510(k) Summary

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1.0 510(k) Summary

This 510(k) summary of safety and effectiveness information is being submitted in accordance with the requirement of 21 CFR Section 807.92(c).

1.1 Submitter

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1.2 Device Information

Trade Name	Regulation Name	Product Code	Regulation No.	Class
Alinity m HIV-1	Human Immunodeficiency virus (HIV) viral load monitoring test	QUM	21 CFR 866.3958	II
	Human immunodeficiency virus (HIV) nucleic acid (NAT) diagnostic and/or supplemental test	QST	21 CFR 866.3957	II

1.3 Predicate Device

Device Name	Predicate Device	PMA	Approved
Alinity m HIV-1	Alinity m HIV-1	BP200455	7/2/2020

1.4 Device Description

Alinity m HIV-1 is an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay for the quantitation of HIV-1 RNA.

This device is similar to the predicate device originally approved (PMA BP200455) with the exception that the subject device may use a new DNA Polymerase as an alternative to original DNA Polymerase and a new Reverse Transcriptase as an alternative to original Reverse Transcriptase in the reagent formulation of the assay. These formulation differences do not introduce any changes to sample processing, assay procedure, or data reduction.

The steps of the Alinity m HIV-1 consist of sample preparation, RT-PCR assembly, amplification/detection, and result calculation and reporting. All steps of the Alinity m HIV-1 procedure are executed automatically by the Alinity m System. Manual dilutions may be performed for low-volume specimens to meet the minimum volume requirement and for high-titer specimens above the upper limit of quantitation (ULoQ). The Alinity m System is designed to be a random-access analyzer that can perform the Alinity m HIV-1 assay in parallel with other Alinity m assays on the same instrument.

Alinity m HIV-1 requires three separate assay specific kits as follows:

- **Alinity m HIV-1 AMP Kit (List No. 08N45-095)**, consisting of two types of multi-well assay trays. The amplification trays (AMP Trays) contain lyophilized, unit-dose RT-PCR amplification/detection reagents and lyophilized, unit-dose IC in separate wells, and the activation trays (ACT Trays) contain liquid activation reagent. The intended storage condition for the Alinity m HIV-1 AMP Kit is 2°C to 8°C.

- **Alinity m HIV-1 CTRL Kit (List No. 08N45-085)**, consisting of negative controls, low positive controls, and high positive controls, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m HIV-1 CTRL Kit is –25°C to –15°C.
- **Alinity m HIV-1 CAL Kit (List No. 08N45-075)**, consisting of two calibrator levels, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m HIV-1 CAL Kit is –25°C to –15°C.

HIV-1 RNA from human plasma or serum is extracted using the Alinity m Sample Prep Kit 2, Alinity m Lysis Solution, and Alinity m Diluent Solution. The Alinity m System employs magnetic microparticle technology to facilitate nucleic acid capture, wash, and elution. The resulting purified RNA is then combined with liquid unit-dose Alinity m HIV-1 activation reagent and lyophilized unit-dose Alinity m HIV-1 amplification/detection reagents and transferred into a reaction vessel. Alinity m Vapor Barrier Solution is then added to the reaction vessel which is then transferred to an amplification/detection unit for reverse transcription, PCR amplification, and real-time fluorescence detection of HIV-1.

At the beginning of the Alinity m HIV-1 sample preparation process, a lyophilized unit-dose IC on the AMP Tray is rehydrated by the Alinity m System and delivered into each sample preparation reaction. The IC is then processed through the entire sample preparation and RT-PCR procedure along with the specimens, calibrators and controls to demonstrate proper sample processing and validity.

The Alinity m HIV-1 amplification/detection reagents consist of enzymes, primers, probes and activation reagents that enable reverse transcription, polymerization, and detection. The Alinity m HIV-1 amplification/detection reagent also contains Uracil-DNA Glycosylase (UDG) as a contamination control for amplicons containing uracil, which may be present in molecular laboratories.

An HIV-1 calibration curve is required for determination of HIV-1 RNA concentration in plasma specimens and for HIV-1 RNA detection in serum specimens. Two levels of calibrators are processed through sample preparation and RT-PCR to generate the

calibration curve. The concentration of HIV-1 RNA in controls and concentration/ detection of HIV-1 RNA in specimen is then determined from the stored calibration curve.

Assay controls are tested at or above an established minimum frequency to help ensure that instrument and reagent performance remains satisfactory. During each control event, a negative control, a low-positive control, and a high-positive control are processed through sample preparation and RT-PCR procedures that are identical to those used for specimens. Plasma specimens may be tested for viral load determination and for supplemental confirmatory evaluation. Serum specimens may only be tested for supplemental confirmatory evaluation.

