>
HIV-negative	2121 <sup>3</sup>	1176	1	3298
Total HIV Positive	68 (3.2%)	39 (3.2%)	33	140
Concordant Reactive POC Tests	51 (75.0%)	31 (79.5%)	18	100
Discordant POC Antibody Tests	7 (10.3%)	3 (7.6%)	13	23
All POC Tests Negative/EIA-Positive	2 (2.9%)	4 (17.9%)	0	6 <sup>4</sup>
Acute (EIA-Negative / NAAT-Positive)	8 <sup>5</sup> (11.9%)	1 (2.6%)	2 <sup>6</sup>	11

PIC: University of Washington Primary Infection Clinic; POC: point-of-care; EIA: enzyme immunoassay; NAAT: nucleic acid amplification test

<sup>1</sup> Participants at the UW PIC were referred because of suspicion or recent diagnosis of acute HIV infection.

<sup>2</sup> Number of study visits. Subjects at the PHSKC STD Clinic and Gay City could participate quarterly.

<sup>3</sup> Includes one participant with reactive EIA, indeterminate Western blot, and negative NAAT

<sup>4</sup> Includes five participants screened by Determine Combo

<sup>5</sup> Includes one participant with positive p24 antigen of four participants screened by Determine Combo

<sup>6</sup> These participants had a negative Determine Combo, reactive ARCHITECT, negative Multispot HIV-1/HIV-2 Rapid Test and Western blot, and HIV RNA levels of 33,000 and 72,000 copies/mL.

## Session F: Performance of CLIA-Waived HIV Tests

### 17. Performance of the Alere Determine HIV-1/2 Ag/Ab Combo Rapid Test in the Miami Health Department STD clinic: A review of the first 9 months of use

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<sup>2</sup>Laboratory Services, Florida Department of Health- Miami

**Project:** To pilot the implementation of the first FDA approved rapid point-of-care (POC) 4th generation HIV-1/2 Ag/Ab Combo (Determine Combo) test into the practice of STD clinics in the state of Florida. Miami-Dade County ranks first in the number of diagnosed HIV and AIDS cases in Florida. FDOH Miami-Dade County Laboratory is AHCA/CLIA-certified for moderate complex and waived testing, performing approximately 5000 rapid HIV-1/2 tests annually in its high HIV-1 seroprevalence public health population.

**Implementation:** The Determine Combo detects and distinguishes HIV-1 p24 Antigen (Ag) from HIV-1 and HIV-2 Antibodies (Ab) and thus has the potential to improve diagnosis of acute HIV-1 infection. The transition from CLIA-waived Clearview Complete HIV-1/2 to Determine Combo involved laboratory staff training, test performance verification, PT (AAB) enrollment, CLIA and AHCA license upgrade and test performance monitoring. Per the established testing algorithm, POC reactive serum specimens were sent to the FBPHL-Miami for confirmation by Abbott Combo IA, Multispot HIV-1/HIV-2 differentiation and HIV-1 NAT for any discordant results. Determine Combo nonreactive results were reported as HIV-1/2 negative.

**Results:** A total of 3,272 Determine Combo tests were performed, 2.8% (91/3272) were preliminary HIV-1 Ab positive, 75.8% (69/91) were confirmed by the laboratory-based algorithm. The observed specificity of 99.32% (3203/3225) is within the Determine 95% CI (97.7-99.5%). In addition, 50 Determine Combo reactive specimens were also tested by Clearview Complete (table 1). More false-positive HIV-1 Ab results were observed with Determine Combo and there was an absence of p24 Ag detection in the first nine months of use.

**Lessons Learned:** Determine Combo was successfully implemented. HIV-1 antibody specificity was comparable to package insert specifications for high risk population, but more data is needed to verify Ag sensitivity and specificity. The clinic linkage-to-care process was modified due to the Determine Combo HIV-1 Ab false positive frequency. In addition the testing algorithm was modified to test Determine Combo nonreactive specimens for acute infections by the Abbott Combo IA. Alere Determine is a higher cost to the clinic due to PT enrollment and additional license fee. Use of Determine with serum/plasma requires more specimen preparation and licensed technical staff to perform the test.

Test	Total	Ab +	P24+	Negative	False-positives
Determine Combo Reactive	50	47	3		13
Clearview Complete	50	38	N/A	12	1
Abbott Combo IA	50	37	0	13	

## Session F: Performance of CLIA-Waived HIV Tests

### 18. New York State (NYS) Experience in Implementing Alere Determine HIV-1/2 Ag/Ab Combo in STD Clinics

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<sup>1</sup> Bureau of HIV/STD Field Services, New York State Department of Health AIDS Institute

**Project:** As part of the New York State (NYS) expanded HIV testing project, integrated HIV and STD testing is supported in STD clinics. Two high volume County Health Department STD clinics implemented the Alere Determine HIV-1/2 Ag/Ab Combo (Determine) test into laboratory services to provide same day results. The sites performed the Determine as a moderate complex test using venous whole blood specimens collected from clinic patients.

**Issue:** The specificity of the Determine test for venous whole blood fingerstick for low risk population is 100% (95% confidence interval (CI) 99.6, 100.0%) (according to the package insert). A low risk population is defined as <1% HIV prevalence regardless of sexual risk behaviors. Specificity was not within the 95% CI and there was a high number of false positives from Determine tests in the two STD clinics.

**Results:** Data were collected from standard CTR forms. Between June 2014 – December 2015, 6,739 Determine tests were conducted. Of those, 75 were reactive, 5 were reactive for HIV-1 p24 antigen, 69 were reactive for HIV-1/HIV-2 antibodies and 1 was reactive for HIV-1 p24 antigen and HIV-1/HIV-2 antibodies. Of those, 37 were true positives and 38 were false positives. Specificity was 99.4% and positive predictive value was 49.3%. Of the 38 false positives, Organics and Alere™ quality assurance department in Scarborough completed 11 investigations of the clinic specimens at one site. The Determine performance was assessed by testing retention strips and reviewing history and batch records. The patient serum sample was tested twice with the retained lot kit from the original test. Of those 4 results were replicated, 5 results were not replicated, and 2 had no sample provided for investigation. The product performance did not exceed the upper control limit for further action on all 11 specimens.

**Lessons Learned:** Though quality control testing was performed, no clear reasons were determined for the false positive test results. As stated in the manufacturer insert, it is feasible to have false positive test results from individuals with certain infections commonly found in STD clinics. These issues highlight the need for further data to evaluate the use of Determine in this setting.

## Session F: Performance of CLIA-Waived HIV Tests

### 19. Michigan State-Wide Roll Out of the 4<sup>th</sup> Generation Alere Determine HIV-1/2 Ag/Ab Combo

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**Project:** Michigan State-Wide Roll Out of the 4<sup>th</sup> Generation Alere Determine HIV-1/2 Ag/Ab Combo

**Issue:** Michigan Department of Health and Human Services (MDHHS) was unable to detect new HIV infection when an individual is most infectious to others and would not test positive on a 2<sup>nd</sup> generation rapid test.

**Result:** MDHHS introduced the Alere Determine HIV-1/2 Ag/Ab Combo (Determine) in January 2015 at the two highest volume tests sites in Michigan; Oakland County Health Department and Detroit Receiving Hospital, which average over 700 tests per month. On February 2015, MDHHS funded agencies attended a preliminary training on the Determine device. Attendees discussed the testing algorithm and received hands-on experience with the testing device. In March 2015, regional, small group trainings were held and provided further hands-on practice with the Determine. Quality assurance procedures were in place, requiring sites to complete a 20-sample validation panel before beginning testing as well as several requirements for proficiency testing for HIV test counselors. Agencies who did not transition in early spring 2015, received refresher training prior to using the Determine. As of October 2015, 90% of funded agencies are using Determine.

