2022 Advancing HIV, STI and Viral Hepatitis Testing Conference

Multisite Evaluation of an HIV-1 panel on the Alinity m HIV-1 assay and its relevance to critical clinical decision points

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Disclosure: WC is an employee of Abbott Molecular Diagnostics

Background

- **Alinity m HIV-1 Viral Load (VL) Assay**
  - RT-PCR
  - VL monitoring
- **Alinity m System**
  - Random access
  - Continuous access
    - ✓ Shared reagents across assays
    - ✓ Assay-specific amplification reagents/Kits
- **Real-World**
  - No peer group data for performance comparison
  - Analyzed performance across multiple sites/instruments
  - Understand greatest contributors to variability and impact at critical decision points

ALINITY M

HIV-1 Intended Use

The Alinity m HIV-1 assay is an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay for the quantification of Human Immunodeficiency Virus type 1 (HIV-1) RNA on the automated Alinity m System in human plasma from HIV-1 infected individuals. The Alinity m HIV-1 assay is intended for use in the clinical management of HIV-1 infected individuals in conjunction with clinical presentation and other laboratory markers.

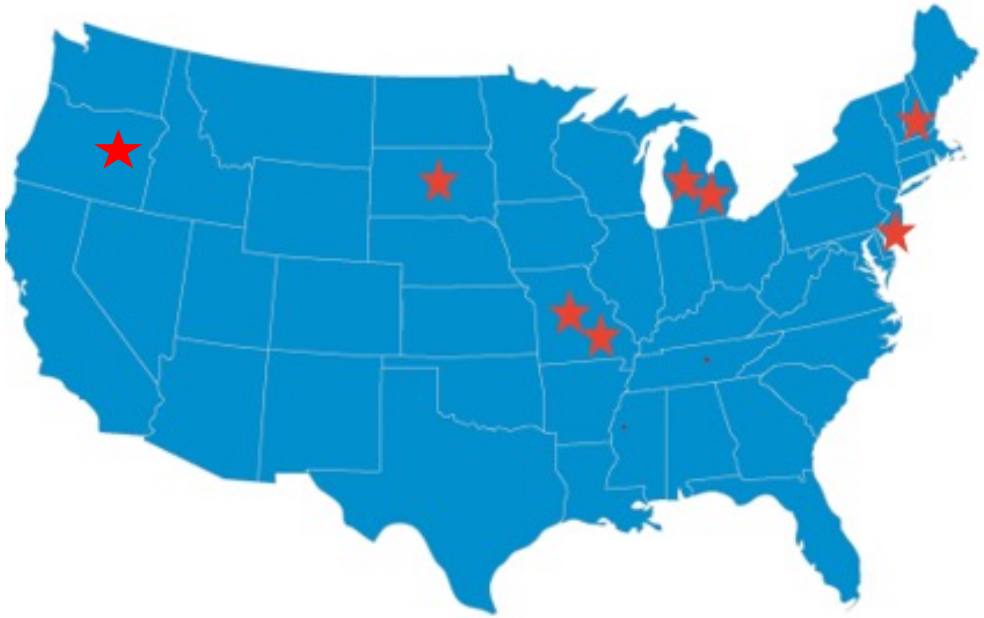
The Alinity m HIV-1 assay may be used to monitor disease prognosis by measuring the baseline plasma HIV-1 RNA level and to assess response to antiretroviral treatment by measuring changes in plasma HIV-1 RNA levels. The results from the Alinity m HIV-1 assay must be interpreted within the context of all relevant clinical and laboratory findings.

This assay is not intended for use in screening blood, blood products, tissue or organ donors for HIV. The assay is not intended as an aid in diagnosis or to confirm HIV-1 infection.

Methods/Study Design

Testing

- 8 sites/9 Alinity m instruments
- HIV – VL Reference Panel (Exact Diagnostics)
- Concentrations 3.0, 2.30, 1.70, and 1.30 Log cp/mL
- Genotypes: Non subtype B, Subtype AG, Subtype B
- 3 reps x 3 days, 2 operators
- 6 months
- All sites same lot reference panel
- N= 317-380



Assay Evaluation

- Mean observed concentrations
- Precision overall and across multiple components of variance
- Sigma/Process capability (Tolerance =+/- 0.5 log cp)
- Impact if any at critical clinical decision points

Methods/Study Design, cont.