The Alinity m HIV-1 assay also utilizes the following:

Alinity m HIV-1 Application Specification File, (List No. 08N45-03C)

Alinity m System and System Software (List No. 08N53)

Alinity m Sample Prep Kit 2 (List No. 09N12-001)

Alinity m Specimen Dilution Kit I (List No. 09N50-001)

Alinity m System Solutions, (List No. 09N20):

- Alinity m Lysis Solution (List No. 09N20-001)
- Alinity m Diluent Solution (List No. 09N20-003)
- Alinity m Vapor Barrier Solution, (List No. 09N20-004)

Alinity m Tubes and Caps (List No. 09N49):

- Alinity m LRV Tube (List No. 09N49-001)
- Alinity m Transport Tubes Pierceable Capped (List No. 09N49-010)
- Alinity m Transport Tube (List No. 09N49-011)
- Alinity m Pierceable Cap (List No. 09N49-012)
- Alinity m Aliquot Tube (List No. 09N49-013)

1.5 Intended Use

The Alinity m HIV-1 assay is an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay for the detection and quantification of Human Immunodeficiency Virus type 1 (HIV-1) RNA on the automated Alinity m System for confirmation of HIV-1 infection or for monitoring 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 is intended for use to monitor disease prognosis by measuring baseline plasma HIV-1 RNA level and to assess response to antiretroviral treatment by measuring changes in plasma HIV-1 RNA levels. Performance for quantitative monitoring is not established with serum specimens.

The Alinity m HIV-1 assay is also intended for use as a supplemental test to confirm HIV-1 infection in individuals who have reactive results with HIV immunoassays. Performance for supplemental use is established with both plasma and serum specimens.

The results from the Alinity m HIV-1 assay must be interpreted within the context of all relevant clinical and laboratory findings.

This device is not intended for use as a first line diagnostic test or for screening donors of blood, blood products, or human cells or tissues, or cellular and tissue-based products (HCT/Ps).

1.6 Similarities and Differences to Predicate Device

The Alinity m HIV-1 assay has the same intended use as the predicate device, the current on-market Alinity m HIV-1 assay (PMA BP200455), which is a legally marketed Nucleic Acid-Based Human Immunodeficiency Virus Ribonucleic Acid Test. The subject device and predicate device differ only in the DNA polymerase and Reverse Transcriptase enzymes that may be used in manufacture of the assay.

These devices are similar in that they are designed to prepare nucleic acids for amplification, amplify specific HIV-1 RNA sequences, detect the amplified products, and report quantitative results.

The primary similarities and differences between the Alinity m HIV-1 assay and the predicate device are shown in **Table 1** and **Table 2**.

Table 1. Similarities Between Alinity m HIV-1 and Predicate Device

Description	Subject Device	Predicate Device
	Alinity m HIV-1	**Alinity m HIV-1 (BP200455)**
Intended Use	Same	The Alinity m HIV-1 assay is an in vitro reverse transcription-polymerase chain reaction (RT-PCR) assay for the detection and quantification of Human Immunodeficiency Virus type 1 (HIV-1) RNA on the automated Alinity m System for confirmation of HIV-1 infection or for monitoring 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 is intended for use to monitor disease prognosis by measuring baseline plasma HIV-1 RNA level and to assess response to antiretroviral treatment by measuring changes in plasma HIV-1 RNA levels. Performance for quantitative monitoring is not established with serum specimens. The Alinity m HIV-1 assay is also intended for use as a supplemental test to confirm HIV-1 infection in individuals who have reactive results with HIV immunoassays. Performance for supplemental use is established with both plasma and serum specimens. The results from the Alinity m HIV-1 assay must be interpreted within the context of all relevant clinical and laboratory findings. This device is not intended for use as a first line diagnostic test or for screening donors of blood, blood products, or human cells or tissues, or cellular and tissue-based products (HCT/Ps).
Assay Type	Same	Quantitative
Assay Targets	Same	Highly conserved sequences within the Integrase (INT) region of the pol gene and the Long Terminal Repeat (LTR) region of the HIV-1 genome.
Specimen Types	Same	Plasma and Serum
Sample Preparation Procedure	Same	Automated liquid handling and robotic manipulation platform
Amplification Technology	Same	Real-time polymerase chain reaction
Assay Controls	Same	• Internal Control (IC) • Negative Control

Table 1. Similarities Between Alinity m HIV-1 and Predicate Device		
Description	**Subject Device**	**Predicate Device**
	Alinity m HIV-1	**Alinity m HIV-1 (BP200455)**
		• Positive Control • High Positive Control

Table 2. *Differences* Between Alinity m HIV-1 and Predicate Device		
Description	**Subject Device**	**Predicate Device**
	Alinity m HIV-1	**Alinity m HIV-1 (BP200455)**
Enzymes	Original DNA Polymerase *or alternative DNA Polymerase* is the enzyme used for DNA amplification.	Original DNA Polymerase is the enzyme used for DNA amplification.
	Original Reverse Transcriptase *or alternative Reverse Transcriptase* is the enzyme used to convert target RNA into complementary DNA.	Original Reverse Transcriptase is the enzyme used to convert target RNA into complementary DNA.

1.7 Performance Data

The following performance data were provided in support of safety, effectiveness, and substantial equivalence determination of the device.

1.7.1 Specific Performance Characteristics

The subject device is similar to the predicate device originally approved (BP200455) with the exception that the subject device may use a new DNA Polymerase and a new Reverse Transcriptase as an alternative to original DNA Polymerase and original Reverse Transcriptase in the reagent formulation of the assay. Apart from the DNA polymerase and Reverse Transcriptase enzymes used, the reagent formulation, including all oligonucleotide primers and probes (components and concentrations) is identical between the subject device and predicate device. There are no differences in the intended use, end-user workflow, instrument workflow, assay software, reagent manufacturing, or final product release specifications.