**Lessons Learned:** Selecting and transitioning to a new a testing device requires agencies buy-in. MDHHS staff, working with agency representatives, analyzed data and science and ultimately selected the Determine. Strategies to foster success included collaborating with funded agency staff; the test roll-out to high volume agencies; providing training and ongoing technical assistance for agencies moving to the Determine; and working with representatives from Alere. To date, three positive antigen tests have been reported and confirmed through supplemental tests. Implications for using the testing device are that we are able to diagnose an individual where they would have been missed by an older device and in turn gone on to infect others. Additionally it allows agencies to link those that test positive to care services quicker which allows for overall better health outcomes.

## Session F: Performance of CLIA-Waived HIV Tests

### 20. New Raw Materials for the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test Design

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**Objective:** OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test, reformulated with new raw materials, has been approved with 24 month expiration dating. The need for a soft launch with matched kit controls is investigated.

**Methods:** Performance of the new OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test was evaluated through design validation. Studies were conducted to characterize functional performance in selected samples, low titer panels, seroconversion panels, and unrelated medical conditions. In seroconversion panels, results were compared to the current, approved OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test and the 3<sup>rd</sup> generation Bio-Rad GS HIV-1/HIV-2 PLUS O published in the seroconversion panel package inserts EIA by assessment of the first consecutive reactive specimen to the respective FDA-approved EIA result. Oral fluid specificity and sensitivity performance of the test was verified by execution of clinical studies.

**Results:** Use of a new in-house streptavidin conjugate and other process improvements were compared to the current product where selected samples yielded concordant reactivity. In 749 fresh negative samples, the validation lots generated a cumulative 99.7% specificity compared to control lot specificity of 99.3%. Specificity was demonstrated with 237 specimens from 27 unrelated medical conditions with concordance for oral fluid at 99.8% and fingerstick whole blood at 99.5%. Reproducibility was established with 3 operators at 3 testing sites. Acceptable sensitivity was noted in low/mixed titer panels and a worldwide panel. In 201 samples from 23 seroconversion panels, the 95% confidence intervals (CIs) for the test overlapped and are within the 95% CIs range of the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test. Moreover, the 95% CIs for the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test indicates sensitivity comparable to the Bio-Rad GS HIV-1/HIV-2 PLUS O enzyme immunoassay. Sensitivity was 100.0% in 60 positives, agreement (95% CI: 94.0% - 100.0%).

**Conclusions:** The performance of the OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test utilizing the new raw materials was comparable to that of current approved OraQuick ADVANCE® Rapid HIV-1/2 Antibody Test and to seroconversion sensitivity performance of a 3rd Gen EIA. This requires the preparation of matched Kit Controls and a coordinated launch.



## Session F: Performance of CLIA-Waived HIV Tests

### 21. Implementation of Alere Determine HIV-1/2 Ag/Ab Combo in NYS CLIA waived Point of Care Testing Sites

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<sup>1</sup> Bureau of HIV/STD Field Services, New York State Department of Health AIDS Institute

**Project:** NYS supports targeted HIV testing through agencies that serve individuals at highest risk for HIV infection. Agencies providing targeted HIV testing for high risk individuals are expected to use the most sensitive test. The Alere Determine HIV-1/2/Ag/Ab Combo (Determine) test has the ability to detect HIV-1 infection earlier than other rapid tests, offering potential public health benefits. A multisite review of NYS CLIA waived sites using Determine under a CLIA-waiver was conducted to evaluate utilization and performance outcomes.

**Issue:** Despite a NYS Department of Health Dear Colleague letter encouraging programs to use the most sensitive and appropriate HIV screening test, few point of care testing sites have implemented Determine. HIV rapid test results were collected from 5 sites using the AIDS Institute Reporting System (AIRS) from March 2014 – January 2015 (pre-implementation) and March 2015 – January 2016 (post-implementation).

**Results:** Prior to implementation, there were 1662 tests conducted by the 5 sites using either Clearview® Complete HIV 1/2 or OraQuick Advance® HIV-1/2. Of those, 11 were antibody reactive and confirmed positive using the HIV diagnostic algorithm. Post-implementation, there were 1464 Determine tests conducted by 5 sites. Of those, 0 were reactive for HIV-1 p24 antigen, 2 were reactive for HIV-1/HIV-2 antibodies and 0 were reactive for HIV-1 p24 antigen and HIV-1/HIV-2 antibodies. The 2 reactive tests were confirmed positive using the HIV diagnostic algorithm. There was a decrease in the number of positive tests following implementation of Determine from 11 to 2 at these high-risk testing sites.

**Lessons Learned:** Determine utilization is currently low. A number of reasons have been identified as contributing factors to the slow uptake, including new device, device open format, and cost. Of the point of care sites that have implemented Determine, none have had a reactive for the HIV-1 p24 antigen. Further data is needed to evaluate the performance and cost-effectiveness to determine the appropriate sites to use Determine.

## Session F: Performance of CLIA-Waived HIV Tests

### 22. Sensitivity of the Alere Determine™ HIV-1/2 Ag/Ab Combo Rapid Test in a South Florida Population with a High Prevalence of HIV Infection

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**Objective:** To determine the sensitivity of the Alere Determine™ HIV-1/2 Ag/Ab Combo Rapid Test (Determine Combo) compared to an instrument-based HIV-1/2 Combo Immunoassay (IA) on specimens from individuals that self-refer for HIV diagnosis at a Miami-Dade County STD clinic from Sept. 8, 2015 to Dec. 9, 2015. Miami-Dade County ranks first in the number of reported HIV cases in Florida (23%, Jan–Oct. 2015).

**Methods:** Bloods collected at Point of Care (POC) from individuals regardless of their Determine Combo rapid results were submitted to the Florida Department of Health, Bureau of Public Health Laboratories – Miami for comparative performance testing using the new HIV Diagnostic Algorithm (CDC, June 2014), which is an instrument-based HIV-1/2 Combo Immunoassay (IA), specifically the ARCHITECT™ HIV Ag/Ab Combo Assay (Abbott Combo) for this analysis. Sensitivity of the Determine Combo assay was defined as concordant positive results between the Determine Combo rapid test and algorithm-defined established or acute HIV-1 infections.

**Results:** Of the 679 specimens pre-screened by a Determine Combo rapid test, 16 (2.3%) were concordant positive Determine Combo (Ag or Ab reactive), Abbott Combo and Multispot HIV-1 reactive (supplemental differentiation IA). Of the remaining 663 Determine Combo negative specimens, 661 were Abbott Combo nonreactive and two were found to be false negative (FN) Determine Combo results using the algorithm-defined acute HIV-1 infection methodology (Abbott Combo repeatedly reactive, Multispot HIV-1 nonreactive and APTIMA HIV-1 RNA reactive).

**Conclusions:** The sensitivity of the Determine Combo rapid test used to pre-screen individuals in this high prevalence public health population was found to be 88.9% (16/18). The package insert claim for serum sensitivity is 99.9% with a 95% CI of 99.4% - 100%. The detection of two algorithm-defined acute HIV-1 infections with FN Determine Combo results in a relative short time period strengthens our public health recommendation to seek additional laboratory-based HIV-1/2 Combo IA testing for individuals with symptoms of recent HIV infection or disclosure of recent high risk behaviors.

