July 28, 2025

Abbott Molecular Inc.
Jennifer Peterson
Associate Director Regulatory Affairs
1300 E Touhy Ave
Des Plaines, Illinois 60018

Re: K243489
Trade/Device Name: Alinity m EBV
Regulation Number: 21 CFR 866.3183
Regulation Name: Quantitative Viral Nucleic Acid Test For Transplant Patient Management
Regulatory Class: Class II
Product Code: QLX
Dated: November 8, 2024
Received: November 12, 2024

Dear Jennifer Peterson:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-

assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Uwe Scherf -S

Uwe Scherf, M.Sc., Ph.D.
Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K243489

Device Name
Alinity m EBV

Indications for Use *(Describe)*
Alinity m EBV is an in vitro polymerase chain reaction (PCR) assay for the quantitation of Epstein-Barr Virus (EBV) DNA in human EDTA plasma on the automated Alinity m System.
Alinity m EBV is intended for use as an aid in the management of EBV in transplant patients. In patients undergoing monitoring of EBV, serial DNA measurements can be used to indicate the need for potential treatment changes and to assess viral response to treatment.
The results from Alinity m EBV must be interpreted within the context of all relevant clinical and laboratory findings.
Alinity m EBV is not cleared for use as a screening test for donors of blood, blood products, or human cells, tissues, and cellular and tissue-based products (HCT/Ps) for EBV.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

Table of Contents

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

Applicant Name and Address: Abbott Molecular Inc.
1300 E. Touhy Avenue
Des Plaines, IL 60018

Contact Person: John Bates
Director Regulatory Affairs
Abbott Molecular, Inc.
1300 E. Touhy Avenue
Des Plaines, IL 60018
Phone: 224-361-7007
Fax: 224-361-7269

Date Prepared: October 15, 2024

1.2 Device Information

Trade Name	Regulation Name	Product Code	Regulation No.	Class
Alinity m EBV	Quantitative viral nucleic acid test for transplant patient management	QLX	21 CFR 866.3183	II

1.3 Predicate Device

Device Name	Predicate Device	510(k)	Cleared
Alinity m EBV	Alinity m EBV	K212778	07/15/2022

1.4 Device Description

Alinity m EBV is an in vitro polymerase chain reaction (PCR) assay for the quantitation of EBV DNA in human plasma.

This device is similar to the predicate device originally cleared (K212778) with the exception that the subject device may use MomentaTaq DNA Polymerase as an

alternative to KAPA2G DNA Polymerase in the reagent formulation of the assay. This formulation difference does not introduce any changes to sample processing, assay procedure, or data reduction.

Additional studies were initiated to support the formulation of the assay with MomentaTaq DNA Polymerase. Supplemental data from these studies were used with data previously obtained from the analytical and clinical testing studies submitted in K212778.

The steps of the Alinity m EBV consist of sample preparation, real-time PCR assembly, amplification/detection, result calculation, and reporting. All stages of the Alinity m EBV procedure are executed automatically by the Alinity m System. No intermediate processing or transfer steps are performed by the user. The Alinity m System is designed to be a random-access analyzer that can perform the Alinity m EBV assay in parallel with other Alinity m assays on the same instrument.

Alinity m EBV requires three separate assay specific kits as follows:

- **Alinity m EBV AMP Kit (List No. 09N43-095)**, consisting of 2 types of multi-well assay trays. The amplification trays (AMP TRAY 1) contain lyophilized, unit-dose PCR amplification/detection reagents and lyophilized, unit-dose IC in separate wells, and the activation trays (ACT TRAY 2) contain liquid unit-dose activation reagent. The intended storage condition for the Alinity m EBV AMP Kit is 2°C to 8°C.
- **Alinity m EBV CTRL Kit (List No. 09N43-085)**, 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 EBV CTRL Kit is –25°C to –15°C.
- **Alinity m EBV CAL Kit (List No. 09N43-075)**, consisting of 2 calibrator levels, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m EBV CAL Kit is –25°C to –15°C.