Additional analytical performance studies listed in **Table 3** were conducted to confirm the ability of the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase

and Reverse Transcriptase (subject device) to meet the performance claims established in the corresponding studies submitted in BP200455 for the Alinity m HIV-1 assay formulated with original DNA Polymerase and Reverse Transcriptase (predicate device).

Table 3. Additional Supporting Studies (Alternate Enzymes Formulation)	
Study Description/Performance Characteristic	**510(k) Summary Section**
Limit of Detection – Plasma	**1.7.1.1**
Limit of Detection – Serum	**1.7.1.2**
Linear Range	**1.7.1.3**
Precision	**1.7.1.4**
Lower Limit of Quantitation	**1.7.1.5**
Specificity	**1.7.1.6**
Potential Cross-Reactants	**1.7.1.7**
Potentially Interfering Endogenous Substances	**1.7.1.8**
Potentially Interfering Drugs	**1.7.1.9**

All other specific performance characteristics of the subject device are supported by the studies submitted in BP200455 (Refer to **Table 4)** and BP200455-S007 (Refer to **Table 5**).

Table 4. Supporting Studies Submitted in BP200455	
Study Description/Performance Characteristic	**Reference**
Metrological Traceability	Original submission
Limit of Detection Across Groups and Subtypes	Original submission
Linearity Across Groups and Subtypes	Original submission
Carryover	Original submission
Alinity m HIV-1 Testing Using Dilution Procedure	Original submission
Precision of Alinity m HIV-1 Using Dilution Procedures	Original submission

Table 5. Supporting Studies Submitted in BP200455-S007	
Study Description/Performance Characteristic	**Reference**
Limit of Detection Across Groups and Subtypes (Serum)	PMA Supplement
Serum Reproducibility	PMA Supplement
Performance with HIV-1 Negative Specimens	PMA Supplement
Seroconversion	PMA Supplement
Detection in Diluted Serum Specimens	PMA Supplement
AMP Tray Carryover	PMA Supplement

1.7.1.1 Limit of Detection - Plasma

A limit of detection (LoD) study was conducted previously to support the approval of BP200455. Please refer to the Summary of Safety and Effectiveness for BP200455.

An additional study was conducted to confirm the LoD claim of Alinity m HIV-1 (20 Copies/mL) in plasma for the alternate enzymes formulation of the assay.

The Limit of Detection (LoD) for HIV-1 in plasma was determined by testing two panels prepared by dilution of an HIV-1 WHO Standard (NIBSC code 10/152) viral intermediate stock in HIV-1 negative human plasma at a concentration of 20 Copies/mL. Testing was performed with (b) (4) lots of amplification reagents over the course of (b) (4) days.

The data from the study demonstrated that the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase had an overall detection rate of 97.9% in plasma at 20 Copies/mL. Refer to **Table 6**.

Table 6. HIV-1 Sensitivity Plasma Percent Detection Rates

Panel	Target Concentration (Copies/mL)	AMP Kit Lot	Total No. of Replicates	No. of Replicates Detected	Detection Rate (%)	95% Exact Confidence Interval (%)
1[a]	20	All Combined	214	211	98.6	(96.0, 99.7)

[a] Panel 1 represents combined panels 1AP, 1BP and HIVLODP.

1.7.1.2 Limit of Detection – Serum

A limit of detection (LoD) study was conducted previously to support the approval of BP200455. Please refer to the Summary of Safety and Effectiveness for BP200455.

An additional study was conducted to confirm the LoD claim of Alinity m HIV-1 (20 Copies/mL) in serum for the alternate enzymes formulation of the assay.

The Limit of Detection (LoD) for HIV-1 in plasma was determined by testing two panels prepared by dilution of an HIV-1 WHO Standard (NIBSC code 10/152) viral intermediate stock in HIV-1 negative human plasma at a concentration of 20 Copies/mL. Testing was performed with (b) (4) lots of amplification reagents over the course of (b) (4) days.

The data from the study demonstrated that the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase had an overall detection rate of 97.9% in serum at 20 Copies/mL. Refer to **Table 7**.

Table 7. HIV-1 Sensitivity Serum Percent Detection Rates

Panel	Target Concentration (Copies/mL)	AMP Kit Lot	Total No. of Replicates	No. of Replicates Detected	Detection Rate (%)	95% Exact Confidence Interval (%)
1[a]	20	All Combined	216	212	98.1	(95.3, 99.5)

[a] Panel 1 represents combined panels 1AS, 1BS and HIVLODS.

1.7.1.3 Linear Range

A linearity study was conducted previously to support the approval of BP200455. Please refer to the Summary of Safety and Effectiveness for BP200455.

An additional study was conducted to confirm that the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase was linear across the intended dynamic range (20 Copies/mL to 10,000,000 Copies/mL)

Linearity was evaluated by testing (b) (4) panel members (prepared with an HIV-1 viral stock representing Group M, subtype B, diluted in HIV-1 negative human plasma) that spanned the intended quantitation range of the assay (20 Copies/mL to 10,000,000 Copies/mL), including a panel member below the expected Lower Limit of Quantification (LLoQ) at 15 Copies/mL and a panel member exceeding the expected Upper Limit of Quantification (ULoQ) at 20,000,000 Copies/mL. Refer to **Table 8**.