## Session F: Performance of CLIA-Waived HIV Tests

### 23. Determining Where it Fits

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**Project:** Performance and real life experience of Alere HIV 4<sup>th</sup> Gen Determine. Since June 1<sup>st</sup> 2015 we have run about 2,100 Determine tests in different settings including non-clinical setting, mobile testing, street fairs, etc.

**Issues:** San Francisco performs acute HIV testing on 80% of 25,000 tests a year, which we feel has helped decrease new infection from 439 to 302 over the last five years. Meanwhile, the city's smaller volume sites have struggled with getting enough tests to maintain infrastructure needed to do acute testing, e.g. maintaining phlebotomy coverage, quality assurance (QA) measures. Even for sites that are testing the highest risk groups or those with most need to access to acute testing these infrastructure barriers have proven to be large. We wanted to reduce barriers to acute testing and the Alere Determine test seemed to offer that opportunity.

During implementation we encountered many real world issues such as: How to craft a window period time frame in the absence of in the field data. Would we find acute infections? How to train lay users in running, reading, and maintaining QA? Is there something better? Will all the work to implement this change be worth it? How to manage the "spin" from manufacturers of 2nd and 3rd generation test.

**Results:** Determine test Run in SF from June 2015 \*

Number of Test	Number of AB +	Number AG+, AB+	Number of AG+	False Positives
2,100	8	0	0	3

\* Additional data is being analyzed

**Lessons Learned:** Change is hard; this is not novel but often forgotten. We learned that using change management techniques helps with the change process. Additionally, we had to have extensive discussions around window period messaging. This was a combination of addressing the needs of those at risk for HIV and of clinical and laboratory staff. Changes were required not only to how technicians were trained but also upon existing QA measures. Lastly, the value of finding one acute person and did this warrant the resources required for this structural change. Our conclusion is that it did.

## Session G: Special Testing Circumstances

### 24. Performance of Rapid HIV Testing in the High Throughput Environment of County Jails

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**Project:** The US incarcerates more persons than any other nation. Most entrants to the criminal justice system enter through jails. Nine million persons cycle through jail an average of 1.4 times/year; the median length of stay is 48 hours. HIV prevalence among correctional populations is 3x higher than the general population. Jails have high population turn-over; they are a fitting place for rapid HIV testing. In 2011, under a CDC cooperative agreement, rapid opt-out HIV testing by jail nurses was integrated into the medical intake process at Fulton County Jail (FCJ) in Georgia. Successful screening at FCJ led to sustaining the project beyond the grant period and to state support for replication of the rapid HIV testing program in the DeKalb County Jail (DCJ).

**Issue:** Challenges of jail screening include providing test results before release. Test results are now available as soon as 60 seconds after HIV testing, in contrast with the conventional method where detainees left jail between testing and delivery of results. Patient privacy may be perceived as limited in a jail setting. There is evidence that patients do not fully disclose HIV risk factors, such as same sex relationships. Finally, HIV + detainees may not be jailed long enough to access care inside jail; starting care post-release has its own challenges.

**Results:** 29,021 HIV tests were conducted at FCJ between February 2013 and July 2015. Over a 12 month period, FCJ diagnosed 89 new cases of HIV. Historically, Fulton County has only diagnosed 535 cases/year. 20% of inmates who were diagnosed with HIV identified their risk as being a man who has sex with other men (MSM). In contrast, by ACASI survey 75% of HIV + inmates identify as MSM. A program at FCJ aimed at linking HIV + detainees to community care has shown success. When the screening program was replicated at DCJ, out of 2,199 individuals, 12 new HIV diagnoses were identified (0.55%).

**Lessons Learned:** Since the HIV epidemic is intertwined with hyper-incarceration in the south, jails here are an opportune setting for HIV testing. Implementation of our nurse-led model for HIV testing has been sustained and replicated.

## Session G: Special Testing Circumstances

### 25. Increase in HIV Testing During European Testing Week and Type of Test Used

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<sup>2</sup>AIDS Action Europe

<sup>3</sup>Public Health England

<sup>4</sup>European Centre for Disease Prevention and Control

<sup>5</sup>The AIDS Healthcare Foundation

<sup>6</sup>European AIDS Treatment Group

<sup>7</sup>Hepatitis B and C Public Policy Association

<sup>8</sup>Correlation Network

<sup>9</sup>European AIDS Clinical Society & University of Zagreb, School of Medicine

<sup>10</sup>Individual Consultant

<sup>11</sup>Terrence Higgins Trust

<sup>12</sup>European AIDS Treatment Group & International HIV partnerships

<sup>13</sup>International Gay, Lesbian, Bisexual, Transgender, Queer and Intersex Youth and Student Organisation

<sup>14</sup>GAT

<sup>15</sup>Eurasian Harm Reduction Network

**Objective:** Around one in three of the 2.5 million people living with HIV in the WHO European Region are unaware that they are HIV positive. The purpose of the European Testing Week (ETW) is to promote HIV testing alongside optimal HIV care in the WHO European Region.

**Methods:** ETW is a partnership including civil society, health care professionals, governmental and other policy organisations. A dedicated website ([www.testingweek.eu](http://www.testingweek.eu)) provides a hub for interested organisations to sign up and download materials to support planned activities. In 2015, ETW took place from 20-27 November 2015 and organisations who took part were invited to complete an online survey in REDCap.

**Results:** Of the 416 organisations that signed up for ETW, 181 (44%) submitted the evaluation survey. The majority of respondents were civil society organisations (76%) and 35 health care professionals (24%). The respondents covered 35 countries. Of the 181 respondents, 173 (96%) reported carrying out HIV activities and 143 (83%) HIV testing activities specifically during ETW. Of the 143 organisations that carried out HIV testing activities, more than 75% reported an increase in HIV testing rates as compared to an average week. More than 20% reported a more than 200% increase in HIV testing during ETW.

The majority of the 90 civil society organisations that carried out HIV testing during ETW reported using rapid tests (blood and saliva) (81%) followed by HIV antibody tests (57%), as did the 28 healthcare professionals with 93% and 54% reporting use of rapid tests (blood and saliva) and HIV antibody tests respectively. Governmental and other policy organisations (N=13) most frequently used HIV antibody/antigen tests (77%) followed by rapid tests (blood and saliva) (62%) (Table 1).

**Table 1:** HIV tests used\* during testing week

	Civil society (N=90)	Healthcare professionals (N=28)	Governmental and other policy organisations (N=13)	Other (N=12)	Total number of respondents (N=143)
<b>Rapid blood test (incl. INSTI test)</b>	58 (64%)	22 (79%)	7 (54%)	7 (58%)	94 (66%)
<b>HIV antibody/antigen test</b>	51 (57%)	15 (54%)	10 (77%)	7 (58%)	83 (58%)
<b>Saliva test</b>	15 (17%)	4 (14%)	1 (8%)	1 (8%)	21 (15%)
<b>Home sampling/postal testing</b>	3 (3%)	2 (7%)	0 (0%)	0 (0%)	5 (3%)
<b>Do not know</b>	1 (1%)	0 (0%)	0 (0%)	2 (20%)	3 (2%)

\* More than one test were reported by some participants

**Conclusion:** Overall, more than 75% of participating organisations reported an increase in HIV testing during ETW. More than half of the organisations saw an above 50% increase in testing, and 20% a more than 200% increase. Both civil society organisations and healthcare professionals reported the rapid blood test as the most frequently used test, while HIV antibody/antigen tests were most frequently used by governmental and other policy organisations.

