An Improved 4th Generation Prototype Assay for Earlier Detection of Acute HIV Infection

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Disclosure

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Global HIV Statistics

Number of people Living with HIV

Total	**36.9 million**	[31.1 million-43.9 million]
Adults	35.1 million	[29.6 million-41.7 million]
Women (15+ years)	17.8 million	[15.4 million-20.3 million]
Children (<15 years)	1.8 million	[1.3 million-2.4 million]

People newly infected with HIV in 2017

Total	**1.8 million**	[1.4 million-2.4 million]
Adults	1.6 million	[1.3 million-2.1 million]
Children (<15 years)	180 000	[110 000-260 000]

AIDS-related deaths in 2016

Total	**1.0 million**	[830 000-1.2million]
Adults	890 000	[740 000-1.1 million]
Children (<15 years)	120 000	[79 000-160 000]

Ref. UNAIDS Fat Sheet- World AIDS Day 2018

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UNAIDS Targets by 2020
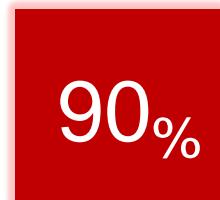
90% Diagnosed

90% On treatment

90% Viral suppressed

UNAIDS

Reductions in New Infections are off Target
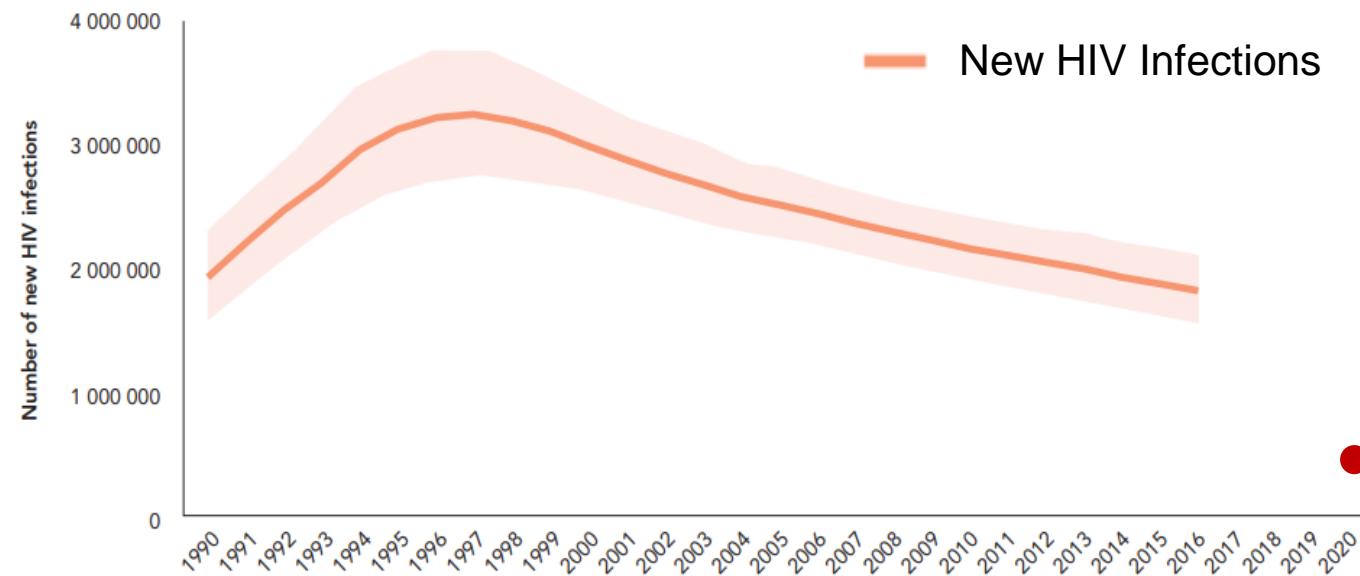
New HIV Infections

The 2020 target is fewer than 500,000 new HIV infections, equivalent to a 75% reduction since 2010.

Ref. UNAIDS DATA 2017

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An Improved 4th Generation HIV Prototype Assay

- Chemiluminescence immunoassay without biotin labeled reagents
- Designed for Architect and Alinity automated platforms
- Research Use Only (RUO)

Architect Platform
(1999 FDA approved)

Alinity Platform
(2017 FDA approved)

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Objective

- Compare performance of the Prototype (RUO) to two FDA-approved 4th generation tests: ARCHITECT HIV Ag/Ab Combo (2010) and Roche Elecsys HIV Combi PT (2017).

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Study Design

- **Sensitivity Evaluation**

  — WHO international HIV-1 p24 antigen standard (NIBSC 90/636)

  — HIV-1/HIV-2 virus isolates (n=17) and acute HIV-1 infections (AHI, n=4)

  — Commercial seroconversion panels (n=14)

  — Patient samples at different stages of HIV infection (n=543)

  — HIV-1/HIV-2 antibody subtypes (n=473)

- **Specificity Evaluation**

  — Blood donors (n=4,316)

  — Prospective collection of individuals with low risk for HIV infection (n=1,690)

  — Heterophilic antibody interference samples (n=9)

- **Evaluation sites and tests**

  — **John Hopkins Medical Institutions**:

    Sensitivity evaluation of the Prototype, ARCHITECT HIV Combo (ARCHITECT) and Roche Elecsys HIV Combi PT (Elecsys).

  — **Abbott Diagnostics**:

    Sensitivity/specificity evaluation of the Prototype and ARCHITECT. Also evaluation of Alinity platform (2017 FDA-approved).