EBV DNA from human plasma is extracted automatically on-board in the Alinity m System 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 nucleic acids are then combined with liquid unit-dose Alinity m EBV activation reagent and lyophilized unit-dose Alinity m EBV 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 PCR amplification, and real-time fluorescence detection of EBV targets.

At the beginning of the Alinity m EBV 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 real-time PCR procedure along with the specimens, calibrators, and controls to demonstrate proper sample processing and validity.

The Alinity m EBV amplification/detection reagents consist of enzymes, primers, probes, and activation reagents that enable polymerization and detection.

An EBV calibration curve is required for determination of EBV DNA concentration. Two levels of calibrators are processed through sample preparation and PCR to generate the calibration curve. The concentration of EBV DNA in specimens and controls is then calculated 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 PCR procedures that are identical to those used for specimens.

The Alinity m EBV assay also utilizes the following:

- Alinity m EBV Application Specification File, (List No. 09N43-05B)
- Alinity m System and System Software (List No. 08N53-002)
- 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

Alinity m EBV is an in vitro polymerase chain reaction (PCR) assay for the quantitation of Epstein-Barr Virus (EBV) DNA in human EDTA plasma on the automated Alinity m System.

Alinity m EBV is intended for use as an aid in the management of EBV in transplant patients. In patients undergoing monitoring of EBV, serial DNA measurements can be used to indicate the need for potential treatment changes and to assess viral response to treatment.

The results from Alinity m EBV must be interpreted within the context of all relevant clinical and laboratory findings. Alinity m EBV is not intended to be used as a screening test for donors of blood, blood products, or human cells, tissues, and cellular and tissue-based products (HCT/Ps) for EBV.

1.6 Similarities and Differences to Predicate Device

The primary functional components of the Alinity m EBV assay are substantially equivalent to the current on-market Alinity m EBV assay (K212778), which is a legally marketed nucleic acid amplification test (NAAT) for the quantitative detection of EBV DNA.

The Alinity m EBV assay has the same intended use as the predicate device. The subject device and predicate device differ only in the DNA polymerase that may be used in manufacture of the assay (MomentaTaq vs. KAPA2G); this formulation difference does not raise new types of safety or effectiveness questions.

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

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

Table 1. Similarities Between Alinity m EBV and Predicate Device

Description	Subject Device	Predicate Device
	Alinity m EBV	**Alinity m EBV (K212778)**
Intended Use	Same	Alinity m EBV is an in vitro polymerase chain reaction (PCR) assay for the quantitation of Epstein-Barr Virus (EBV) DNA in human EDTA plasma on the automated Alinity m System. Alinity m EBV is intended for use as an aid in the management of EBV in transplant patients. In patients undergoing monitoring of EBV, serial DNA measurements can be used to indicate the need for potential treatment changes and to assess viral response to treatment. The results from Alinity m EBV must be interpreted within the context of all relevant clinical and laboratory findings. Alinity m EBV is not intended to be used as a screening test for donors of blood, blood products, or human cells, tissues, and cellular and tissue-based products (HCT/Ps) for EBV.
Assay Type	Same	Quantitative
Assay Targets	Same	2 highly conserved regions of the EBV genome (gp350 and EBNA1)
Specimen Types	Same	EDTA Plasma
Sample Preparation Procedure	Same	Automated liquid handling and robotic manipulation platform
Amplification Technology	Same	Real-time polymerase chain reaction
Assay Controls	Same	• Negative Control • Low Positive Control • High Positive Control • Internal Control (IC)

Table 2. *Differences* Between Alinity m EBV and Predicate Device

Feature	Current Application	Predicate Device
	Alinity m EBV	**Alinity m EBV (K212778)**
Amplification Enzymes	KAPA2G HotStart DNA Polymerase *or MomentaTaq HotStart DNA Polymerase* is the enzyme used for DNA amplification.	KAPA2G HotStart DNA Polymerase is the enzyme used for DNA amplification.

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 cleared (K212778) with the exception that the subject device may use MomentaTaq DNA Polymerase as an alternative to KAPA2G DNA Polymerase in the reagent formulation of the assay. Apart from the DNA polymerase enzyme 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 EBV assay formulated with MomentaTaq DNA Polymerase (subject device) to meet the performance claims established in the corresponding studies submitted in K212778 for the Alinity m assay formulated with KAPA2G DNA Polymerase (predicate device).