## Session H: Testing Alternatives using Dried Blood Specimens

### 26. Validation of the GEN-PROBE® APTIMA® HIV-1 RNA Qualitative Assay for Use with Dried Blood Spots

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**Objective:** Currently, we perform the Western blot on dried blood spots (DBS) submitted for confirmation of a reactive HIV rapid test. When antibodies do not confirm, we have no additional tests available to resolve the discordance. We sought to validate the APTIMA® HIV-1 RNA Qualitative Assay for use with DBS specimens.

**Methods:** DBS were prepared by pipetting 50µL of blood onto Whatman 903 cards, dried overnight and stored with desiccant at -20°C until use, except for DBS undergoing stability analyses which were stored at room temperature and 37°C without desiccant. A DBS dilution series was prepared from blood spiked with quantitated RNA-positive plasma and used for limit of detection (LOD) and stability studies. Blinded accuracy studies were conducted using DBS prepared from 20 HIV-1 positive and 10 HIV-1 negative clinical blood specimens. For testing, two 6-mm punches were added to 530µl of elution buffer (1mM EDTA, 1mM EGTA, 3% lithium lauryl sulfate in phosphate buffered saline), and incubated overnight at 4°C. After brief centrifugation, 500µl of eluate was tested on the APTIMA® HIV-1 RNA Qualitative Assay according to the manufacturer's instructions.

**Results:** Data from the dilution series tested on three separate days indicated that the LOD was 2500 copies/mL or 50 copies/reaction. Ten replicates of the 2500 copies/mL-dilution were re-tested and 9 (90%) were reactive for RNA. The full dilution series was also tested after DBS were stored at room temperature and 37°C for 21 days. All DBS with at least 2500 copies/mL were reactive under these conditions. To assess accuracy, DBS from 20 HIV-1-positive and 10 HIV-1-negative specimens were blinded and tested. HIV-1 RNA was detected in 18 of 20 HIV-1-positive DBS. Testing was repeated for the 2 false-negative DBS and RNA was detected in both. Additional testing of the corresponding plasma suggested that the RNA in both was near the LOD. HIV-1 RNA was not detected in the 10 HIV-1 negative DBS.

**Conclusion:** Our results indicate that the APTIMA® HIV-1 RNA Qualitative Assay can detect HIV-1 RNA in DBS specimens with at least 2500 RNA copies/mL, including DBS stored at elevated temperatures for up to 21 days.

## Session H: Testing Alternatives using Dried Blood Specimens

### 27. Diminishing Returns on Increased Dried Blood Spot Sample Quantity

L. Gravens<sup>1</sup>, P. Sullivan<sup>1</sup>, and A. McNaghten<sup>2</sup>

<sup>1</sup> Emory University Rollins School of Public Health

<sup>2</sup> Centers for Disease Control and Prevention

**Objective:** Self-collected dried blood spot (DBS) specimens have been used in several studies to determine or confirm HIV status, but utility may be limited by insufficient samples. We examined differences in sample quality and adequacy for HIV testing when using a 1-, 3- or 5-spot DBS specimen collection card.

**Methods:** In 2014, 45 men who have sex with men were recruited and 15 men each were randomized to receive a 1-, 3- or 5-spot DBS collection card. Written instructions were provided on how to collect the specimen(s). The DBS cards were reviewed by staff from the Centers for Disease Control and Prevention lab and rated on overall quality and adequacy.

**Results:** A higher percentage of circles were completely filled for the 1-spot cards (73%), than 3-spot cards (60%) or 5-spot cards (37%). An average of 2 punches per spot were obtained from 1-spot and 3-spot cards; and average 1 punch per spot was obtained from 5-spot cards. The 3-spot card yielded an average of 6 full punches per card compared with 5 punches for the 5-spot card.

There was no significant difference by card type in adequacy for testing ( $X^2=1.6$ ,  $p=0.82$ ). There was a significant difference in number of punches between the 1-spot cards (mean 2.33, SD=1.21) and the 3-spot cards (mean=6.60 SD=3.11) ( $t=-5.00$ ,  $p<0.001$ ). There was a significant difference in number of punches between the 1-spot cards (mean 2.33, SD=1.12) and the 5-spot cards (mean=7.73, SD=5.16) ( $t=-3.96$ ,  $p<0.001$ ). There was no significant difference in number of punches between 3-spot cards (mean=6.60 SD=3.11) and 5-spot cards (mean=7.73, SD=5.16) ( $t=-0.73$ ,  $p=0.07$ ).

**Conclusion:** There is a benefit of 3- or 5-spot cards over a 1-spot card regarding the number of punches available for testing per card. There is no marginal benefit of a 5-spot card over a 3-spot card in regard to number of punches available for testing. Studies using self-collected DBS samples for HIV testing may want to consider using a 3-spot collection card in preference to a 1- or 5-spot collection card in efforts to decrease participant burden without affecting the adequacy of the sample for testing or sample quality.



## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

### 28. Comparison of Two Digital PCR Platforms and Development of an HIV-2 Quantitative Assay

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**Objective:** Digital PCR (dPCR) is an interesting alternative to traditional quantitative real-time PCR because quantitation does not require standard curves and several digital PCR platforms are now available. We present a comparison between the Bio-Rad QX200™ Droplet Digital™ PCR System and Life Technologies' QuantStudio™ 12K Flex Real-Time PCR System using international WHO-NIBSC HIV-1 and HIV-2 standards. Following the digital PCR evaluation, we developed an HIV-2 quantitative assay.

**Methods:** To compare digital PCR systems, an External Quality Assurance Program Oversight Laboratory (EQAPOL) HIV-1 RNA and the WHO-NIBSC HIV-1 controls were extracted, amplified into cDNA, quantified and compared on the two different dPCR platforms.

The HIV-2 quantitative assay used primers and probes targeting the gag region of HIV-2. The WHO HIV-2 (1000IU/mL) International Standard was used as an external in-house control to validate the assay. A dilution series of 7 replicates using the WHO HIV-2 control was used to establish the lower limit of the assay.

**Results:** The quantification of the EQAPOL reagent was comparable to within 0.20 log of the previously calculated value for the control (68,700cp/ml [4.84]). Interestingly, when using a one-step RT-PCR system specific for each digital PCR platform a significantly lower quantitation was observed for the EQAPOL reagent on the QuantStudio™ 12K Flex Real-Time PCR System (24,193cp/ml [4.38]) and the QX200™ Droplet Digital™ PCR System (12,953cp/mL [4.11]).

The WHO HIV-2 standard curves demonstrated that the assay was sensitive and reproducible. All 7 replicates at 125IU/mL were quantifiable. 6/7 at 62.5IU/mL and 4/7 at 31.25IU/mL were quantifiable therefore the lower limit of detection was then set at 100 IU/mL.

**Conclusion:** All digital PCR systems evaluated gave comparable quantitation values for the HIV-1 controls. Finally, when quantifying RNA the choice of a 1-step or 2-step RT-PCR system may have significant impact on quantitation. Presently there is no quantitative HIV-2 assay commercially available and the lack of HIV-2 control reagents which makes development of in-house methods problematic. With the recent introduction of Bio-Rad's Automated Droplet Generator coupled with digital droplet PCR, we effectively identified HIV-2 in plasma as low as 100IU/mL. We have since been providing HIV-2 determinations to Canadian stakeholders.