Panel concentrations and relevance to clinical guidelines' definitions of viral failure

1,000 (3.0 log) cp/mL	WHO, 2 consecutive VL measurements in 6 mos. NIH/ACTG persistent VL range of 200-1,000 cp/mL – resistance?
200 (2.3 log) cp/mL	NIH < 200 cp/mL Acceptable viral suppression
50 (1.7 log) cp/mL	Optimal viral suppression
20 (1.3 log) cp/mL*	Optimal viral suppression Alinity m HIV-1 claimed LoD*

Results – Precision Analysis

Operational Variance

Genotype	N	Mean Concentration (Log Copies/mL)	Within-Day Component SD	Within-Day Component % CV	Between-Day Component SD	Between-Day Component % CV	Between-Instrument Component SD	Between-Instrument Component % CV	Total[a] SD	Total[a] % CV
Non subtype B	127	3.07	0.0622	2.03	0.0431	1.40	0.0366	1.19	0.0841	2.74
	127	2.29	0.1092	4.77	0.0505	2.21	0.0506	2.21	0.1306	5.71
	125	1.62	0.1642	10.14	0.0393	2.43	0.0473	2.92	0.1753	10.83
	108	1.38	0.1780	12.91	0.0557	4.04	0.0672	4.87	0.1983	14.38
Subtype A-G	126	2.97	0.0943	3.18	0.0515	1.73	0.0525	1.77	0.1196	4.03
	127	2.24	0.1229	5.48	0.0666	2.97	0.0244	1.09	0.1419	6.32
	122	1.59	0.2355	14.77	0.0391	2.45	0.0783	4.91	0.2512	15.76
	97	1.34	0.1979	14.77	0.0000	0.00	0.0819	6.11	0.2142	15.99
Subtype B	127	2.99	0.0638	2.13	0.0393	1.32	0.0234	0.78	0.0785	2.63
	127	2.19	0.1055	4.81	0.0444	2.03	0.0303	1.38	0.1183	5.40
	127	1.72	0.1873	10.92	0.0000	0.00	0.0453	2.64	0.1927	11.23
	112	1.32	0.2023	15.32	0.0000	0.00	0.1277	9.67	0.2392	18.11

[a] Total includes Within-Day, Between-Day and Between-Instrument Components.