HIV-1 p24 Analytical Sensitivity
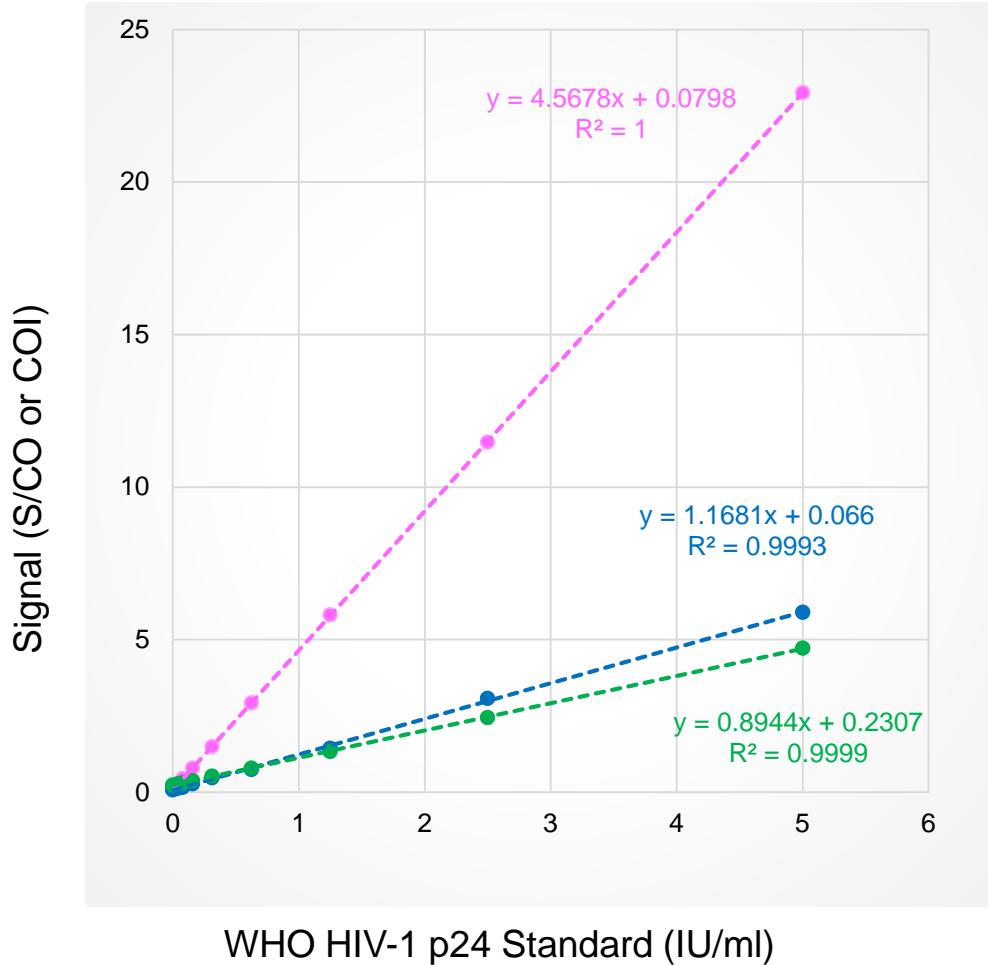
| 4th Generation HIV test	LOD WHO Std (IU/ml)
● **Prototype**	**0.20**
● **ARCHITECT** (2010)	**0.80**
● **Elecsys** (2017)	**0.86**

■ The Prototype demonstrated the best HIV-1 Ag analytic sensitivity, ~4 fold improvement over ARCHITECT and Elecsys.

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Detection of HIV-1 Antigen Genotypes
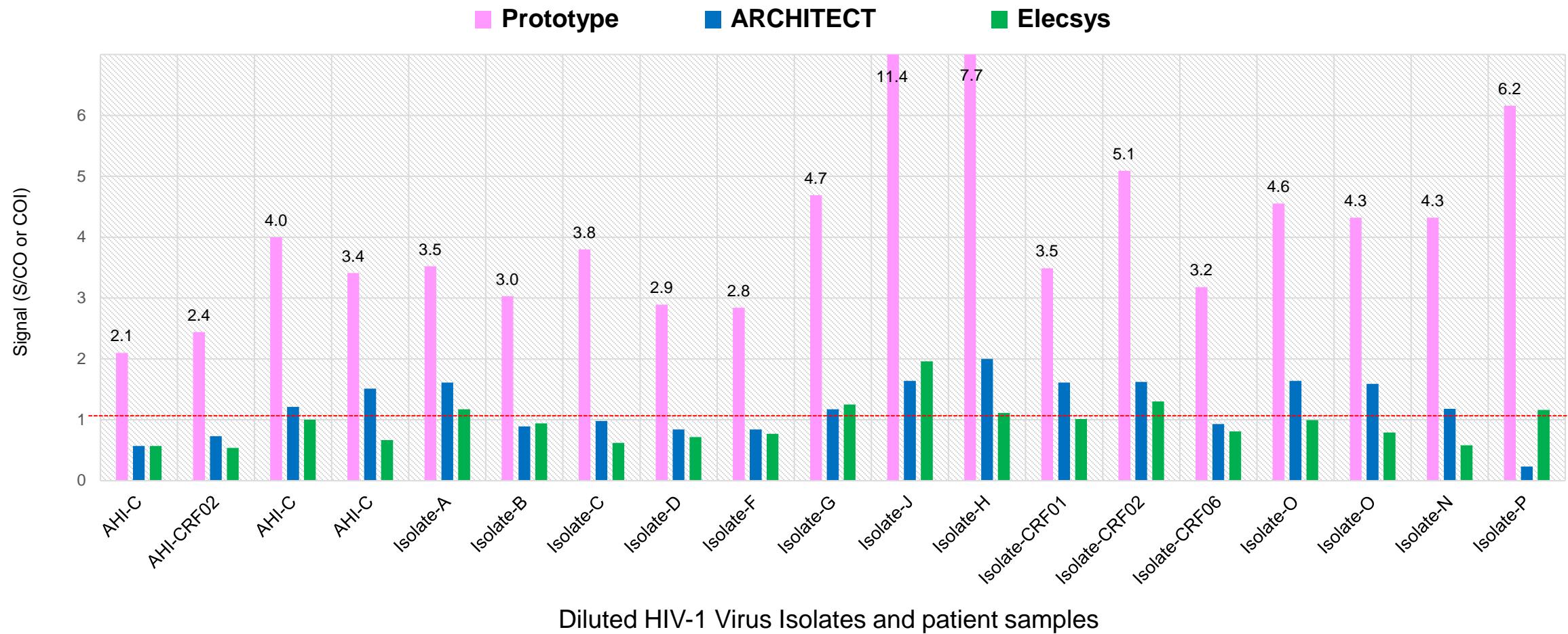
All 19 diluted HIV-1 genotypes were detected by the Prototype with enhanced antigen sensitivity (1.6-5.3 fold) relative to ACHITECT and Elecsys.