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

### 29. Dynamic Monitoring of Replication-competent Virus in HIV-positive Individuals Under ART in Support of HIV cure

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<sup>1</sup> University of Alaska Fairbanks

<sup>2</sup> Alaska State Public Health Virology Laboratory

**Objective:** Highly effective antiretroviral therapy (ART) can reduce HIV viral load to levels below the limit of detection by standard HIV assays. Given the extreme variability of the virus, HIV variants resistant to ART may be present as minority population in HIV infected individuals under ART. Current PCR assays fail to detect all these variants. In addition, the “one-fits-all” HIV primers used in current PCR assays do not have the flexibility for the dynamic monitoring of HIV variants and drug resistant strains occurred during ART.

**Methods:** We developed a highly sensitive HIV detection assay using a method we called “Preferential Amplification of Pathogenic Sequences (PATHseq)”, coupled with next generation sequencing (NGS) technology. The PATHseq method uses a set of short oligonucleotides (8-10 mer) called “non-human” primers that do not match the sequences of human transcripts (RNAs). Instead of using random primers in the construction of cDNA library for sequencing, the PATHseq method recruits these short non-human primers, which in turn, preferentially amplifies non-human, presumably pathogenic sequences. The PATHseq method has pending US patent.

**Results:** 1) To accurately reflect individual genome diversity and HIV polymorphisms, a set of “non-human” primers were developed to match an individual’s transcriptome and HIV variation; 2) A serial dilution of HIV RNA is used to determine the lower limit of detection. The sensitivity is compared with current PCR-based assays. Spiked various human viruses is used to test the specificity; 3) De-identified HIV positive specimens from infected individuals under ART are used to test the feasibility of this assay in detecting minute HIV RNA and compare it to commercial HIV nucleic acid-based tests.

**Conclusion:** PATHseq method can be used to greatly enrich pathogenic sequences in NGS library. This method does not require prior knowledge of the pathogen or assumption of the infection, and therefore, provides a fast and target-independent approach to identify human pathogens.

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

### 30. Performance Evaluation of cobas<sup>®</sup> HIV-1 for High Throughput HIV Viral Load Testing

P. Loetscher<sup>1</sup>, S. Templer<sup>2</sup>, B. Seiverth<sup>1</sup>, A. Cobernuss-Rahn<sup>1</sup>, E. Marins<sup>2</sup>, C. Simon<sup>2</sup>, and **R. Luo<sup>2</sup>**

<sup>1</sup> Roche Diagnostics International

<sup>2</sup> Roche Molecular Systems

**Objective:** HIV viral load testing is recommended for all patients on antiretroviral treatment. As viral load testing continues to scale up worldwide, highly sensitive and specific HIV viral load tests that support high throughput testing are needed to provide timely and accurate results. The objective of the current study was to evaluate the performance characteristics of the new **cobas<sup>®</sup>** HIV-1 test, which allows for high throughput HIV viral load testing.

**Methods:** The performance of the **cobas<sup>®</sup>** HIV-1 test was evaluated for limit of detection (LOD), linearity, accuracy, precision, sensitivity, specificity, comparison with the COBAS<sup>®</sup> AmpliPrep/COBAS<sup>®</sup> TaqMan<sup>®</sup> HIV-1, v2.0 Test (TaqMan<sup>®</sup> v2.0), potential interfering substances, and primary tube equivalency.

**Results:** **cobas<sup>®</sup>** HIV-1 demonstrated a LOD of 13.2 copies/mL and a linear range of 20-10,000,000 copies/mL. Precision and accuracy were both within  $\pm 0.17 \log_{10}$ . Sensitivity on clinical samples was between 99.25-100%, with a specificity of 100%. The assay demonstrated excellent correlation to TaqMan<sup>®</sup> v2.0, and results varied less than  $\pm 0.20 \log_{10}$  from potential exogenous or endogenous interfering substances. Both lavender top EDTA plasma tubes and Becton Dickinson and Company (BD) Vacutainer<sup>®</sup> Plasma Preparation Tubes can be used with similar results.

**Conclusions:** **cobas<sup>®</sup>** HIV-1 is a highly sensitivity and specific method for viral load monitoring that has an improved limit of detection, lower sample volume, and increased throughput capability compared to TaqMan<sup>®</sup> v2.0.

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

### 31. Performance of the VITROS® Immunodiagnostic Products HIV Combo Assay\*

P. Contestable<sup>1</sup>, C. Noeson<sup>1</sup>, K. Smith<sup>1</sup>, A. Tweedie<sup>1</sup>, C. Waasdorp<sup>1</sup>, and L. Colt<sup>1</sup>

<sup>1</sup> Assay Research and Development, Ortho Clinical Diagnostics

**Objective:** Assess the sensitivity, specificity and precision performance of the VITROS Immunodiagnostic Products HIV Combo Assay\* on VITROS Systems. The assay simultaneously detects both HIV antibodies and p24 antigen to enable earlier diagnosis of HIV infection.

**Methods:** Antibody detection in the VITROS HIV Combo Assay\* is achieved using recombinant transmembrane envelope proteins for HIV-1 group M and O and HIV-2. The p24 antigen detection is accomplished using monoclonal antibodies (MAbs) against HIV-1 p24. Biotinylated antigen or MAb are pre-bound to microwells coated with streptavidin. Sample is added to the coated wells in the first stage of the reaction and HIV analyte from the sample is captured by the biotinylated proteins. After washing, HRP conjugated envelope proteins and anti-p24 MAbs are added. Following a final wash, bound HRP conjugates are detected using the VITROS signal reagent.

Testing was performed using three lots on three VITROS Systems. Clinical specificity was assessed using 5077 blood donors and 608 clinical specimens. Clinical sensitivity evaluation included 500 known HIV positive samples and 34 seroconversion panels. The p24 antigen sensitivity was evaluated via dilution of the NIBSC HIV-1 p24 Antigen Dilution standard (90/636) and the AFSSAPS HIV-1 p24 Antigen Dilution standard. Each assay lot was evaluated for total within lab precision over 20 occasions in accordance with CLSI EP05-A3.

**Results:** Donor specificity was determined to be 99.84% (95% CI: 99.69% to 99.93%) for blood donors and 100% (95% CI: 99.39% to 100%) for hospitalized patients. All known positive samples tested generated reactive results, including a commercially available panel of antibody subtypes. When used to test 34 commercially available seroconversion panels the HIV Combo assay was comparable to the commercially available 4th generation assay. The assay detects AFSSAPS p24 antigen at  $\leq 13.1$  pg/mL and NIBSC at  $\leq 0.48$  IU/mL. Precision of the assay ranged from 3.4 to 10.5% near the assay cut-off.

**Conclusion:** The VITROS HIV Combo Assay\* is designed to help enable earlier detection of HIV infection and demonstrates acceptable seroconversion sensitivity, clinical specificity and analytical performance.

\*Under Development

## Session J: New Tests for Diagnosis, Clinical Staging, and Surveillance

### 32. Development and Evaluation of a New Immunoassay Method for Detection of Recent HIV Infection

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<sup>2</sup> Institute of Human Virology

**Objective:** Accurate estimation of HIV incidence is an important factor for evaluation of prevention programs. Current methods for detection of recent infection have limitations such as varying performance in different clades and populations and low specificity. This study focused on development of an immunoassay method based on the antibodies against HIV-1 integrase, as it is the last antibody to turn positive in Fiebig staging (approximately 100 days), giving a longer window of opportunity to identify cases.

