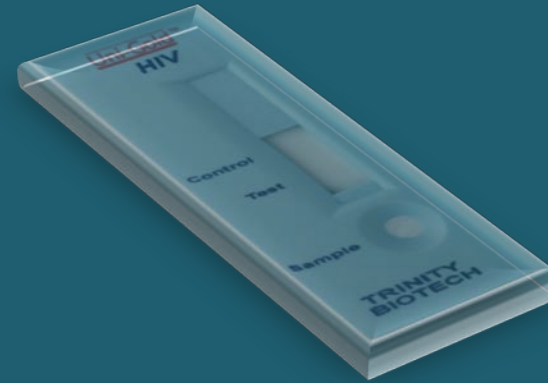


Rapid testing algorithm performance in a low prevalence environment: NJ 2015-8



Alere Determine™
HIV-1/2 Ag/Ab Combo



Trinity Biotech Uni-Gold
HIV1/2 Recombigen

Eugene G. Martin, PhD

HIV Diagnostics Conference - March 2019



• FINANCIAL DISCLOSURES

- **Eugene G. Martin, PhD** - Rutgers University - Robert Wood Johnson Medical School, Pathology and Laboratory Medicine, Somerset, NJ
- **Debbie Ysmin Mohammed, DrPH, MS, MPH, BSN, AACRN** – William Paterson University, Wayne, New Jersey
- **Gratian Salaru, MD** - Rutgers University - Robert Wood Johnson Medical School, Pathology and Laboratory Medicine, Somerset, NJ

- None of the authors have relevant personal financial interests, arrangements or affiliations with any organization related to the commercial products or services discussed
- NJ HIV, the rapid test support program, is funded by grants from the NJ Department of Health, Division of HIV, STD & TB Services & Division of Mental Health & Addiction Services.

HIV TRANSMISSIONS

UNITED STATES Percentage of People with HIV	Status -2016	Accounts for Percentage of New Transmissions
15%	DON'T KNOW	38%
23%	KNOW, BUT NOT IN CARE	43%
11%	NOT VIRALLY SUPPRESSED	20%
51%	VIRALLY SUPPRESSED	0%

Source: CDC Vital Signs, 2019

	NEW JERSEY - Age > 13 - 2014		
	Number	EAPC	p Value
Estimated HIV incidence	1,100	-3.5	0.11
Estimated HIV prevalence	39,200	0.9	0.19
Est Pct living with undiagnosed HIV infection	10.4	-4.7	0.11

EAPC: Estimated Annual Percentage Change

Source: Johnson AS, Song R, Hall HI. State-Level Estimates of HIV Incidence, Prevalence, and Undiagnosed Infections. CROI. Seattle, WA, March 4-5, 2019.

Undiagnosed HIV infection continues to contribute disproportionately to the spread of disease



First Step along the Continuum of Care

DIAGNOSTICS



Background

- A sequential, two-step, rapid testing algorithm (RTA) eliminates confirmatory delay and improves linkage processes by reducing false positive referrals.
- The bulk of RTA discordant specimens are processed centrally through our Somerset offices.
- In use since 2009, the NJ-RTA was modified in 2015 after statewide adoption of Determine HIV-1/2 Ag/Ab Combo (DC) as the initial rapid screening test. This allowed immediate, on-site verification of initial antibody results and expedited linkage into care. We report here a summary of DC screening test results observed since 2015.
- We require that all sites that receive rapid HIV devices utilize a 'Preliminary Positive Tracking Form' to allow outcome tracking for initial DC screens reactive for either p24Ag+, HIV1/2 Ab+ or both.