Reagent/ Lot Variance

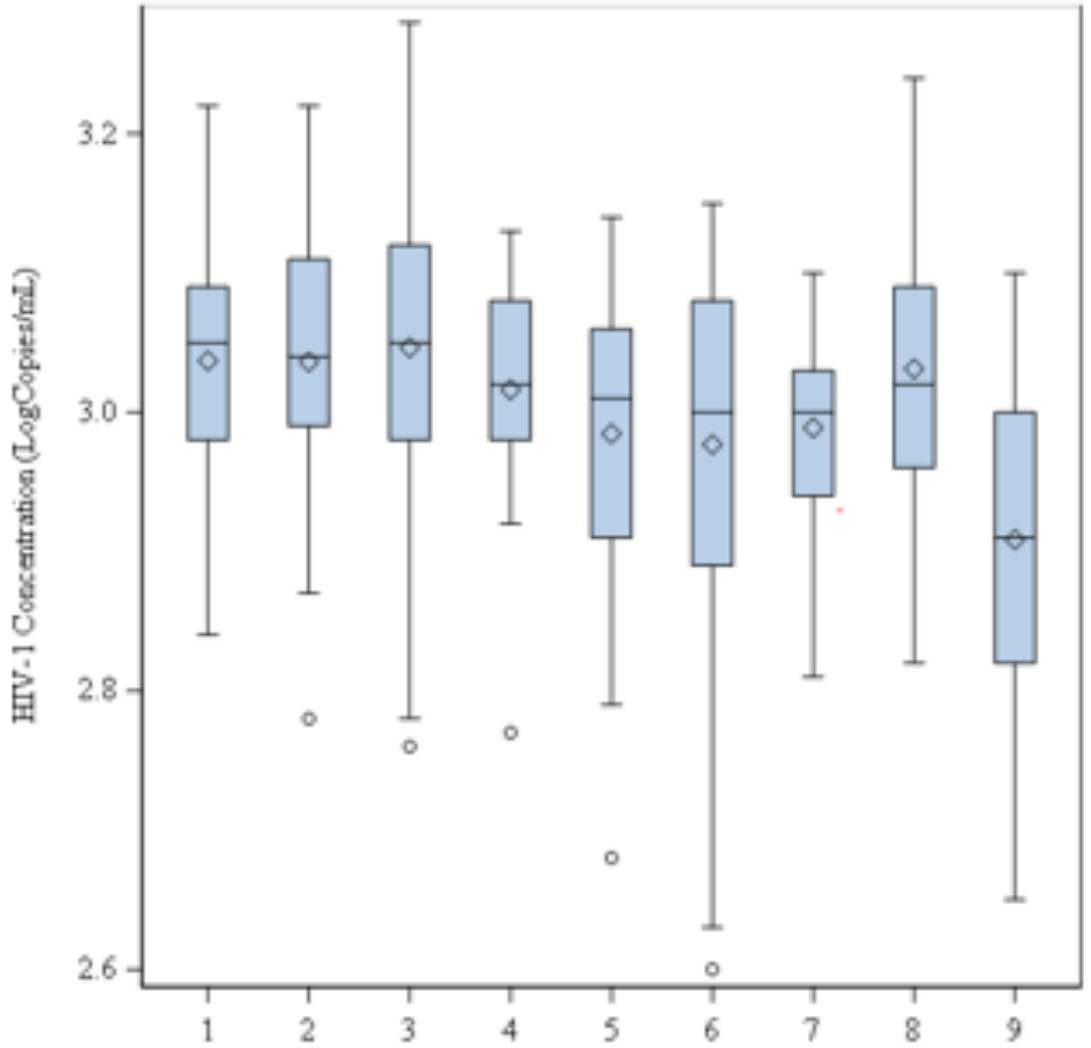
Genotype	N	Mean Concentration (Log Copies/mL)	Within-Lot Component SD	Within-Lot Component % CV	Between-Lot Component SD	Between-Lot Component % CV	Total[a] SD	Total[a] % CV
Non subtype B	127	3.07	0.0709	2.31	0.0535	1.74	0.0888	2.89
	127	2.29	0.1227	5.36	0.0504	2.20	0.1326	5.80
	125	1.62	0.1691	10.44	0.0538	3.32	0.1774	10.96
	108	1.38	0.1981	14.36	0.0000	0.00	0.1981	14.36
Subtype A-G	126	2.97	0.1137	3.83	0.0390	1.31	0.1202	4.05
	127	2.24	0.1354	6.03	0.0496	2.21	0.1442	6.43
	122	1.59	0.2390	14.99	0.0903	5.66	0.2555	16.02
	97	1.34	0.1959	14.63	0.0229	1.71	0.1973	14.73
Subtype B	127	2.99	0.0762	2.55	0.0193	0.65	0.0786	2.63
	127	2.19	0.1122	5.12	0.0443	2.02	0.1206	5.51
	127	1.72	0.1864	10.87	0.0348	2.03	0.1896	11.06
	112	1.32	0.2218	16.79	0.0000	0.00	0.2218	16.79

[a] Total includes Within-Lot and Between-Lot Components.