**Methods:** The recombinant integrase was produced in *E.coli* and used in different ELISAs to discriminate the lower titer and avidity of anti-integrase antibodies in recent vs. non recent infected individuals. The evaluated formats were: lowering the concentration of coated integrase, treatment of attached antibodies by 4M urea and combination of low concentration and urea treatment. The performance of the different ELISAs was evaluated by 12 members of a BBI panel (PRB601), including recent and non-recent samples. The arbitrary cutoff value was determined as 3 SD above the mean ODs of the recent samples. The specificity of the final developed assay was determined by 100 HIV positive sera (from Iranian infected individuals, ART naïve or under ART) in comparison to BED-CEIA and LAg-avidity assays.

**Results:** The best discriminative assay was including 0.1 µg/ml of integrase for coating in combination with urea treatment. The mean OD of recent samples was 0.133 vs. 1.086 for non-recent samples. And the arbitrary cutoff point was 0.32. The False Recent Rate (FRR) of the integrase-based ELISA, BED-CEIA and LAg-avidity was 2, 14 and 2%, respectively.

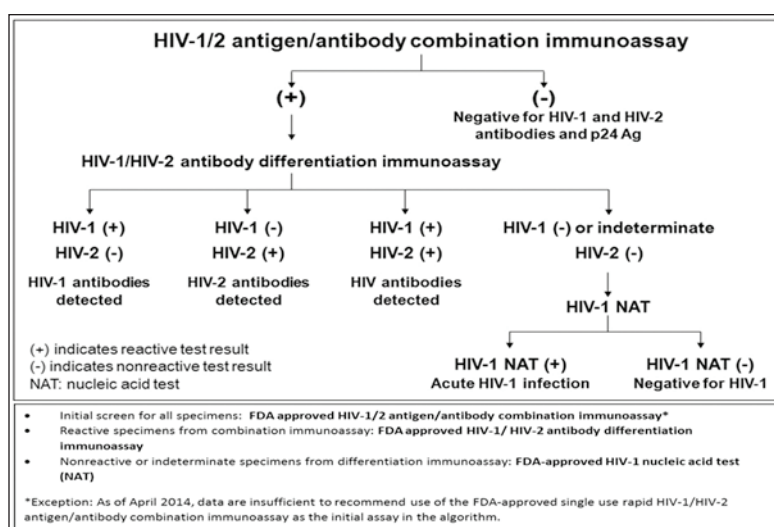
**Conclusion:** Integrase is a conserved and immunogenic antigen of HIV and the anti-integrase antibodies are the latest to develop among all HIV antigens, making it an appropriate marker to discriminate recent and non-recent infections. The FRR of 3 different assays show that our assay (an early generation integrase-based ELISA) performed as well or better than the BED-CEIA and LAg-avidity assays. We plan on further refining the test and using a multi assay algorithm to improve its predictive value of detecting recent HIV infection.

## Overcoming the Challenges and Barriers to Implementing the HIV Diagnostic Testing Algorithm in Your Laboratory

Diagnostic testing for HIV infection has dramatically improved since the 1980's:

1. There are now rapid and simple point-of-care diagnostic tests available.
2. There are powerful drugs to treat and prevent HIV infection.
3. There has been a shift in prevention efforts from identifying those with established HIV infections to detection of HIV infected persons in the acute (and established) phase with the goals of early treatment and prevention of transmission.

The 3 step algorithm for HIV testing, recommended by the Centers for Disease Control and Prevention and the Association of Public Health Laboratories, published in June 2014, is designed to improve the detection of acute infections and differentiate between HIV-1 and HIV-2 antibodies. Although many labs have implemented the algorithm, universal adoption of this has yet to be achieved.



The primary advantage of the new algorithm is the ability to identify HIV infection earlier. This is critical because the risk of HIV-1 transmission from persons with acute and early infection is much higher than that from persons with established infections. Therefore, identifying these cases as early as possible and initiating antiretroviral therapy (ART) can benefit patients and reduce HIV transmission. The new algorithm takes advantage of the advances in HIV diagnostic testing by using a sequence of tests that concurrently detect HIV-1 and HIV-2 antibodies and HIV-1 p24 antigen. The algorithm also includes an HIV antibody differentiation assay as a supplemental test and HIV-1 RNA testing, as needed. This algorithm produces fewer indeterminate results and has a faster turnaround time for HIV-1 antibody positive samples compared to previous algorithms that utilized the Western blot (WB) for confirmation.

A minority of labs continue to perform the HIV-1 Western Blot (WB) on plasma and serum specimens despite the fact that the WB is not able to detect acute infection and has the potential to misclassify HIV-2 infection as an HIV-1 infection. Based on the Association of Public Health Laboratories survey of HIV Diagnostic Testing Methods, in 2009 78.6% (48/61) of responding state and local public health laboratories who performed confirmatory testing used the Western Blot. In 2012, 66.2% (43/65) used the Western Blot. By 2015, 13.5% of (10/74) responding state and local public health laboratories continued to use the Western Blot for confirmatory testing. While there is not a survey of clinical labs to determine which still perform HIV Western Blot, data from the CAP Proficiency Test Participant Summary Reports indicates that in 2012 there were 220 participants; in 2013, there were 200 participants, a 9% decline; and in 2014 there were 174 participants, a 21% decline from 2012. We do not know if these labs who get discordance between the WB and the initial test go on to perform RNA testing.

**Questions for the audience:**

1. What are barriers to adopting the algorithm?
2. If your lab has adopted the new algorithm, what challenges did you face?
3. What reasons can you provide to help labs abandon the western blot?
4. How has your lab overcome obstacles to the new algorithm?
5. What recommendations would you make to labs that have not yet adopted the algorithm?
6. From data with BioRad MultiSpot, this algorithm is thought to produce fewer indeterminate results will this hold true with Geenius? In general, does the introduction of the BioRad Geenius incentivize the adoption of the algorithm or is it an additional barrier?
7. Does new instrumentation (BioPlex) that is able to differentiate with the screening test change your perspective of the algorithm when you consider turnaround time, cost, approved tests, and the need for verification of results.

## Challenges and Successes of Implementing the HIV Diagnostic Testing Algorithm: Reports from Four HIV Surveillance Programs

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The Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories (APHL) issued updated recommendations in June 2014 for HIV diagnostic laboratory testing. The three step HIV Diagnostic Testing Algorithm (algorithm) highlights existing challenges and poses new challenges for public health reporting of laboratory data. This roundtable will discuss the challenges and successes as experienced by the four HIV surveillance programs.

### 1. Challenges:

- a. Incomplete reporting of components of the algorithm is common.
- b. Alternate algorithms and laboratory-specific reporting nuances complicate interpreting and processing algorithm results.
- c. The involvement of multiple laboratories in completing the algorithm necessitates linking results to determine the final test result.
- d. Inconsistently used Logical Observation Identifiers Names and Codes (LOINC) and or laboratory specific proprietary test panel coding need to be leveraged for public health to consume the electronic laboratory reporting (ELR) stream and correctly interpret algorithm results.
- e. In some cases, initial screening (i.e., rapid screening or CLIA-waived point of care testing) begins outside of the laboratory and protocols vary on how to integrate this point of care testing with the laboratory components of the algorithm.
- f. Partial execution of the algorithm is common as some laboratories do not automatically perform nucleic acid testing when required, rather relying on a specific clinician order.
- g. Scenarios of the conduct of inappropriate lab testing without effort by lab to investigate or clarify the request with the ordering clinician.
- h. Reports to the ordering clinician generated by some laboratories are neither clear nor specific enough for the clinician to determine whether the patient has confirmed laboratory evidence of HIV infection.