Overview: NJ HIV Screening Locations

2019				
RWJMS Oversight	Venue	Stationary	Mobile Vans	Totals
	CBO	26	12	38
	CLINICS	3		3
	CORRECTIONS	4		4
	FQHC	9	2	11
	HEALTH DEPT	22	2	24
	HOSPITALS	1		1
	UNIVERSITIES	4		4
DMHAS FUNDING	SUBSTANCE ABUSE	7	0	7
		76	16	92
NON-RWJMS Oversight	Venue	Stationary	Mobile Vans	Totals
	CBO	1		1
	CLINICS	1		1
	CORRECTIONS	0		0
	FAMILY PLANNING	4		4
	FQHC	13		13
	HEALTH DEPT	3		3
	HOSPITALS	20		20
	UNIVERSITIES	2		2
	SUBSTANCE ABUSE	0		0
		44	0	44
3/14/2019	NEW JERSEY (ALL SITES)	120	16	136



Centralized Discordant Handling

NJ HIV PRELIMINARY POSITIVE TRACKING

NJ RAPID HIV TEST ALGORITHM

Initial Rapid HIV Screen
Determine Combo

If NEG,
Results within 20-30 minutes

HIV1/2 Ab +

Second Rapid HIV Screen
Trinity Unigold

DISCORDANT WORKUP: →
CDC HIV DIAGNOSTIC ALGORITHM with NAAT

How often is the initial DC screen wrong (?)

Free P24 Ag+

CONFIRMED
"PRESUMPTIVE POSITIVE"

How often do both rapid tests 'Confirm' Infection?

How many True Positives are missed by the second rapid (?)

LINKED TO CARE DIAGNOSTIC & STAGING WORKUP

How often is p24Ag+ observed?
Is it confirmed at the linkage site?

Factors Impacting Rapid Test Results

- In a RAPID TEST setting.. Little things DO matter!
 - Who tests
 - How they test
 - How the devices are handled (temperature/timing/expiration dates)
 - How thoroughly operators are trained
 - What they understand about the test and its limits
 - Internal or external pressures that operate on testers

Tracking Discordants: Case Study D17-18

Site # 1 – Initial Rapid HIV Screen Results – Determine Combo

← Test 1 Reagent Lot #

Site # 2 – Second Rapid HIV Screen Results – Usually Trinity Unigold, occasionally Orasure Oraquick

← Test 2 Reagent Lot #

← NJ HIV picks up and refers specimen to reference lab (Quest) for CDC Laboratory based 4th gen screening PLUS an HIV quantitative viral load or we receive data from non-RWJ laboratory that follows on their own

← Linkage information with

← Laboratory data if being reported to us



NJ HIV Positive Tracking Form Transcribed for Presentation

Client ID # NJDH540024 First Rapid HIV Test Result Date: 05-12-2017 D17-18

First Test Site ID Number 6371 First Test Site Name: JCMC-RWJBH, CTS-002

First Test Site Counselor Name: Brian R. Robles First Test Site Counselor Number: 6921

First Rapid HIV Test Type: Determine INSTI Other

Result: Positive HIV 1/2 Antibody Positive HIV Antigen (Determines ONLY)

Specimen (circle one): Oral Fingertick Test Kit Lot Number: 161027

Positive ANTIGEN ONLY (Determine): No rapid tests can validate this result. Collect discordant work-up samples for confirmation, call NJHIV support for assistance and REFER client to care IMMEDIATELY. This may represent an acute HIV case; confirmation may take 7-10 days. ENTER CONFIRMATORY RESULTS BELOW.

For Single Rapid Test Sites and Non-Clinical Rapid-Rapid Test sites, this form MUST ACCOMPANY the patient to test site where second test will be performed and must go to the treatment site. The form must be returned to the first test site to capture the positive result and referral to care.

SECOND Rapid HIV Test Result Date: 05-12-2017

NOT DONE BECAUSE: Client Walked OUT Determined to be KNOWN POS ALREADY IN CARE Check off ALL THAT APPLY

Enter site information ONLY if Second Test Site is different from First Test Site: R2R

Second Test Site ID Number: 6371 Also, enter in Local Field 1 in Evaluation Second Test Site Name: JCMC-RWJBH, CTS-002

Second Test Site Counselor Number: 6921 Also, enter in Local Field 2 in Evaluation Second Test Site Counselor Name: B.R. Robles

Second HIV Test Type: Rapid: Unigold OraQuick Result: Positive Negative

Specimen (circle one): Oral Fingertick Venipuncture Test Kit Lot Number: F287008

Test Result: Fax to 732-235-9012. When Rapid HIV test results part is completed DO NOT SEND the EvalWeb Form to this number