- Overall operational: mean CV%= 9.43, within-day mean CV% =8.44
- Overall reagent/lot: mean CV%=9.27, within- lot mean CV%= 8.94

Results – Precision Analysis: HIV-1 by Instrument

3.01 Log cp/mL
USL=3.51 log cp/mL
LSL= 2.51 cp/mL
N=380



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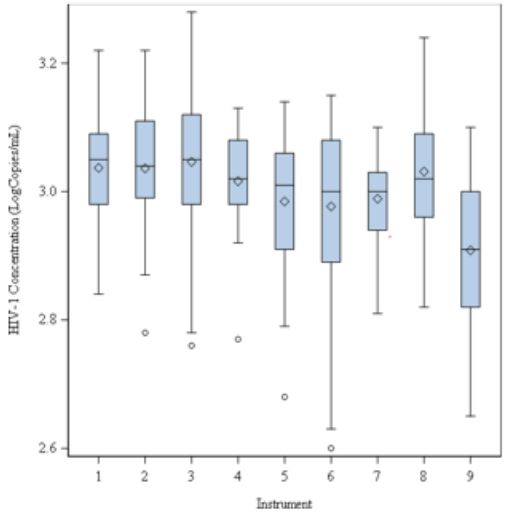
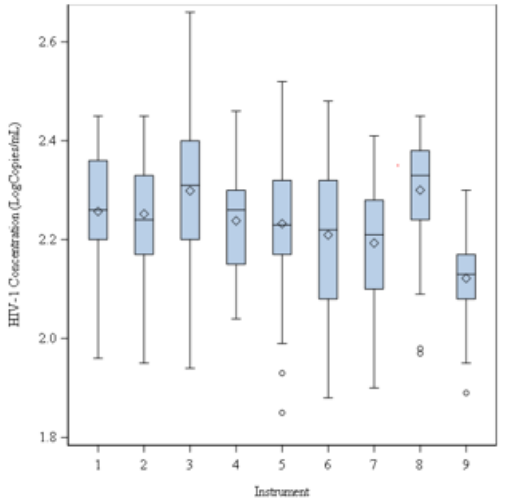
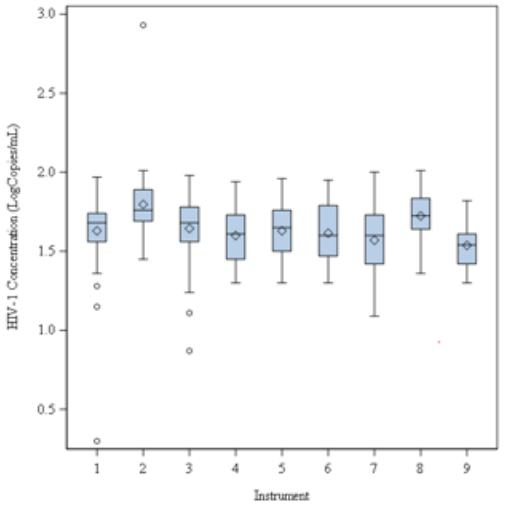
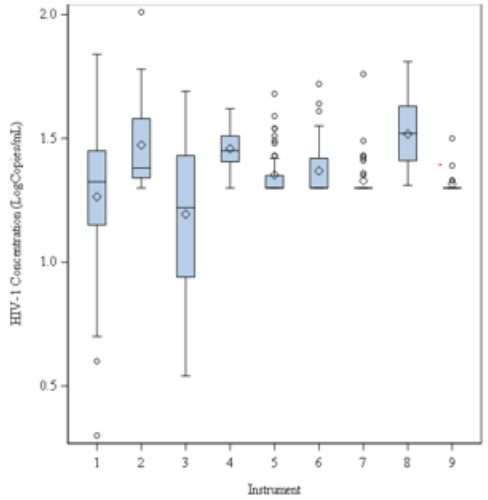




2.24 Log cp/mL
USL= 2.74 cp/mL
LSL=1.74 cp/mL
N=381

1.64 Log cp/mL
USL=2.14 log cp/mL
LSL=1.14 log cp/mL
N=374





1.35 Log cp/mL
USL=1.85 log cp/mL
LSL= 0.85 log cp/mL
N= 317

Results – Process Capability Index (CpK)

C_{pk}	Process Yield
0.5	86.8%
0.8	98.4
1.0	99.7%
1.2	99.97%
1.33	99.99%

What is it?