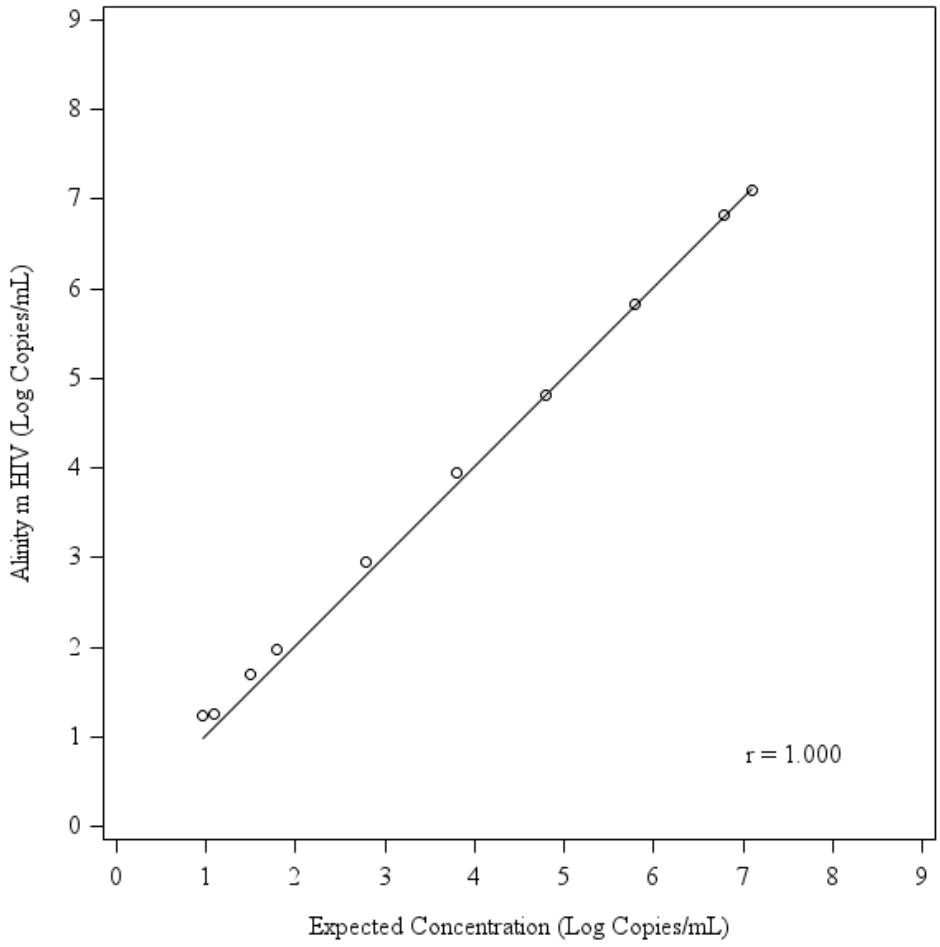
Table 8. Panel Members for Linearity

Panel Member	Panel Member Targeted HIV-1 Concentration (Copies/mL)	Panel Member Targeted HIV-1 Concentration (Log Copies/mL)	Minimum Total No. of Replicates
01	20,000,000	7.30	24
02	10,000,000	7.00	24
03	1,000,000	6.00	24
04	100,000	5.00	24
05	10,000	4.00	24
06	1,000	3.00	24
07	100	2.00	24
08	50	1.70	24
09	20	1.30	24
10	15	1.18	24

[a] The assay's claimed ULoQ is 10,000,000 Copies/mL per package insert.
[b] The assay's claimed LLoQ for plasma is 20 Copies/mL per package insert

The data from the study demonstrated that the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase was linear across the quantitation range from 15 Copies/mL to 20,000,000 Copies/mL. Representative results for Alinity m HIV-1 linearity performance are shown in **Figure 1**.

Figure 1. Alinity m HIV-1 (Alternate Enzyme Formulation) Linearity Weighted Least Squares Regression Plot



The data in the image is described in the text.

1.7.1.4 Precision

A precision study was conducted previously to support the approval of BP200455. Please refer to the Summary of Safety and Effectiveness for BP200455.

An additional study (as follows) was conducted to confirm the precision claim of Alinity m HIV-1 for the alternative DNA Polymerase and Reverse Transcriptase formulation of the assay:

- Within-laboratory standard deviation (SD) of ≤ 0.25 Log Copies/mL for samples between 200 Copies/mL to 10,000,000 Copies/mL (2.30 Log Copies/mL to 7.00 Log Copies/mL) HIV-1 RNA

  Within-laboratory SD of ≤ 0.46 Log Copies/mL for samples with target concentrations ≤ 3x LLoQ (60 Copies/mL or 1.78 Log Copies/mL) HIV-1 RNA

Precision was evaluated by testing 8 panel members with HIV-1 concentrations ranging from 20 Copies/mL to 15,000,000 Copies/mL (1.30 Log Copies/mL to 7.18 Log Copies/mL). Panel members were prepared by diluting cultured virus stock (Group M, subtype B) into in HIV-1 negative human plasma.