Table 3. Additional Supporting Studies (MomentaTaq formulation)

Study Description / Performance Characteristic	**510(k) Summary Section**
Limit of Detection	**1.7.1.1**
Linear Range	**1.7.1.2**
Precision	**1.7.1.3**
Lower Limit of Quantitation	**1.7.1.4**

All other specific performance characteristics of the subject device are supported by the studies submitted in K212778 (original submission and Amendments 1 and 2). Refer to **Table 4**.

Table 4. Supporting Studies Submitted in K212778

Study Description / Performance Characteristic	Reference
Traceability to the WHO Standard	Original submission
Limit of Detection for EBV Type 2	Original submission
Linearity for EBV Type 2	Amendment 2
Analytical Specificity – Potential Cross-Reactants	Original submission
Analytical Specificity – Potentially Interfering Substances	Original submission
Carryover	Amendment 1
Alinity m EBV Testing Using Dilution Procedure	Original submission
Precision of Alinity m EBV Using Dilution Procedure	Original submission
Confirmation of LLoQ Using Dilution Procedure	Original submission

1.7.1.1 Limit of Detection

A limit of detection (LoD) study was conducted previously to support the clearance of K212778. Please refer to the decision summary for K212778.

An additional study was conducted to confirm the LoD claim of Alinity m EBV (20 IU/mL) for the MomentaTaq formulation of the assay.

LoD for EBV type 1 was evaluated by testing dilutions of the 1st World Health Organization (WHO) International Standard for Epstein-Barr Virus for Nucleic Acid Amplification Techniques (NIBSC code 09/260) prepared in EBV negative human plasma. Testing for each EBV DNA concentration was performed with 3 lots of amplification reagents across multiple days. The data from the study demonstrated that the Alinity m EBV assay formulated with MomentaTaq DNA Polymerase had an overall detection rate of 97.2% at 20 IU/mL for all reagent lots combined with a 95% Confidence Interval of (93.0%, 98.9%). Refer to **Table 5**.

Table 5. Alinity m EBV (MomentaTaq formulation) Limit of Detection (LoD) Results

Panel	Target Concentration (IU/mL)	AMP Kit Reagent Lot	Total No. of Valid Replicates	No. of Replicates Detected	Detection Rate (%)	95% Score Confidence Interval (%)
1	15	1	48	45	93.8	(83.2, 97.9)
		2	48	46	95.8	(86.0, 98.8)
		3	47	45	95.7	(85.8, 98.8)
		All Combined	143	136	95.1	(90.2, 97.6)
2	20 [a]	1	47	47	100.0	(92.4, 100.0)
		2	48	46	95.8	(86.0, 98.8)
		3	47	45	95.7	(85.8, 98.8)
		All Combined	142	138	97.2	(93.0, 98.9)
3	50	1	48	48	100.0	(92.6, 100.0)
		2	48	48	100.0	(92.6, 100.0)
		3	47	47	100.0	(92.4, 100.0)
		All Combined	143	143	100.0	(97.4, 100.0)
4	100	1	48	48	100.0	(92.6, 100.0)
		2	47	47	100.0	(92.4, 100.0)
		3	47	47	100.0	(92.4, 100.0)
		All Combined	142	142	100.0	(97.4, 100.0)

[a] Alinity m EBV assay limit of detection (LoD) claim

1.7.1.2 Linear Range

A linearity study was conducted previously to support the clearance of K212778. Please refer to the decision summary for K212778.

An additional study was conducted to confirm that the Alinity m EBV assay formulated with MomentaTaq was linear across the claimed quantitation range (50 IU/mL [1.70 Log IU/mL] to 200,000,000 IU/mL [8.30 Log IU/mL]).