Check One Both Tests Positive

Evaluation Web Result Form with client information mailed to Surveillance Date Mailed: _____ Mailed By: _____

Discordant Result (First test is positive and second test is negative. Also for Antigen ONLY positives). Draw 2 serum separator tubes and 2 white top tubes & Call NJ HIV Program at 732-743-3624 or 732-743-3620 for pick-up. Process collected tubes according to instructions. Discordant - Physician Line: 732-236-7013

Second Test Not Done: Client refused - Contact Partner Services and complete Partner Services Form

Client Referral to Treatment: Fax to 732-235-9012 when appointment information is completed

Date client referred to treatment: _____ Appointment kept: Yes No

Date of Appointment: _____ If No, Why? _____

Patient Navigated By: _____

CONFIRMATORY Laboratory Results or DISCORDANT Laboratory Results:

Sent to Laboratory: Blood drawn for antigen confirmation _____

4th gen Reflex: POS NEG; Biorad MultiSpot HIV-1 HIV-2 NEG

Optima Qual HIV-1 RNA POS NEG

Quantitative Viral Load: _____ copies/mL or < 20 copies/mL NEG CD4 count: _____

Please use assigned CTS number, de-identify and fax lab confirmation to: (732) 235-9012

Section 2.3.1 FORM NJ-HIV 1-31-2017

THE RTA DISCORDANT PATHWAY

- We order two tests to resolve a discordant result: A reflex (RFL) lab-based HIV combo screen AND a quantitative viral load assay looking for HIV-1 RNA. Provides internal check on the reference laboratory and gives us hints within a couple of days (IF POSITIVE).
- **HIV-1 RNA, QN, RT-PCR**
- **HIV 1/2 AG/AB, 4TH GEN RFL** - Laboratory-based HIV screen (More Sensitive than any rapid test)
 - Should also be reactive if truly positive. Sensitive to both HIV p24 Ag AND HIV1/2 Ab.
 - If reactive → a REFLEX TEST: **HIV1/2 AB DIF, SUPPLEM USE** is performed to confirm the presence of HIV antibodies
 - If the confirmatory, differentiation assay is negative, the process moves to the only FDA approved diagnostic RNA assay: **HIV-1 RNA, QL TMA.**