One lot of Alinity m HIV-1 amplification reagents manufactured with the alternative DNA Polymerase and Reverse Transcriptase was run on one Alinity m System. (b) (4) replicates of each panel member were run twice each day for (b) (4) days with a minimum separation of (b) (4) hours between successive runs of a panel member.

The overall precision analysis summary for the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase is presented in **Table 9**.

The results demonstrated that the Alinity m HIV-1 assay has a within-laboratory SD of 0.25 Log Copies/mL or less for samples targeted between 200 Copies/mL to 10,000,000 Copies/mL (2.30 Log Copies/mL to 7.00 Log Copies/mL) HIV-1 RNA, and a within-laboratory SD of 0.46 Log Copies/mL or less for samples with target concentrations ≤ 3x LLoQ (60 Copies/mL or 1.78 Log Copies/mL) HIV-1 RNA.

Table 9. Precision Analysis

Panel	N	Mean Concentration (Log Copies/mL)	Within-Run Component SD	Within-Run Component %CV	Between-Run Component SD	Between-Run Component %CV	Between-Day Component SD	Between-Day Component %CV	Within-Laboratory [a] SD	Within-Laboratory [a] %CV
01	115	1.24	0.26	21.0	0.00	0.0	0.00	0.0	0.26	21.0
02	120	1.58	0.19	12.1	0.00	0.0	0.03	1.9	0.19	12.3
03	120	2.28	0.09	4.0	0.00	0.0	0.02	1.0	0.09	4.2
04	119	3.01	0.06	1.9	0.00	0.0	0.01	0.4	0.06	2.0
05	120	4.02	0.05	1.2	0.02	0.4	0.00	0.0	0.05	1.3
06	119	4.95	0.03	0.6	0.00	0.1	0.01	0.2	0.03	0.6
07	119	5.99	0.02	0.4	0.02	0.3	0.00	0.0	0.03	0.5
08	119	7.07	0.07	0.9	0.00	0.0	0.00	0.0	0.07	0.9

[a] Within-Laboratory includes Within-Run, Between-Run, and Between-Day Components.

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1.7.1.5 Lower Limit of Quantitation (LLoQ)

A lower limit of quantitation (LLoQ) study was conducted previously to support the approval of BP200455. Please refer to the Summary of Safety and Effectiveness for BP200455.

An additional study was conducted to confirm the LLoQ claim of Alinity m HIV-1 (20 Copies/mL) for the alternative DNA Polymerase and Reverse Transcriptase formulation of the assay.

a) From the results of the Alinity m HIV-1 Sensitivity- Limit of Detection Plasma (**Section 1.7.1.1**) and Serum (**Section 1.7.1.2**) verification studies, the lowest HIV-1 target concentration level verified resulting in an HIV-1 detection rate of 95.0% or greater was confirmed.

b) From the results of the Alinity m HIV-1 Linearity study (**Section 1.7.1.3**), the HIV-1 target concentration corresponding to the lowest panel member of linear range, as determined in the analysis, was identified.

c) From the results of the Alinity m HIV-1 Precision study (**Section 1.7.1.4**), the HIV-1 lowest target concentration that meets the product requirement for Precision was identified. Note: all higher panels must also meet the product requirement for Within-Laboratory Precision.

The LLoQ was defined as highest HIV-1 concentration determined in steps (a) through (c) above.

Panel members were dilutions of an HIV-1 World Health Organization (WHO) Standard (NIBSC code 10/152) prepared in HIV-1 negative human plasma.

The results of the calculations are shown in **Table 10** and **Table 11**.

The results of these analyses support a claimed LLoQ of 20 Copies/mL.

Table 10. Alinity m HIV-1 Lower Limit of Quantitation Analysis Results

Study	Panel	N[a]	Target Concentration (Log Copies/mL)
Sensitivity (Plasma)	1	140	20[b]
Sensitivity (Serum)	1	141	20[b]
Linearity	10	24	15[c]
Precision	01	115	20[d]

[a] N represents the valid detected replicates for each respective study.

[b] The HIV-1 Sensitivity target concentration that resulted in a detection rate of 95.0% or greater is 20 Copies/mL.

[c] The HIV-1 Linearity target concentration corresponding to the lowest panel member tested that falls within the linear range is 15 Copies/mL.

[d] The HIV-1 Precision lowest target concentration that meets the product requirement is 20 Copies/mL.

Table 11. Alinity m HIV-1 Lower Limit of Quantitation Overall Summary

Linearity	Sensitivity (Plasma)	Sensitivity (Serum)	Precision	LLoQ	Acceptance Criteria
15	20	20	20	20	Met

1.7.1.6 Specificity

The specificity of the Alinity m HIV-1 assay was determined by testing negative specimens, demonstrated to be HIV-1 negative using an HIV-1 Ag/Ab test and the on-market Alinity m HIV-1 assay.

All specimens included in the analysis were identified as “HIV-1 RNA Not Detected” by the Alinity m HIV-1 assay, resulting in 99.6% (764/767) specificity (95% CI 98.9% to 99.9%) for all results (400 plasma and 367 serum). The data demonstrates that the Alinity m HIV-1 assay has specificity of 99.6% (**Table 12**).