Detection of HIV-2 Antigen Subtypes

End point dilution of HIV-2 Virus Isolates
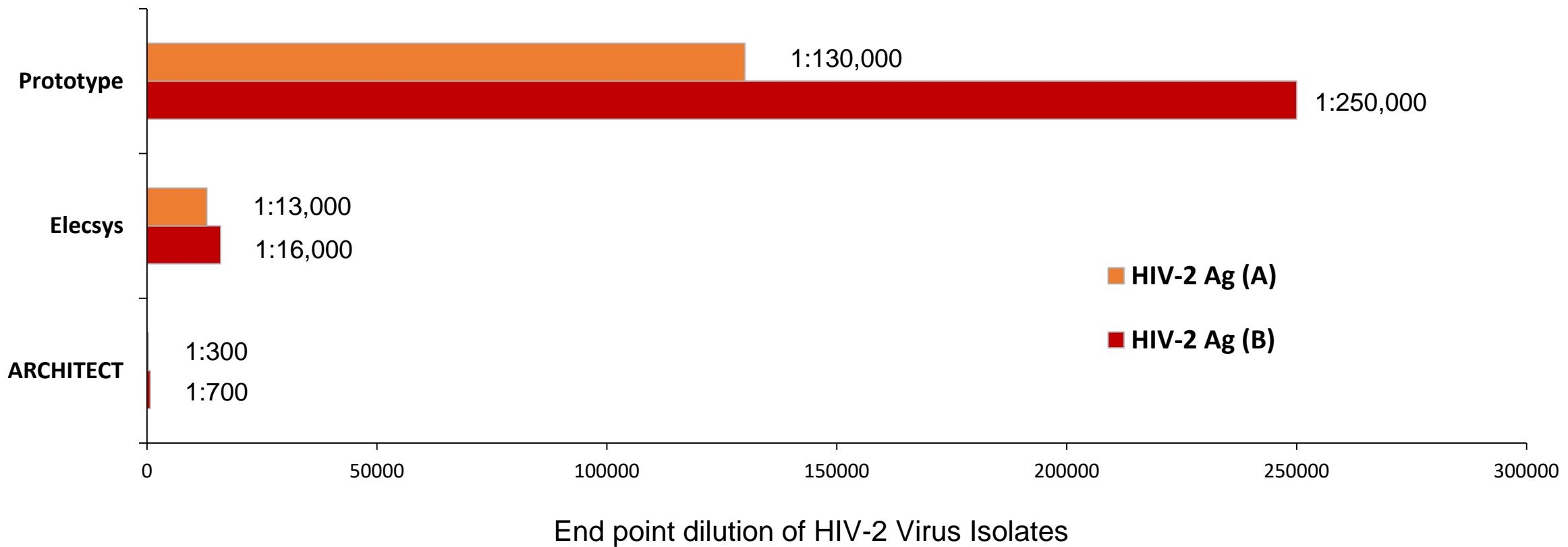
- HIV-2 Ag sensitivity of the Prototype was ~ 10 and 100 fold higher than ARCHITECT and Elecsys HIV Combo tests.

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Seroconversion Sensitivity (14 panels)

Seroconversion Panel	# RNA+ panel bleeds	# Reactive panel bleeds			Days Prototype ahead of ARCHITECT/Elecsys
		Prototype	ARCHITECT	Elecsys	
9012	7	4	3	3	2
9013	3	2	1	1	2
9018	5	4	3	3	3
9022	4	3	2	2	2
9024	2	2	1	1	4
9031	7	4	3	3	8
6244	3	1	1	1	0
ANT9017	9	5	3	3	NA
9089	4	3	3	3	0
9032	9	5	4	3	2-ARCH., 7-Elecsys
9014	1	4	4	4	0
PRB969	7	4	3	3	7
PRB973	4	2	2	2	0
12008	7	6	5	5	5
Total detected bleeds	72	51	40	38	Avg. 2.7-3.1 days

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Seroconversion Sensitivity (Ag only Panel)