### 2. Public Health Efforts:

- a. Educational efforts directed towards laboratories
  - i. New York State general educational materials
  - ii. New York State's public health reporting recruitment process
  - iii. New York State and Michigan periodic assessments/lab report cards
  - iv. Best practices around working with laboratories to address partial execution and incomplete reporting of the algorithm
- b. Procedures to collect and process reported laboratory algorithm results
  - i. Review health department procedures to interpret laboratory specific coding for processing of ELR
  - ii. Tedious, manual linking of individual lab results
- c. Educational efforts directed towards clinicians
  - i. Education regarding what they are ordering, what the test results mean and what follow up testing is required
  - ii. Michigan HIV Testing Guidance
  - iii. Michigan reporting various diagnostic testing situations on the case report form
- d. Roles of Health Department Partner Services and Surveillance investigation
  - i. Partner Services priority
    1. Incomplete algorithm results – facilitate blood draw for NAT
    2. Results indicative of acute infection
  - ii. Surveillance medical record review to confirm diagnosis, acute infection, HIV-2





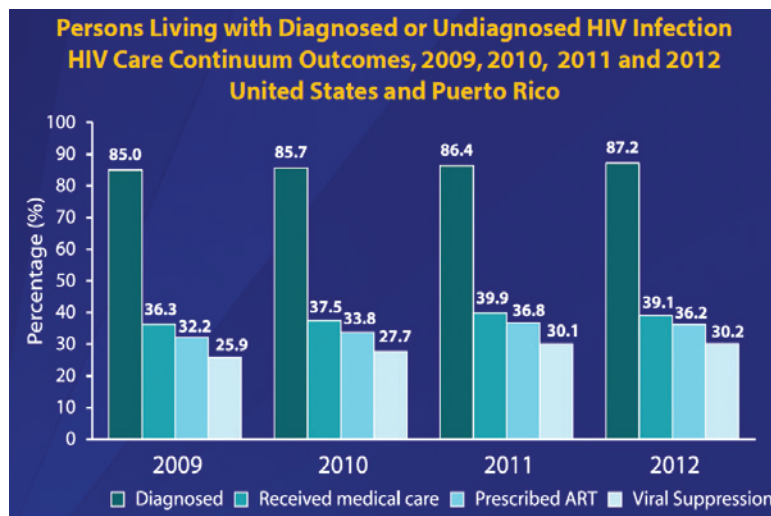
## ROUNDTABLE HANDOUTS

2. Ongoing challenges:
  - a. Mixed success with reporting of the preferred and most appropriate LOINCs
  - b. Changing testing technologies lead to the continual need to revise procedures and validate submission of new lab results
  - c. Ongoing laboratory, clinician and Health Department staff education needs
  - d. Alternate algorithms
  - e. Not all reports of the algorithm represent new diagnoses

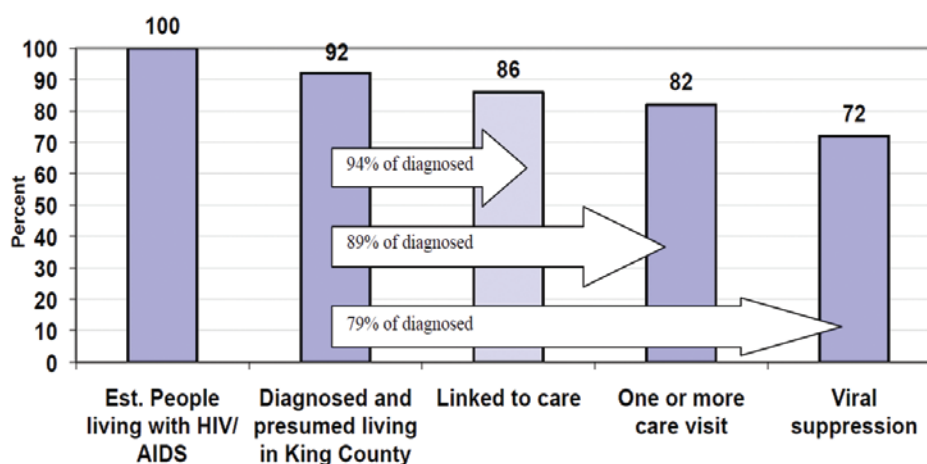
## Improving the Impact of HIV Testing Through Better Linkage and More Timely Viral Suppression

In the US, HIV screening in clinical settings and targeted testing in non-clinical settings is widely implemented and has successfully identified many people with HIV infection.

However, testing is only the entry point to medical care. If the final goal for both the patient and public health is treatment leading to viral suppression, we haven't been doing so well in the US as a whole.



**Figure 1: 2014 King County HIV Care Cascade as of June 30, 2015**



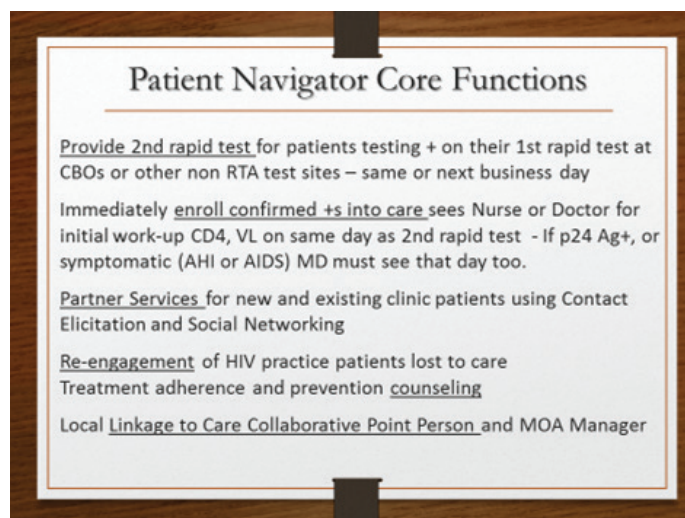
But some places like Seattle, San Francisco and New Jersey, who are represented on the panel today, do much better than the US as a whole: Why?

## WHERE CAN WE MAKE IMPROVEMENTS?

### Reducing time to care initiation and re-engaging those lost to care

The New Jersey HIV Prevention Patient Navigator program

- The combined efforts of the Navigator Program, i.e., the rapid testing and the Navigator components, resulted in 912 newly diagnosed or out-of-care HIV positives linked to care in 2013.
- The Navigator budget was \$1,975,431. In 2013, each HIV positive individual was linked to care at an average cost of \$2145.



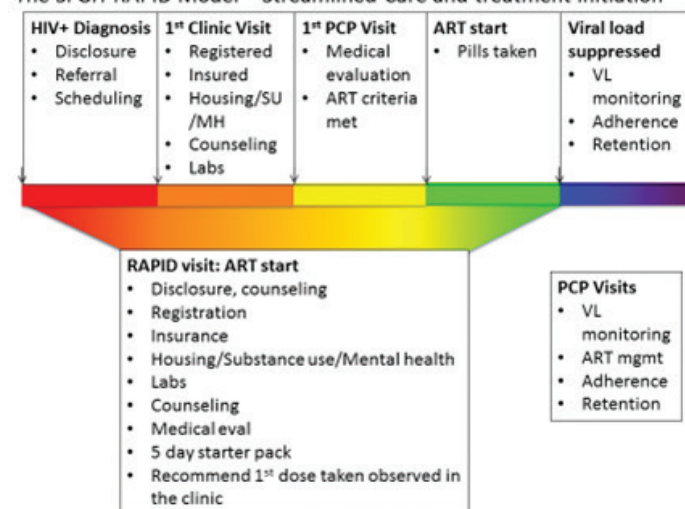
### Reducing time to viral suppression by streamlining treatment initiation

San Francisco General Hospitals RAPID HIV treatment program July 2013 to Present

**Provides same day, observed ART to newly diagnosed HIV+ outpatients**

- Started with a focus on recently infected (Negative test < 6 months from diagnosis)
- Expanded to all newly diagnosed
- All RAPID clients received same day ART, mean time to VL < 200 copies/ml was 56 days
- Reduced time to VL suppression by nearly 60%, compared to 132 days observed in patients newly diagnosed between 2010-June 2013

The SFGH RAPID Model – Streamlined Care and treatment initiation



Please be thinking about other examples of ways to improve care engagement and viral suppression, as well as barriers you face in meeting this goal.