Table 12. Alinity m HIV-1 Percent Specificity and Two-Sided 95% Exact Confidence Interval

N Tested	N True Negatives	N False Positives	Diagnostic Specificity (%)	95% Confidence Interval (%)
767	764	3	99.6	(98.9,99.8)

1.7.1.7 Potential Cross-Reactants

The analytical specificity of Alinity m HIV-1 was evaluated with a panel of microorganisms (**Table 13**) in HIV-1 negative plasma, positive plasma containing 60 Copies/mL HIV-1 RNA and positive plasma containing 200 Copies/mL HIV-1 RNA. No cross-reactivity or interference in the performance of Alinity m HIV-1 was observed in the presence of the tested microorganisms.

Table 13. Potential Cross-Reactants

Potential Cross Reactant
Adenovirus type 5
BK human polyomavirus
Cytomegalovirus
Dengue virus type 1
Epstein-Barr virus
Hepatitis A virus
Hepatitis B virus
Hepatitis C virus
Herpes simplex virus 1
Herpes simplex virus 2
Human herpesvirus 6B
Human herpesvirus 8
Human Immunodeficiency virus 2
Human papilloma virus 16
Human papilloma virus 18
Human T lymphotropic virus type 2
Human T lymphotropic virus type 1
Influenza A
Vaccinia virus
Varicella-zoster virus
Chlamydia trachomatis
Mycobacterium gordonae
Mycobacterium smegmatis
Neisseria gonorrhoeae
Propionibacterium acnes
Staphylococcus aureus
Staphylococcus epidermidis
Candida albicans
Dengue virus type 2
Dengue virus type 3
Dengue virus type 4
GB Virus C / Hepatitis G Virus

1.7.1.8 Potentially Interfering Endogenous Substances

The effects of endogenous substances were evaluated. Potential interference on Alinity m HIV-1 performance was assessed by testing HIV-1 negative samples, HIV-1 positive samples containing 60 Copies/mL HIV-1 RNA, and HIV-1 positive samples containing 200 Copies/mL HIV-1 RNA. No interference was observed in the presence of albumin (60 g/L), hemoglobin (2 g/L), triglycerides (37 mM), conjugated bilirubin (342 µM), unconjugated bilirubin (342 µM) or human genomic DNA (2 µg/mL) that were introduced in the sample.

1.7.1.9 Potentially Interfering Drugs

The effects of the presence of high levels of therapeutic drugs commonly prescribed for the treatment of HIV-1 and related diseases were evaluated. Potential interference on Alinity m HIV-1 performance was assessed by testing HIV-1 negative samples, HIV-1 positive samples containing 60 Copies/mL HIV-1 RNA, and HIV-1 positive samples containing 200 Copies/mL HIV-1 RNA. No interference was observed in the presence of drug compounds tested in pools at a concentration of 3 times the reported Cmax or higher.

Table 14. Potentially Interfering Drugs Tested.

Drug Pool	Drug Compound
1	Abacavir sulfate, Acyclovir, Adefovir, Amitriptyline, Amlodipine, Aspirin, Atazanavir, Atenolol, Atorvastatin, Azithromycin, Celecoxib, Cidofovir, Clarithromycin, Clopidogrel
2	Didanosine, Efavirenz, Entecavir, Fluconazole, Fluoxetine, Ibuprofen, Indinavir, Kaletra (Lopinavir and Ritonavir), Lamivudine, Levofloxacin, Maraviroc, Nelfinavir, Nevirapine, Paroxetine
3	Prednisone, Raltegravir, Ribavirin, Rifamate (Rifampin and Isoniazid), Saquinavir, Sertraline, Stavudine, Stribild (Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir), Bactrim (Sulfamethoxazole and Trimethoprim)
4	Darunavir, Ethambutol, Etravirine, Flucytosine, Fluticasone propionate, Furosemide, Hydrochlorothiazide, Levothyroxine, Rifabutin, Rilpivirine, Salmeterol xinafoate, Simeprevir, Sofosbuvir, Telaprevir, Tenofovir alafenamide, Trazodone, Warfarin, Zalcitabine
5	Fosamprenavir, Keflex (Cephalexin), Metformin, Naproxen, Pyrazinamide
6	Tipranavir
7	Ceftriaxone, Ciprofloxacin, Foscarnet, Lisinopril, Peginterferon alfa-2a, Enfuvirtide, Imipramine

8	Cyclosporine, Telbivudine, Valacyclovir, Valganciclovir, Zidovudine, Amphotericin B, Ganciclovir
9	Acetaminophen, Hydrocodone
10	Biotin

1.7.2 Clinical Performance Characteristics

1.7.2.1 Clinical Reproducibility

A reproducibility study was conducted previously to support the approval of BP200455. Please refer to the Summary of Safety and Effectiveness for BP200455.

An additional study was conducted to evaluate the reproducibility of the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase.

Reproducibility performance of Alinity m HIV-1 was evaluated by testing a 10-member reproducibility panel, which included 10 positive panel members. Panel members were prepared using HIV-1 virus diluted in negative human plasma and spanned the linear range of Alinity m HIV-1 assay.