Tracking Follow-up on an RTA Discordant Result

START BELOW		DC COMPLAINT RANGE: 2009-2013 0.002%-0.14%																	
Discordant or N	RTA DISCORDANT	Client ID	Date of	Site	Lot # - Initial HIV1/2 Score	Lot # - Second Ass	Alert TS Case#	Complaint Rate	Alert TS Resolution	Screen	T	Product	Determine Combo (Ag/Ab/bo)	Second Rap	Resolution	Aptima HIV	Genieus	RNA copies	Ref lab: MS (MultiSpot) EIA
D17-01	N	NJDH510349	12/12/2016	St. Joseph	160721	ND	993976			NON - RTA	1	Determine	DC Ag+	ND	FP DC Ag	ND	ND	<20	EIA 4th gen -
D17-02	Y	NJDH535456	1/4/2017	Complete Care	160721	F141013	993993			RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-03	Y	NJDH516473	1/10/2017	SJFMC-Salem/Cooper EIP	160619	6649343	993993	0.022%	no CAPA	R2R	1	Determine/DraQuick	DC Ab+	OQ-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-04	Y	NJDH092085	1/18/2017	CGE/EBCHC	160605	F270008	993943	0.048%	no CAPA	R2R	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-05	Y	NJDH092086	1/18/2017	CGE/EBCHC	160605	F125056	993948	0.048%	no CAPA	R2R	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-06	N	NJDH531568	3/2/2017	EIP	160808	161027	993967	0.006%/0.022%	no CAPA	NON - RTA	1	Determine	DC Ag+	ND	FP DC Ag	ND	ND	<20	EIA 4th gen -
D17-07rept	N	NJDH476322	2/1/2017	Rutgers ID Clinic	160808	ND	993954	0.006%	no CAPA	NON - RTA	1	Determine	DC Ag+	ND	FP DC Ag	ND	ND	<20	EIA 4th gen -
D17-08	Y	NJDH557757	3/16/2017	Complete Care	161027	F141013	993982	0.022%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-09	Y	NJDH520771	4/3/2017	Chandler Health Ctr	161027	F349004	993987	0.022%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-10	Y	NJDH559020	4/10/2017	Hoboken Family Planning-Union City/JCMC	160406	F252003	993996	0.035%	no CAPA	R2R	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-11	Y	NJDH545159	4/12/2017	Zufall Health Center-Dover	161214	F287008	994006	0.011%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-12	Y	NJDH512042	4/18/2017	Camden AHEC/Cooper EIP	161027	6649343	994014	0.022%	no CAPA	R2R	1	Determine/DraQuick	DC Ab+	OQ-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-13rept	Y	NJDH474564	4/5/2017	Catholic Charities - Union	160619	E287008	993989			RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	ND	EIA 4th gen -
D17-14	Y	NJDH551941	4/26/2017	Newark STD	161027	F190067	994016	0.022%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-15	Y	NJDH544001	4/26/2017	Trinitas	161027	F125056	994019	0.022%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-16	Y	NJDH558095	5/4/2017	VNA	161214	F287008	n/a	true positive	true positive	RR	1	Determine/Unigold	DC Ab+	UG-	TP DC Ab	DETECTED	IND/HIV2	15,125	EIA 4th gen +
D17-17	Y	NJDH545223	5/8/2017	Zufall Health Center-Dover	161214	F287008	994030	0.011%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-18	Y	NJDH540024	5/12/2017	JCMC-RWJBH	161027	F287008	n/a	true positive	true positive	RR	1	Determine/Unigold	DC Ab+	UG-	TP DC Ab	DETECTED	HIV1/2 NEG	273,228	EIA 4th gen +
D17-19	Y	NJDH536363	5/17/2017	Buddies of NJ	170123	F190067	994039	0.020%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-20	Y	NJDH563541	6/1/2017	MRSC - A Team	170223	F228007	994050	0.012%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	NOT DETECTED	HIV1/2 NEG	<20	EIA 4th gen +
D17-21	Y	NJDH538436	6/5/2017	PROJECT	170123	F190062	994058	0.020%	no CAPA	R2R	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-22	Y	NJDH564504	6/6/2017	CGE/EBCHC	170123	F342019	994061	0.020%	no CAPA	R2R	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-23	Y	NJDH563266	6/19/2017	RUTGERS STOP	170123	F270008	994063	0.020%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-24	Y	NJDH563140	6/13/2017	Complete Care	170123	F141013	994067	0.020%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-25	Y	NJDH571923	6/30/2017	Hyacinth Newark	170223	F342109	994081	0.012%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-26	N	NJDH506386	2/14/2017	Joseph's	160605	ND	993959	0.048%	no CAPA	NON - RTA	1	Determine	DC Ab+	ND	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-26rept	N	NJDH556621	6/27/2017	Joseph's	161214	F349004	994072	true positive	true positive	NON - RTA	1	Determine/Unigold	DC Ab+	UG-	TRUE POS	ND	ND	*****	ND
D17-27	Y	NJDH574616	7/10/2017	Atlantic County HD	170123	F342019	994084	0.020%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	ND	EIA 4th gen -
D17-28	Y	NJDH544344	3/27/2017	Atlantic County HD	161027	F270008	993986	0.022%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	ND	EIA 4th gen -
D17-29	Y	NJDH542325	7/27/2017	Cooper University Hospital	161027	6649343	994091	0.022%	no CAPA	RR	1	Determine/DraQuick	DC Ab+	OQ-	FP DC Ab	ND	ND	<20	EIA 4th gen -
D17-30	Y	NJDH572001	7/28/2017	Hyacinth Newark	170223	H132002	994101	0.012%	no CAPA	RR	1	Determine/Unigold	DC Ab+	UG-	FP DC Ab	ND	ND	<20	EIA 4th gen -

Questions:

1. How often did we observe free p24Ag+?
 - How often do they subsequently confirm?
2. How often do both rapid tests 'Confirm' an Infection?
3. When the second rapid fails to confirm, how often is it falsely negative? Or, how often is the initial screen result a false positive?
4. How long does it take to resolve a 'discordant'?