## **Dried Blood Spots (DBS) May Have High Utility Both in Resource Limited Settings and in Hard to Reach Populations for Diagnosis and Treatment Decisions - Handout**

Dried Blood Spots (DBS) have utility both in resource limited settings and in hard-to-reach populations for diagnosis and treatment decisions. This roundtable will review where we are, what remains to be done, and examine the advantages and limitations.

**Chair:** Dr. Joanne Mei, Centers for Disease Control and Prevention, Atlanta, GA

### **Discussants:**

- Dr Silvina Masciotra, Centers for Disease Control and Prevention, Atlanta, GA.
- Adj A/Prof Levinia Crooks AM, La Trobe University, University of NSW, CEO, Australasian Society for HIV Medicine, Australia
- Mr Philip Cunningham, Chief Operating Officer, St. Vincent's Centre for Applied Medical Research, Reference Laboratory, Australia

**Facilitated discussion:** Dr Bernard M Branson, Scientific Affairs LLC, GA

### **Abstract:**

Dried blood spots (DBS) have been used for HIV antibody testing and for HIV nucleic acid testing of neonates born to HIV+ mothers for many years, but have been used rarely in clinical settings until recently. DBS can be used for HIV diagnosis, viral load and potentially, drug resistance testing, and may be particularly useful to overcome difficulties and cost of the specimen collection, transport, and stability that is necessary for HIV antigen and RNA testing, which now play an increasing role in both HIV diagnosis and clinical management. More stringent or rigorous controls may be placed on diagnostic tests over monitoring tests by different regulatory bodies. Yet recent comparative studies indicate that the performance of DBS is comparable if not superior to many alternatives.

DBS can thus facilitate diagnosis and expanded treatment access, particularly in resource limited settings, and to reach people at high risk for HIV with previously low rates of HIV testing, where DBS have attained high acceptance and positive yield. DBS have also been commercialized for testing samples collected at home and used as a surveillance tool, either instead of or in addition to POC rapid tests. But these have only been approved for earlier generation HIV antibody EIA and Western blot.

This roundtable will review existing evidence for the performance of DBS with current HIV assays and practical applications for clinical management and surveillance in both low and high resource settings, examine the current status of validations and regulatory approvals, identify outstanding questions that need to be resolved, and explore interest in a multi-centre evaluation to answer any remaining questions.

### **Discussion Topics:**

#### **Performance - DBS for Antibody Testing**

The performance of DBS (Masciotra, et. al.) concluded promising performance of the GS HIV COMBO Ag/Ab EIA and Geenius HIV 1/2 supplemental assay. Use of these tests can facilitate confirmatory testing and can be used to bank specimens for future testing.

#### **Acceptability of DBS for HIV screening and yield**

The use of targeted DBS testing in populations at elevated risk of HIV and among populations that resist testing or do not test frequently have shown high acceptability (Westrop et.al, 2014). Brady (2014) presented the Terrence Higgins Trust data at the BASH/BHIVA conference, they found a +ve yield of 1.8% in MSM and 3.6% in African samples collected between Jan and Sept 2013 and 0.8% and 2.6% in the sample groups between Nov 2013 and Mar 2014. Thirty-two percent of these populations had never been previously tested.

## Utility of DBS for Viral Load and Resistance monitoring and decision making

Particularly in developing settings the ease at which DBS samples can be collected and transported makes them particularly attractive for individual monitoring and population surveillance.

At a population level resistance screening in developing settings may provide valuable information for second line treatment guidelines. VL is likewise useful for monitoring circulating virus and treatment impacts at a population level.

## Screening versus Clinical or Monitoring Applications

Concerns about performance are greatest in the use of DBS in screening or diagnostic settings. This is an area of particular importance and an issue which the round table will explore.

- What needs to be done?
- What advocacy or specific research or validation is required to have DBS accepted as a screening and diagnostics tool?
- Are appropriate quality assurance programs in place for screening and diagnostic testing?
- While increasingly DBS sample collection is accepted for monitoring, what is required to meet the screening and diagnostic evaluation bar, with regulators?

## Is there interest in collaborative validation studies or further research?

- What practical steps might be taken to progress validation of DBS for use in conventional approved HIV assays?
  - CLIA validation studies that might be submitted to CMS
  - Collaborative pathways to assist a product sponsor in submitting an application
- Can the round table make recommendations for subsequent activity in this area?
- Prototype: submitting validation data to CMS that then allows labs to do limited validations
- Can DBS provide a confirmatory sample for self-test and facilitate a linkage to care?
- Can the same data be used in developing and developed settings?
- Quality Assurance – application of the CDC neonate DBS testing program?
- Nucleic acid tests – particularly those making qualitative diagnostic claims

## Related abstracts which may be of interest to readers

The following are abstracts from this meeting which may be of interest

**E4. Perceptions and Performance of Self-administered Rapid HIV Tests Conducted by Untrained Users in Real-World Settings.** *P. R. Chavez, L. G. Wesolowski, S. M. Owen, L. Gravens, P. Sullivan, and R. J. MacGowan*

**H1. Evaluation of the performance of the Bio-Rad GS HIV Combo Ag/Ab EIA and Bio-Rad Geenius™ HIV-1/2 Supplemental Assay using dried blood spots as an alternative specimen type.** *Silvina Masciotra, Wei Luo, Sarah Adams, Kathy Shriver, Laura Wesolowski, Steve Ethridge, Amanda Smith, Gabriela Paz-Bailey, S. Michele Owen*

This paper will be presented immediately before the round table, and act as an introduction to the roundtable discussion.

Two additional references, which may be of interest are:

**2014 Clinical Virology Symposium, USA Poster# 1165: Dried Blood Spot Testing With the Bio-Rad GS HIV Combo Ag/Ab EIA and Bio-Rad Geenius™ HIV 1/2 Supplemental Assay.** *Silvina Masciotra, Geoff Davis, Wei Luo, LiXia Li, Joanne Mei, M. Kathleen Shriver, Amanda Smith, Christopher Bentsen, Monica Parker, Berry Bennett, Bernard Branson, and S. Michele Owen*

This is initial research comparing the Bio-Rad HIV Combo Ag/Ab and Geenius HIV supplemental Assay. The paper being presented immediately before the round table is continuation of this work.

**AIDS 2014 WEAX0105LB: Testing history and risk behaviour of individuals requesting an HIV test through an online self-sampling service.** *S.J. Westrop, C. James, D. Edwardes, M. Brady, R. Gillespie, O.N. Gill, A. Nardone*

Which reported at the 2014 International AIDS Conference and reported the acceptability of DBS for reaching high risk MSM and African sub-populations in the UK.