Testing utilized two unique lot combinations that consisted of two lots of Alinity m HIV-1 AMP Kit and one lot each of Alinity m HIV-1 CAL Kit, Alinity m HIV-1 CTRL Kit, and Alinity m Sample Prep Kit 2. Testing was performed at three clinical sites on five non-consecutive days with (b) (4) per day. (b) (4) replicates of each panel member were tested on each of five days to ensure a minimum of five valid replicates for analysis.

The reproducibility results are summarized in **Table 15**.

Table 15. Alinity m HIV-1 (Alternate Enzyme Formulation) Overall Variance Component Analysis (Log Copies/mL)

Panel	N[a]	Mean Concentration (Log Copies/mL)	Within-Run/Day Component SD	Within-Run/Day Component %CV	Between-Run/Day Component SD	Between-Run/Day Component %CV	Within Laboratory[b] SD	Within Laboratory[b] %CV	Between-Lot Component SD	Between-Lot Component %CV	Between-Site / Instrument Component SD	Between-Site / Instrument Component %CV	Total[c] (Overall) SD	Total[c] (Overall) %CV
1	179	7.74	0.05	0.6	0.03	0.3	0.05	0.7	0.04	0.5	0.07	0.9	0.10	1.3
2	179	6.82	0.06	0.8	0.01	0.1	0.06	0.9	0.03	0.4	0.07	1.1	0.10	1.4
3	177	6.00	0.04	0.6	0.01	0.1	0.04	0.6	0.03	0.5	0.04	0.7	0.06	1.1
4	175	5.40	0.04	0.7	0.01	0.2	0.04	0.7	0.03	0.6	0.02	0.4	0.06	1.0
5	179	4.45	0.05	1.1	0.00	0.0	0.05	1.1	0.04	1.0	0.00	0.0	0.07	1.5
6	178	3.85	0.05	1.2	0.01	0.4	0.05	1.3	0.04	1.1	0.00	0.0	0.06	1.7
7	179	3.14	0.06	1.8	0.01	0.2	0.06	1.8	0.05	1.5	0.03	0.9	0.08	2.5
8	179	2.41	0.09	3.8	0.00	0.1	0.09	3.8	0.06	2.6	0.03	1.3	0.12	4.8
9	179	1.88	0.16	8.3	0.00	0.0	0.16	8.3	0.04	2.3	0.06	3.1	0.17	9.2
10	177	1.44	0.25	17.5	0.00	0.0	0.25	17.5	0.12	8.5	0.00	0.0	0.28	19.4

[a] Number of valid replicates with detectable viral load

[b] Within-Laboratory includes Within-Run/Day and Between-Run/Day Components.

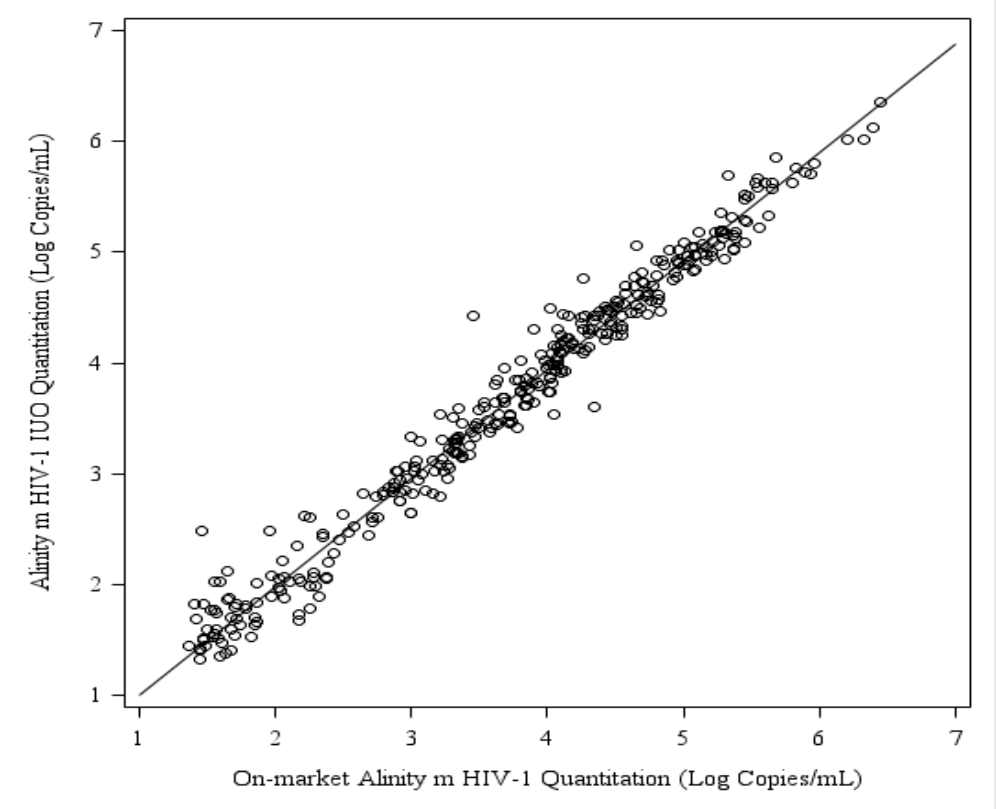
[b] Total (Overall) includes Within-Run/Day, Between-Run/Day, Between-Lot, and Between-Site/Instrument Variance Components.