SC Panel	Viral Load cps/ml	Day Post RNA+	Prototype	ARCH.	Elecsys
9012-2	<50	-5	0.1	0.1	0.2
9012-3	69	0	0.1	0.1	0.2
9012-4	221	3	0.1	0.1	0.2
9012-5	33,740	8	1.0	0.4	0.6
9012-6	101,800	10	3.7	1.0	1.7
9012-7	>500,000	15	68.6	15.2	35.7
9012-8	>500,000	17	173.6	50.0	105.3
9013-4	<50	-4	0.1	0.1	0.2
9013-5	58	0	0.1	0.1	0.1
9013-6	56,350	5	1.9	0.5	0.8
9013-7	185,800	7	8.1	2.1	3.0
9018-6	<50	-3	0.2	0.1	0.2
9018-7	304	0	0.2	0.1	0.2
9018-8	15,280	4	3.3	0.8	0.6
9018-9	193,100	7	33.0	5.5	5.2
9018-10	621,000	11	77.8	12.1	18.4
9018-11	>500,000	15	96.0	20.2	39.6

| SC Panel	Viral Load cps/ml	Day Post RNA+	Prototype	ARCH.	Elecsys
9024-10	<50	-4	0.1	0.1	0.2
9024-11	12,840	0	1.1	0.3	0.4
9024-12	>500,000	4	116.9	35.5	26.5
9031-13	<50	-4	0.1	0.1	0.2
9031-14	197	0	0.3	0.1	0.2
9031-15	1,493	3	0.2	0.1	0.2
9031-16	10,507	7	1.1	0.3	0.3
9031-17	15,166	15	8.5	2.2	1.7
9031-18	173,075	22	16.1	6.1	8.3
9031-19	237,938	26	19.6	7.8	13.2
9032-4	<50	-3	0.1	0.1	0.2
9032-5	134	0	0.1	0.1	0.1
9032-6	1,507	3	0.2	0.1	0.2
9032-7	29,006	8	1.9	0.8	0.5
9032-8	40,815	10	2.9	1.2	0.6
9032-9	20,395	15	2.5	2.4	1.0
9032-11	3,161	21	3.4	2.0	9.0
9032-12	4,052	23	15.8	2.0	38.8

■ Prototype improved detection 1 or 2 bleeds (2-8 days) earlier than ARCHITECT and Elecsys HIV Combo tests.

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Seroconversion Sensitivity (Trough Panel)
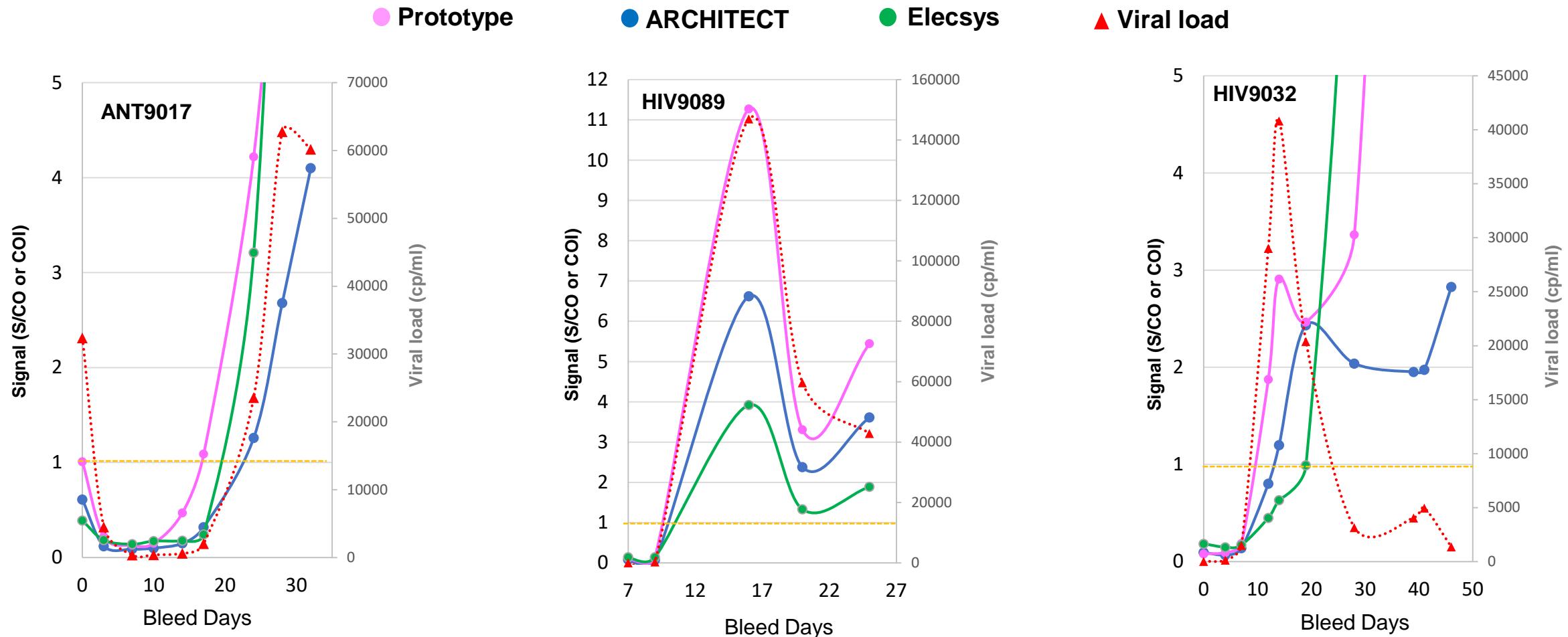
■ Prototype reduced the 2nd diagnostic window or trough effect (2-7 fold).