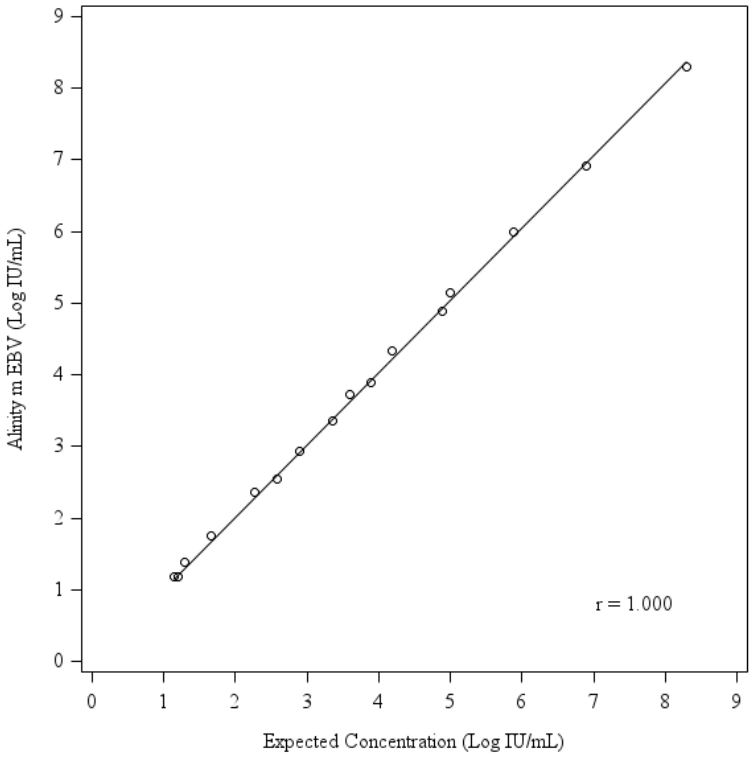
Linearity was evaluated by testing 16 panel members that spanned the intended quantitation range of the assay (50 IU/mL to 200,000,000 IU/mL), including a panel member below the expected Lower Limit of Quantification (LLoQ) at 15 IU/mL and a panel member exceeding the expected Upper Limit of Quantification (ULoQ) at 250,000,000 IU/mL. Panels prepared with different specimen types were designed to have at least a 2 Log IU/mL overlap with adjacent sample types. Refer to **Table 6**.

Table 6. Panel Members for Linearity

Panel Member	Targeted EBV Concentration		Source
	IU/mL	Log IU/mL	
01	250,000,000	8.40	Plasmid DNA
02	10,000,000	7.00	Plasmid DNA
03	1,000,000	6.00	Plasmid DNA
04	130,000	5.11	Plasmid DNA
05	100,000	5.00	Cultured virus
06	20,000	4.30	Plasmid DNA
07	10,000	4.00	Cultured virus
08	5,000	3.70	Plasmid DNA
09	2,500	3.40	Clinical specimen
10	1,000	3.00	Plasmid DNA
11	500	2.70	Cultured virus
12	200	2.30	Clinical specimen
13	50	1.70	Clinical specimen
14	25	1.40	Plasmid DNA
15	20	1.30	Cultured virus
16	15	1.18	Clinical specimen

The data from the study demonstrated that the Alinity m EBV assay formulated with MomentaTaq DNA Polymerase was linear across the quantitation range from 15 IU/mL to 250,000,000 IU/mL (1.18 Log IU/mL to 8.40 Log IU/mL). Representative results for Alinity m EBV linearity performance are shown in **Figure 1**.

Figure 1. Alinity m EBV (MomentaTaq formulation) Linearity



1.7.1.3 Precision

A precision study was conducted previously to support the clearance of K212778. Please refer to the decision summary for K212778.

An additional study was conducted to confirm the precision claim of Alinity m EBV (as follows) for the MomentaTaq formulation of the assay:

- Within-laboratory standard deviation (SD) of ≤ 0.25 Log IU/mL for plasma samples containing 500 IU/mL to 200,000,000 IU/mL (2.70 Log IU/mL to 8.30 Log IU/mL) EBV DNA
- Within-laboratory SD of ≤ 0.50 Log IU/mL for plasma samples containing 20 IU/mL to 500 IU/mL (1.30 Log IU/mL to 2.70 Log IU/mL) EBV DNA

Precision was evaluated by testing 8 panel members with EBV concentrations ranging from 20 IU/mL to 2×10^8 IU/mL (1.30 Log IU/mL to 8.30 Log IU/mL). Panel members were prepared by diluting EBV-positive clinical specimen, EBV cultured virus or synthetic DNA in human plasma. EBV synthetic DNA was only used for panel members with high target concentrations (> 6 Log IU/mL). The quantitation of the panel members was traceable to the 1st WHO International Standard for Epstein Barr virus (EBV) (NIBSC code 09/260).