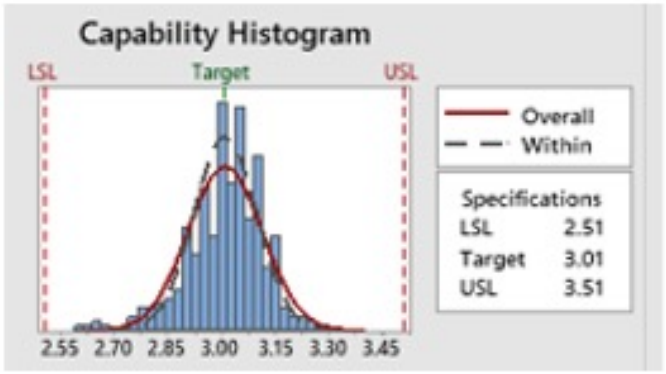
- Measures ability of a process to produce output within a customers' tolerance range Uses specification limits and parts variation (sigma)
- Estimates how close one is to a given target and how consistent around average performance
- Best-case scenario for existing process
- Estimate future performance – assuming it's consistent.

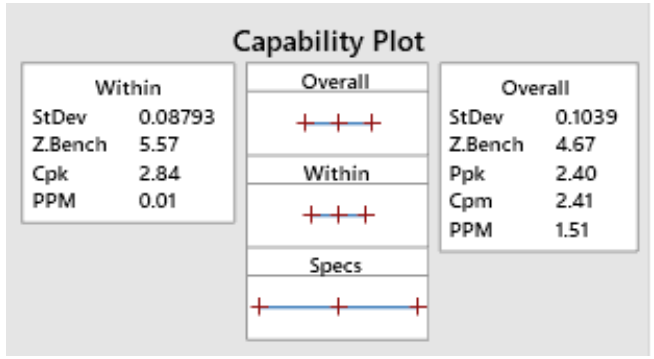
Cpk = of >1.33 indicates that the process is capable and meets specification limits. Any value less than this may mean variation is too wide compared to the specification or the process average is away from the target.

Source: https://www.whatissixsigma.net/process-capability-index-cpk/

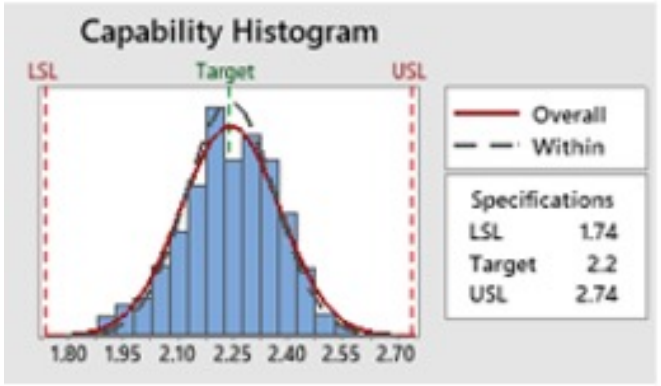
Results – Process Capability Index (CpK)