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Antibody Sensitivity: HIV Patient Samples (n=543)

- Acute (299)
- Symptomatic (128)
- AIDS (116)

$y = 0.868x + 42.368$
$R^2 = 0.8381$

Prototype S/CO (y-axis)

ARCHITECT S/CO (x-axis)
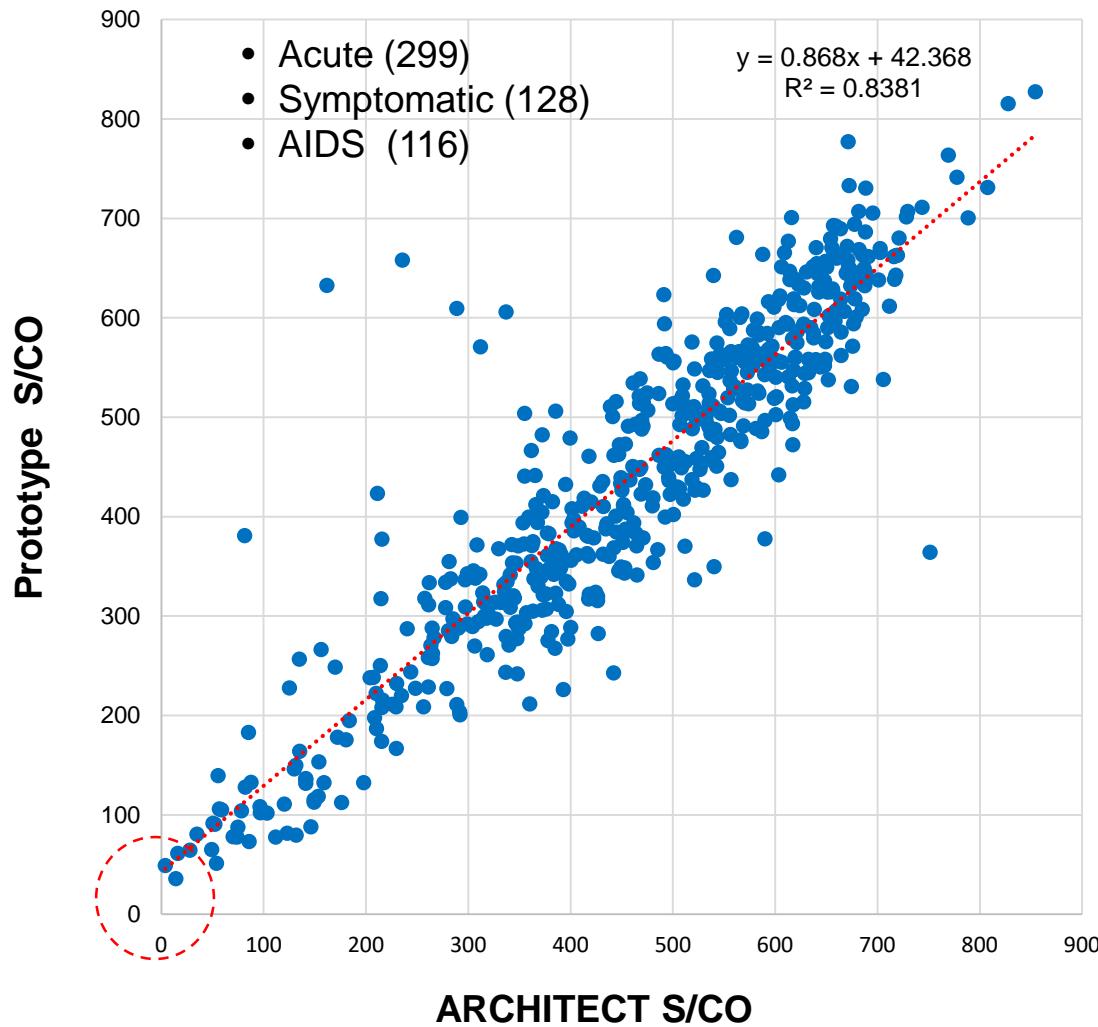
Signal Comparison

HIV-1 M Sample	ARCHITECT	Prototype
	S/CO	S/CO
#243	3.8	48.9
#86	14.0	35.7
#472	16.0	61.7

- All 543 (100%) HIV patient samples were detected by the Prototype and ARCHITECT HIV Combo test.

- Sensitivity of low titer samples was improved 2-13 fold by the Prototype over ARCHITECT HIV Combo.

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Antibody Sensitivity: HIV Subtype/Group (n=473)

**327 HIV-1 Group M Subtype**

- 39 A
- 36 B
- 29 C
- 14 D
- 15 F
- 11 G
- 3 H
- 2 J
- 29 CRF01_AE
- 31 CRF02_AG

- 5 CRF06_cpx
- 5 CRF09_cpx
- 8 CRF11_cpx
- 8 CRF13_cpx
- 5 CRF22_01A1
- 2 CRF36_cpx
- 5 CRF37_cpx
- 3 CRF43_02G
- 113 URF