Three lots of Alinity m EBV amplification reagents manufactured with MomentaTaq DNA Polymerase were run on 1 Alinity m System by 3 operators (each of the 3 operators used 1 lot of amplification reagents). Three replicates of each panel member were run twice each day for 15 days for each lot/operator combination with a minimum separation of 2 hours between successive runs of a panel member.

The overall precision analysis summary for the Alinity m EBV assay formulated with MomentaTaq DNA Polymerase is presented in **Table 7**.

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The results demonstrated that the Alinity m EBV assay has a within-laboratory SD of 0.25 Log IU/mL or less for EBV DNA panels targeted to 500 IU/mL to 200,000,000 IU/mL (2.70 Log IU/mL to 8.30 Log IU/mL) and a within-laboratory SD of 0.50 Log IU/mL or less for EBV DNA panels targeted to 20 IU/mL to < 500 IU/mL (1.30 Log IU/mL to < 2.70 Log IU/mL).

Table 7. Alinity m EBV (MomentaTaq formulation) Precision Analysis – All Reagent Lots

			Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory [a]		Between-Lot Component		Total [b]	
Panel	N	Mean Concentration (Log IU/mL)	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
01	270	1.35	0.24	18.0	0.11	8.2	0.00	0.0	0.27	19.8	0.00	0.0	0.27	19.8
02	270	1.69	0.19	11.1	0.00	0.0	0.06	3.3	0.20	11.6	0.00	0.0	0.20	11.6
03	270	2.78	0.08	2.9	0.00	0.0	0.02	0.7	0.08	3.0	0.00	0.0	0.08	3.0
04	270	3.99	0.07	1.6	0.02	0.4	0.00	0.0	0.07	1.7	0.00	0.0	0.07	1.7
05	270	5.07	0.05	1.0	0.03	0.6	0.01	0.2	0.06	1.2	0.01	0.1	0.06	1.2
06	270	6.10	0.05	0.9	0.03	0.5	0.00	0.0	0.06	1.0	0.01	0.1	0.06	1.0
07	270	7.03	0.06	0.9	0.02	0.3	0.01	0.1	0.07	1.0	0.01	0.1	0.07	1.0
08	270	8.39	0.17	2.0	0.08	1.0	0.00	0.0	0.19	2.3	0.00	0.0	0.19	2.3

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

The Total SD and Total %CV for each panel member in this study were compared with the Total SD and Total %CV from the original precision study submitted in K212778. Refer to **Table 8**.

Table 8. Equivalence Evaluation of Total SD and Total %CV (New [a] vs. Original [b])

	Mean Concentration		Total SD		Total %CV		Ratios and 95% CI		
Panel Member	**New (Log IU/mL)**	**Original (Log IU/mL)**	**New SD**	**Original SD**	**New % CV**	**Original % CV**	**SD**	**%CV**	**Clinically Acceptable? [e]**
01	1.35	1.43	0.27	0.26	19.8	18.4	1.02 (0.90, 1.17)	1.08 (0.95, 1.23)	Yes
02 [c]	1.69	2.2	0.20	0.2	11.6	8.9	1.00 (0.81, 1.23)	1.30 (1.06, 1.60)	Yes
03	2.78	2.77	0.08	0.13	3.0	4.9	0.62 (0.37, 1.03)	0.62 (0.37, 1.02)	Yes
04	3.99	4.06	0.07	0.08	1.7	1.9	0.87 (0.41, 1.82)	0.88 (0.42, 1.85)	Yes
05	5.07	5.05	0.06	0.07	1.2	1.4	0.81 (0.46, 1.42)	0.81 (0.46, 1.41)	Yes
06	6.10	6.09	0.06	0.07	1.0	1.1	0.90 (0.58, 1.39)	0.89 (0.58, 1.38)	Yes
07	7.03	7.05	0.07	0.06	1.0	0.8	1.23 (0.95, 1.58)	1.23 (0.95, 1.59)	Yes
08 [d]	8.39	8.22	0.19	0.08	2.3	0.9	2.48 (1.50, 4.10)	2.43 (1.47, 4.02)	Yes