NJ RAPID HIV TEST ALGORITHM – (2015-8)



Initial Rapid HIV Screen
Determine Combo

310,785

2400 Preliminary Positive Screens

HIV1/2 Ab +

Second Rapid HIV Screen
Trinity Unigold

196 Discordant Screens

DISCORDANT WORKUP: →
CDC HIV DIAGNOSTIC ALGORITHM with NAAT

How often is the RTA discordant screen result correct (92.9%)

182 Initial False DC Positive Screens

P24 Ag+ (13)

CONFIRMED "PRESUMPTIVE POSITIVE"

How often do both rapid tests 'Confirm' Infection? (91.8%)

14 True Positives were missed by the second rapid (7.1%)

2204 Presumptive Confirmation

LINKED TO CARE DIAGNOSTIC & STAGING WORKUP

Only 1 p24Ag+ was confirmed at the linkage site

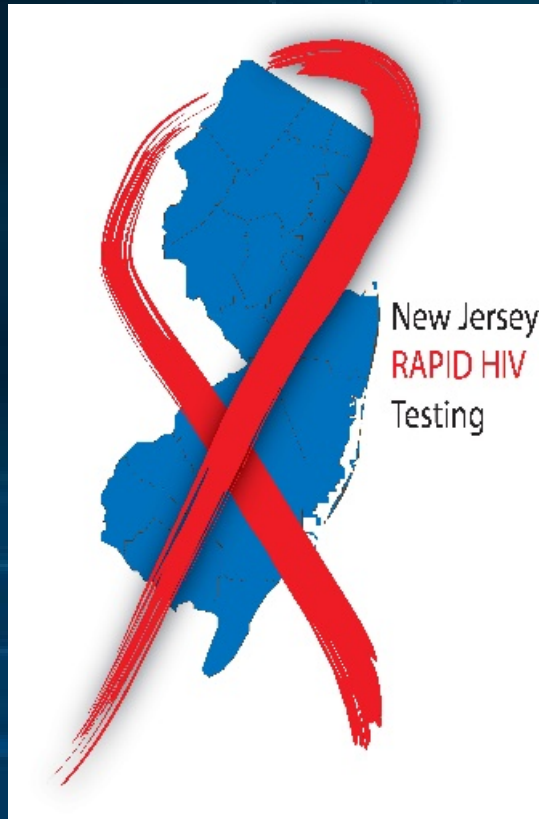
But what about the 14 true HIV infections?

- Average quantitative HIV-1 viral load of positive discordant specimens: 277,385 copies/mL
- Several: 5/14 (35.7%) had viral loads <1000 copies/mL.
- Among 2191 “confirmed positives” identified by the RTA:
 - Three false (3) positive RTAs were subsequently reported (both rapid tests being positive while the subsequent HIV-1/2 Ag/Ab assay and quantitative HIV-1 viral load were negative).
 - Fingerstick DC Ag detection identified a SINGLE INSTANCE of an early infection detected by Determin Combo in >300,000 tests throughout New Jersey. Many true positive discordant cases are associated with viral loads <1000.

CONCLUSIONS:

- By using a rapid test algorithm to insure credible referrals and developing a collaborative network to expedite care and treatment, NJ has achieved the first 90 in the care continuum.
- The RTA has allowed us to tailor a counseling message that fits the realities of our state and the outcomes we have observed
- The RTA sets the groundwork for expedited **screen, confirm & treat strategies** and presents significant opportunities as POC NAT devices become available.

Thanks for your time and attention



Eugene Martin, Ph.D.

Co-Director NJ HIV, PI - DHSTS grant

Gratian Salaru, MD

Co-Director NJ HIV, PI - DMHAS MOA

Parisa Javidian, MD - BLD

Tom Kirn, MD, Ph.D.

Joanne Corbo, MT (ASCP), MBA

Rapid HIV Program Manager

Latasha Adams BS,MT

Moeen Ahmed BS,MT

Aida Gilanchi, BS,MT

Nisha Intwala, BS,MT (ASCP)

Franchesca Jackson, BS

DAS Mobile HIV Counselor

- **Marianela Moreno**

Administration:

- Lisa May
- Karen Williams