50 HIV-1 Group O

96 HIV-2

All samples detected

Group N

Group M

HIV

Group P

Group O

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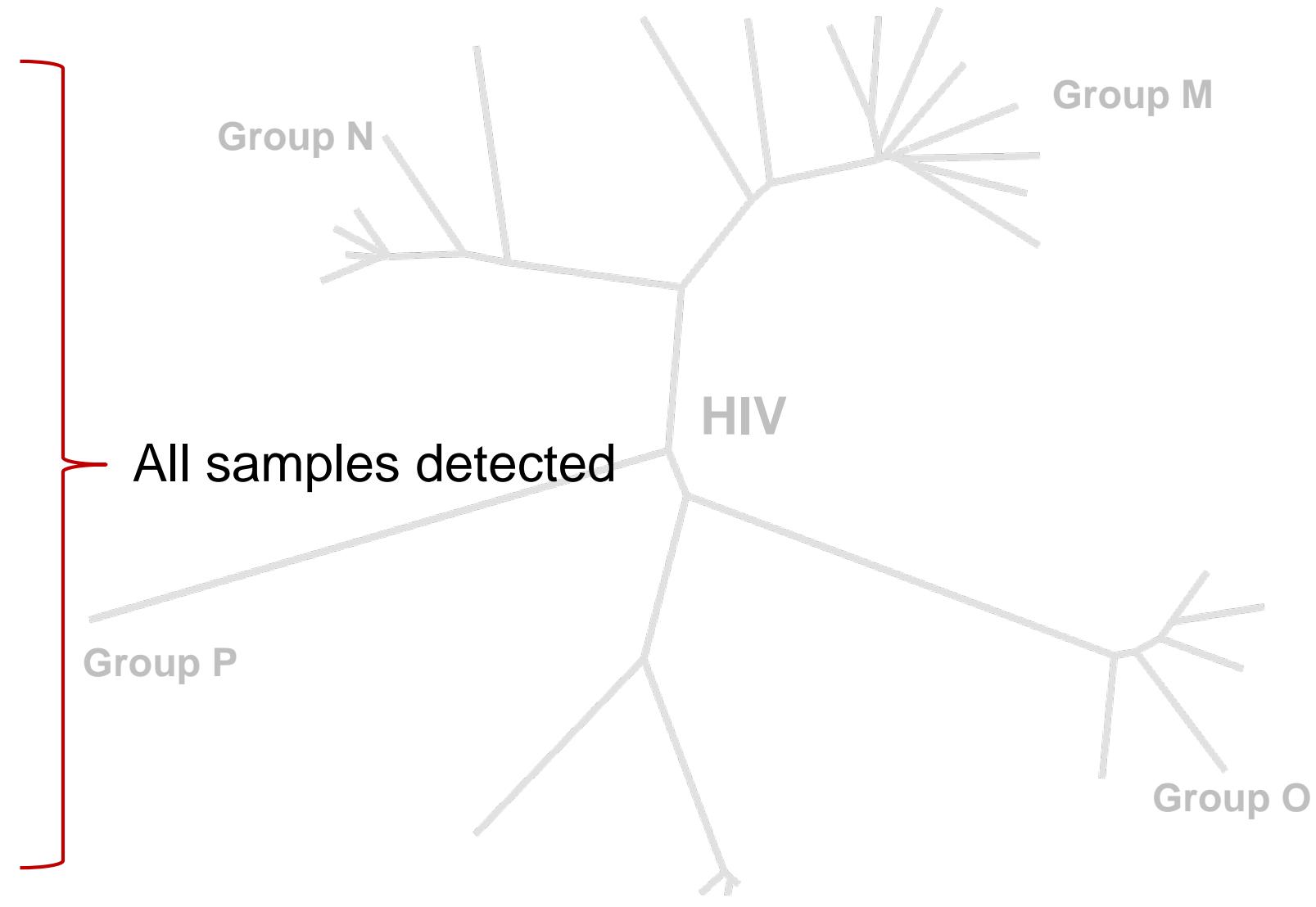
Performance of Prototype on Architect and Alinity Platforms

Ab Detection

$y = 1.1236x - 1.6872$
$R^2 = 0.9963$

Alinity platform (S/CO) vs Architect platform (S/CO)

HIV Ab Subtype (n):
- HIV-1 Group M (250)
- HIV-1 group O (50)
- HIV-1 URF (122)
- HIV-2 (96)

Ag Detection

$y = 1.0383x + 0.2237$
$R^2 = 0.991$

Alinity platform (S/CO) vs Architect platform (S/CO)