[a] "New" Mean Concentration, Total SD, and Total %CV data for Alinity m EBV assay formulated with MomentaTaq DNA Polymerase

[b] "Original" Mean Concentration, Total SD, and Total %CV data for on-market Alinity m EBV assay formulated with KAPA2G DNA Polymerase (submitted in K212778)

[c] Panel 02 in the New precision study targeting 1.7 Log IU/mL is compared to panel 02 in the Original precision study targeting 2.0 Log IU/mL.

[d] Panel 08 in the New precision study targeting 8.3 Log IU/mL is compared to panel 09 in the Original precision study targeting 8.3 Log IU/mL.
NOTE: Panel 08 in the Original precision study targeting 8.0 Log IU/mL is not analyzed for comparison.

[e] Precision results were effectively equivalent if the 95% confidence interval for the ratio of SD or ratio of %CVs between the MomentaTaq DNA Polymerase ("New") and KAPA2G DNA Polymerase ("Original") contained 1.00 or the upper bound of the 95% confidence interval for the ratio of SD or ratio of %CV is < 1.00; these results were therefore "Clinically Acceptable."

1.7.1.4 Lower Limit of Quantitation (LLoQ)

A lower limit of quantitation (LLoQ) study was conducted previously to support the clearance of K212778. Please refer to the decision summary for K212778.

An additional study was conducted to confirm the LLoQ claim of Alinity m EBV (50 IU/mL) for the MomentaTaq formulation of the assay.

The LLoQ is defined as the lowest concentration at which EBV DNA is reliably quantitated within an acceptable total error. Total error was estimated for detected samples from the LoD study (**Section 1.7.1.1**) by 2 methods:

- Total Analytical Error (TAE) = |bias| + 2 × SD, and
- Total Error (TE) = SQRT(2) × 2 × SD

The results of the calculations are shown in **Table 9**.

Panel members were dilutions of the 1st WHO International Standard for Epstein-Barr Virus for Nucleic Acid Amplification Techniques (NIBSC code 09/260) prepared in EBV-negative plasma.

The results of these analyses support a claimed LLoQ of 50 IU/mL (1.70 Log IU/mL), with an acceptable level of accuracy and precision (ie, TAE and TE less than or equal to 1.00 Log IU/mL).

Table 9. Alinity m EBV (MomentaTaq formulation) TAE and TE

Target Concentration (Log IU/mL)	Mean Concentration (Log IU/mL)	Bias [a] (Log IU/mL)	SD (Log IU/mL)	TAE (Log IU/mL)	TE (Log IU/mL)
1.18	0.96	–0.22	0.32	0.86	0.91
1.30	1.07	–0.23	0.33	0.89	0.93
1.70	1.52	–0.18	0.20	0.59	0.57
2.00	1.86	–0.14	0.17	0.48	0.47

1.7.1 Clinical Performance Characteristics

1.7.1.1 Clinical Reproducibility

A reproducibility study was conducted previously to support the clearance of K212778. Please refer to the decision summary for K212778.

An additional study was conducted to evaluate the reproducibility of the Alinity m EBV assay formulated with MomentaTaq DNA Polymerase.

Reproducibility performance of Alinity m EBV was evaluated by testing a 9-member reproducibility panel, which included 8 positive panel members and 1 negative panel member. The positive panel members were prepared using EBV positive clinical specimen, cultured virus, or plasmid DNA diluted in human EDTA plasma. The concentration levels spanned the quantitation range of the assay.

One lot each of Alinity m EBV AMP Kit, Alinity m EBV CAL Kit, Alinity m EBV CTRL Kit, and Alinity m Sample Prep Kit 2 lots were used. Testing was performed at 3 clinical sites on 5 non-consecutive days with 2 runs per day. Four replicates of each panel member were tested on each of 5 days to ensure a minimum of 3 valid replicates for analysis.