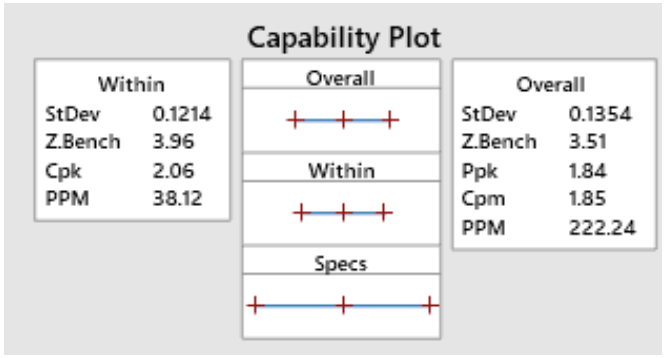
TEa = +/-0.5 log cp/mL





1,000 (3.01 log) cp/mL
Cpk= 2.84

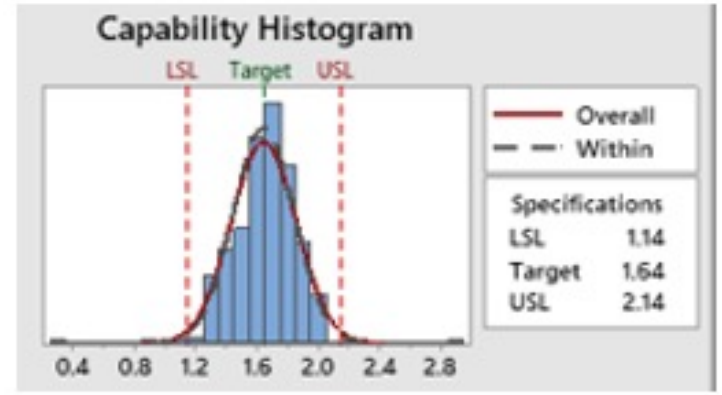




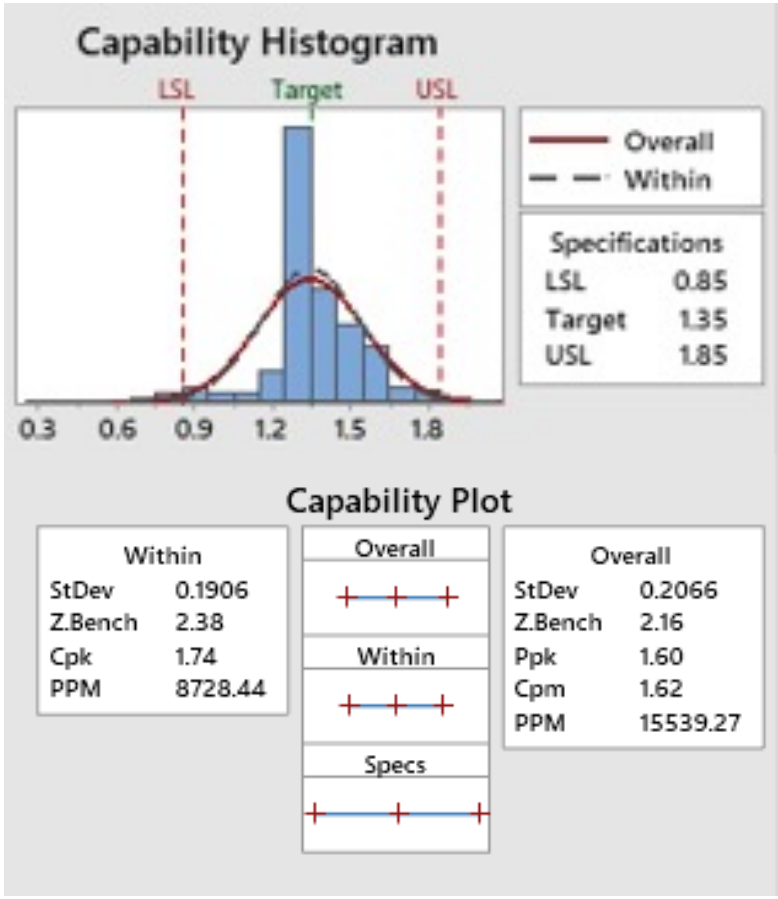
200 (1.74 log) cp/mL
Cpk= 2.06

The actual process spread is represented by 4 sigma

Results – Process Capability Index (CpK)



50 (1.64 log) cp/mL
CpK = 1.67



20 (1.35 log) cp/mL*
Cpk = 1.74

The actual process spread is represented by 3 sigma

Conclusions

- Alinity m HIV-1 is a continuous-access RT assay for viral load monitoring
- We evaluated assay precision across multiple components of variance – including between “peer group”
- Good analytical performance at relevant concentration targets based on clinical performance – what does this mean in terms of claim performance and real-world
- Greatest source of variability was “within-lot”
- Analyzed process capability (Cpk) of the Alinity m HIV assay at clinically relevant concentrations. Cpk indices were ≥ 1.33 at 4-sigma level at 1,000 and 200 cp/mL concentrations and at 3-sigma at “undetectable” concentrations 50 and 20 cp/mL
- Overall, performance of the Alinity m HIV-1 viral load assay demonstrated good analytical performance and ability to meet customer performance goals at clinically relevant VL concentrations

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