52 dilutions of HIV-1 (M/O) & HIV-2 Virus isolates
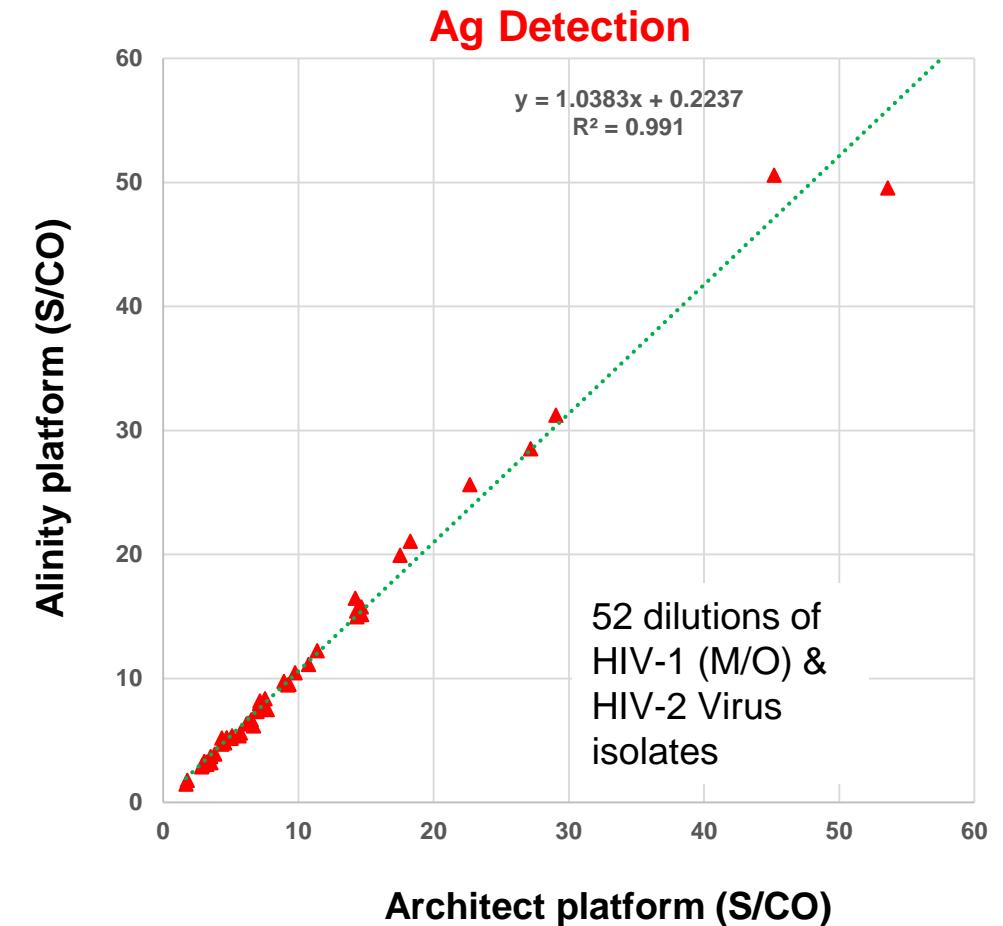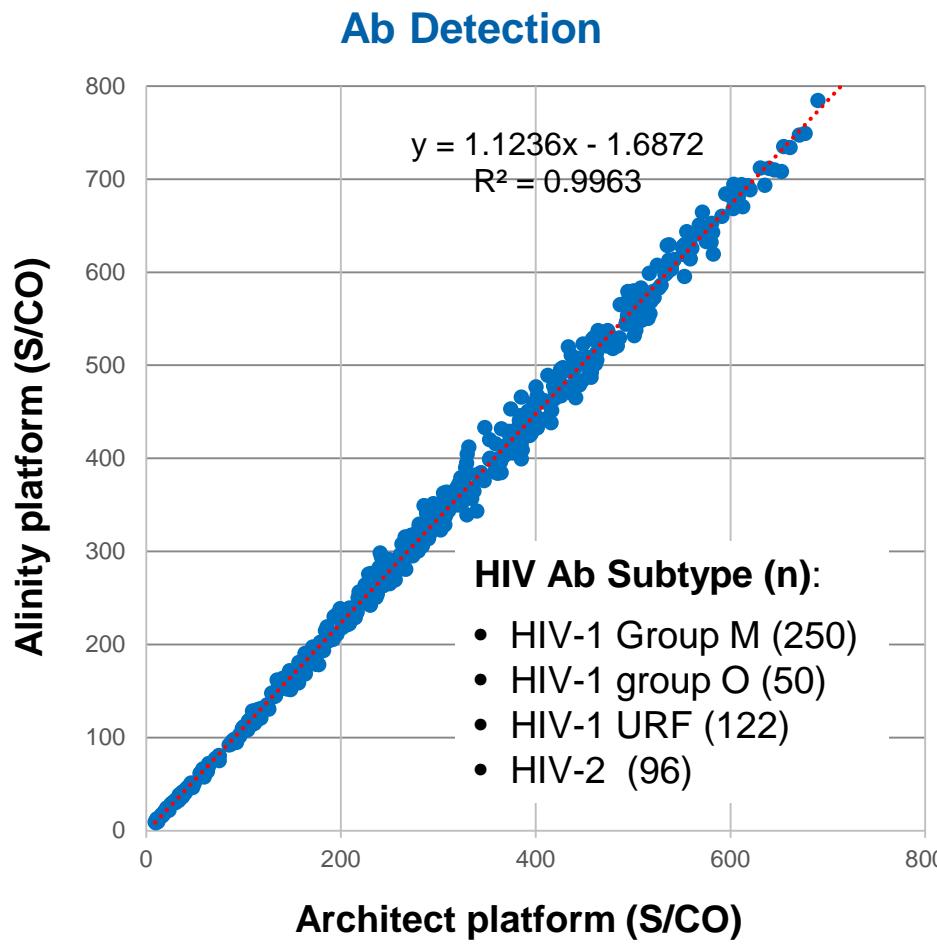
■ The Prototype performed consistently between the platforms

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Clinical Specificity: Blood Donors and Low Risk Diagnostic Specimens