1.7.2.2 Viral Load Quantitation

A method comparison study was conducted with the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase to demonstrate equivalence to the FDA-approved (on-market) Alinity m HIV-1 assay formulated with original DNA Polymerase and Reverse Transcriptase (BP200455).

Regression and bias analysis included a total of 355 samples with results that were within the common quantitation range of both the Alinity m HIV-1 assay with alternate enzymes formulation (subject device) and the comparator assay (on-market Alinity m HIV-1). **Figure 2** shows the results of the Deming regression analysis with a slope of 0.98, an intercept of 0.02 Log Copies/mL, and a correlation coefficient of 0.987. The mean paired difference (bias) between subject device and the comparator (subject device minus comparator) was -0.05 Log Copies/mL with a 95% Confidence Interval of (-0.07, -0.03).

Figure 2. Deming Regression Analysis



The data in the image is described in the text.

1.7.2.3 HIV-1 Clinical Sensitivity

The performance of Alinity m HIV-1 formulated with the alternative DNA Polymerase and Reverse Transcriptase was compared to that of an FDA-approved HIV-1 RNA assay. The specimens were from subjects known to be HIV-1 positive. Samples were repeat reactive in an FDA-approved Ab/Ag assay and had viral loads of ≥100 Copies/mL as determined by an FDA approved comparator assay.

A total of 451 retrospectively collected specimens were included in the analysis. The overall HIV-1 sensitivity of Alinity m HIV-1 was 100.0% (451/451, 95% CI: 99.2% to 100.0%). The HIV-1 sensitivity of Alinity m HIV-1 for serum specimens was 100.0% (227/227, 95% CI: 98.4% to 100.0%). The HIV-1 sensitivity of Alinity m HIV-1 for plasma specimen was 100.0% (224/224, 95% CI: 98.4% to 100.0%). Refer to Table 16.

Table 16: Sensitivity of Plasma and Serum Specimens

Specimen Type	N	Alinity m HIV-1 RNA Detected	Alinity m HIV-1 RNA Not Detected	Sensitivity	95% Exact CI
All	451	451	0	100.0% (451/451)	(99.2%, 100.0%)
Serum	227	227	0	100.0% (227/227)	(98.4%, 100.0%)
Plasma	224	224	0	100.0% (224/224)	(98.4%, 100.0%)

1.7.2.4 Agreement between Alinity m HIV-1 Assay and FDA Approved HIV-1 Nucleic Acid Test (NAT) Comparator Assay for Repeat Reactive Confirmed Negative (RRCN) and Repeat Reactive Confirmed Indeterminate (RRCI) (Combined EDTA Plasma and Serum)

Performance in repeatedly-reactive/confirmed negative and repeatedly-reactive/confirmed indeterminate was evaluated with the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase.

The samples were repeatedly reactive with an initial serological diagnostic test; subsequent confirmation testing produced negative or indeterminate results with an FDA approved serological HIV differentiation assay. These specimen types are referred to as repeatedly reactive confirmed negative (RRCN) and repeatedly reactive confirmed indeterminate (RRCI). Of 71 (16 plasma and 55 serum) valid serological discordant samples evaluated, 53 samples were reported as RRCN and 18 samples reported as RRCI. The PPA and NPA for the Alinity m HIV-1 assay were calculated relative to a NAT comparator result. Refer to Table 17.

Table 17: Agreement between Alinity m HIV-1 Assay and FDA Approved HIV-1 Assay for RRCN and RRCI Specimens

Specimen Type	HIV Differentiation Assay	Sample Matrix	N	Comparator + and Alinity m +	Comparator + and Alinity m -	Comparator - and Alinity m -	Comparator - and Alinity m +	PPA (%) Estimate (95% CI)	PPA (%) n/N	NPA (%) Estimate (95% CI)	NPA (%) n/N
All	Negative and Indeterminate	Serum and EDTA Plasma	71	17	2	51	1	89.5 (66.9, 98.7)	17/19	98.1 (89.7, 100.0)	51/52
RRCN	Negative	Serum	43	7	1	34	1	87.5 (47.3, 99.7)	7/8	97.1 (85.1, 99.9)	34/35
	Negative	EDTA Plasma	10	1	0	9	0	100.0 (2.5, 100.0)	1/1	100.0 (66.4, 100.0)	9/9
RRCI	Indeterminate	Serum	12	8	0	4	0	100.0 (63.1, 100.0)	8/8	100.0 (39.8, 100.0)	4/4
	Indeterminate	EDTA Plasma	6	1	1	4	0	50.0 (1.3, 98.7)	1/2	100.0 (39.8, 100.0)	4/4

1.8 Conclusions Drawn from the Studies

The additional analytical and clinical study results demonstrate that the Alinity m HIV-1 assay formulated with the alternative DNA Polymerase and Reverse Transcriptase is as safe, as effective, and performs as well as the predicate device.