Signal Distribution	Fresh Blood Donors (n=4,316)	Low Risk Population (n=1,690)
Mean	0.08	0.09
SD	0.030	0.042
SD to CO	**31**	**22**
IR/RR	8/3	15/14 (*10 RRs were confirmed HIV positive*)
False Positives	**3**	**4**
Specificity	**99.93%** (4313/4316)	**99.76%** (1676/1680)
LL 95% CI	99.82%	99.44%
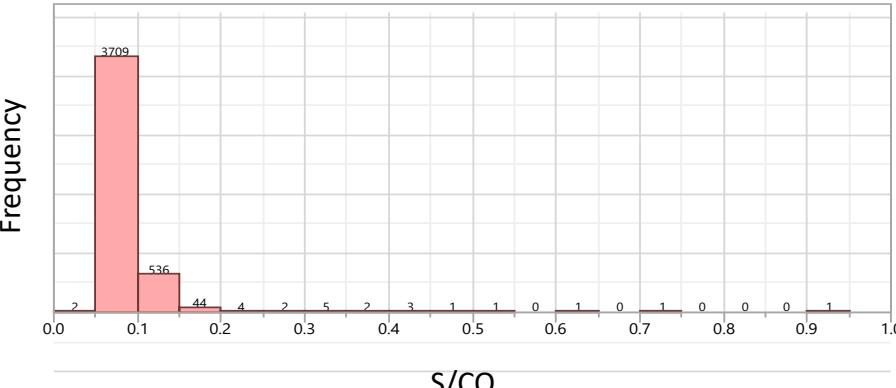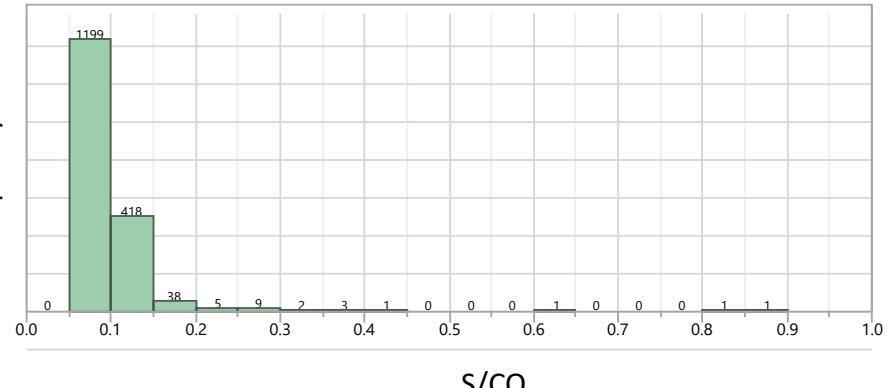
■ The Prototype demonstrated high specificity for both blood donors and low risk population.

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Specificity: Heterophilic Antibody Interference

| False Positive Complaints	ARCHITECT	Prototype
	S/CO	S/CO
UAE 1401400R1383573	450	0.12
US S163520	20	0.20
Canada 0600600R2201391	20	0.20
US 1-1895324311	323	0.27
Qatar 138138RE1017953	401	0.09
US 0560560R2250986	2.4	0.09
Switzerland 0870870C1058028	15	0.14
Italy 0920920R1278937	7	0.11
Slovenia 2332330R1265724	50	0.15

- The Prototype eliminated all 9 ARCHITECT false reactive samples due to heterophilic antibody interference.

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Prototype Performance Summary

- Broad detection of HIV-1 and HIV-2 genotypes with enhanced p24 analytical sensitivity
- Reduction of seroconversion window 2.7-3.1 days over ARCHITECT and Elecsys
- High specificity with minimized heterophilic antibody interference

HAMA Complaints	ARCHITECT S/CO	Prototype S/CO
UAE 1401400R1383573	450	0.12
ARC S163520	20	0.20
Canada 0600600R2201391	20	0.20
US 1-1895324311	323	0.27
Qatar 138138RE1017953	401	0.09
US 0560560R2250986	2.4	0.09
0870870C1058028	15	0.14
0920920R1278937	7	0.11
2332330R1265724	50	0.15
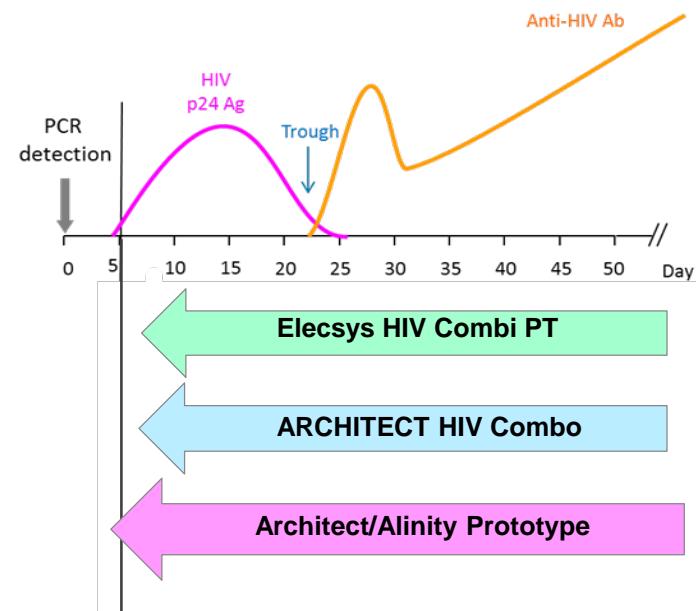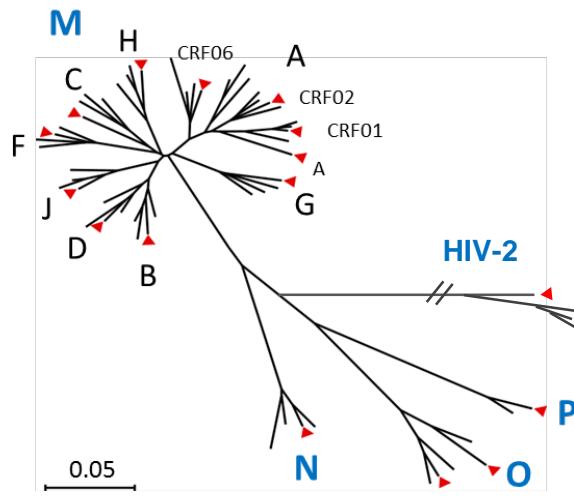
- Broad HIV genotype detection
- Reduced seroconversion window period
- Minimized heterophilic Ab interference

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