The reproducibility results are summarized in **Table 10** (for the positive panel members) and in **Table 11** (for the negative panel member).

Table 10. Alinity m EBV (MomentaTaq formulation) Reproducibility for Positive Panel Members

		Mean Concentration	Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory [a]		Between-Site Component		Total [b]	
Panel	N	(Log IU/mL)	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
1	118	7.88	0.06	0.7	0.01	0.1	0.00	0.0	0.06	0.7	0.00	0.0	0.06	0.7
2	116	6.82	0.04	0.6	0.00	0.0	0.02	0.3	0.04	0.6	0.01	0.2	0.04	0.6
3	120	6.00	0.05	0.8	0.02	0.4	0.01	0.2	0.05	0.9	0.03	0.5	0.06	1.0
4	118	5.02	0.04	0.8	0.02	0.3	0.02	0.4	0.05	0.9	0.04	0.8	0.06	1.2
5	120	4.00	0.05	1.2	0.00	0.1	0.01	0.3	0.05	1.2	0.04	1.1	0.06	1.6
6	118	3.09	0.07	2.4	0.01	0.2	0.00	0.0	0.07	2.4	0.03	1.1	0.08	2.6
7	117	1.74	0.19	10.9	0.00	0.0	0.00	0.0	0.19	10.9	0.04	2.4	0.19	11.1
8	113	1.39	0.29	21.2	0.04	2.5	0.00	0.0	0.30	21.3	0.00	0.0	0.30	21.3

[a] Within-Laboratory includes Within-Run, Between-Run, and Between-Day Variance Components.
[b] Total (Overall) includes Within-Run, Between-Run, Between-Day, and Between-Site Variance Components.

Table 11. Alinity m EBV (MomentaTaq formulation) Reproducibility for Negative Panel Member

		N			Negative	
Panel	Site	Total	Positive	Negative	Agreement Rate	95% CI
9	All	119	1	118	99.2%	(95.4%, 99.9%)

The Total SD and Total %CV for each panel member in this study were compared with the Total SD and Total %CV from the original reproducibility study submitted in K212778. Refer to **Table 12**.

Table 12. Equivalence Evaluation of Total SD and Total %CV (New [a] vs. Original [b])

	Mean Concentration		Total SD		Total %CV		Ratios and 95% CI		
Panel	New (Log IU/mL)	Original (Log IU/mL)	New SD	Original SD	New %CV	Original %CV	SD	%CV	Clinically Acceptable? [c]
1	7.88	8.40	0.06	0.19	0.7	2.3	0.30 (0.07, 1.35)	0.32 (0.07, 1.44)	Yes
2	6.82	7.04	0.04	0.14	0.6	2.0	0.32 (0.07, 1.35)	0.33 (0.08, 1.39)	Yes
3	6.00	5.76	0.06	0.10	1.0	1.8	0.58 (0.21, 1.56)	0.55 (0.20, 1.49)	Yes
4	5.02	5.04	0.06	0.12	1.2	2.4	0.49 (0.19, 1.26)	0.49 (0.19, 1.26)	Yes
5	4.00	4.01	0.06	0.09	1.6	2.2	0.72 (0.36, 1.44)	0.73 (0.36, 1.45)	Yes
6	3.09	3.07	0.08	0.09	2.6	2.8	0.94 (0.64, 1.37)	0.93 (0.63, 1.36)	Yes
7	1.74	1.64	0.19	0.23	11.1	14.0	0.84 (0.56, 1.26)	0.80 (0.53, 1.20)	Yes
8	1.39	1.20	0.30	0.30	21.3	25.1	0.98 (0.80, 1.21)	0.85 (0.69, 1.04)	Yes

[a] "New" Mean Concentration, Total SD, and Total %CV data for Alinity m EBV assay formulated with MomentaTaq DNA Polymerase

[b] "Original" Mean Concentration, Total SD, and Total %CV data for on-market Alinity m EBV assay formulated with KAPA2G DNA Polymerase (submitted in K212778)

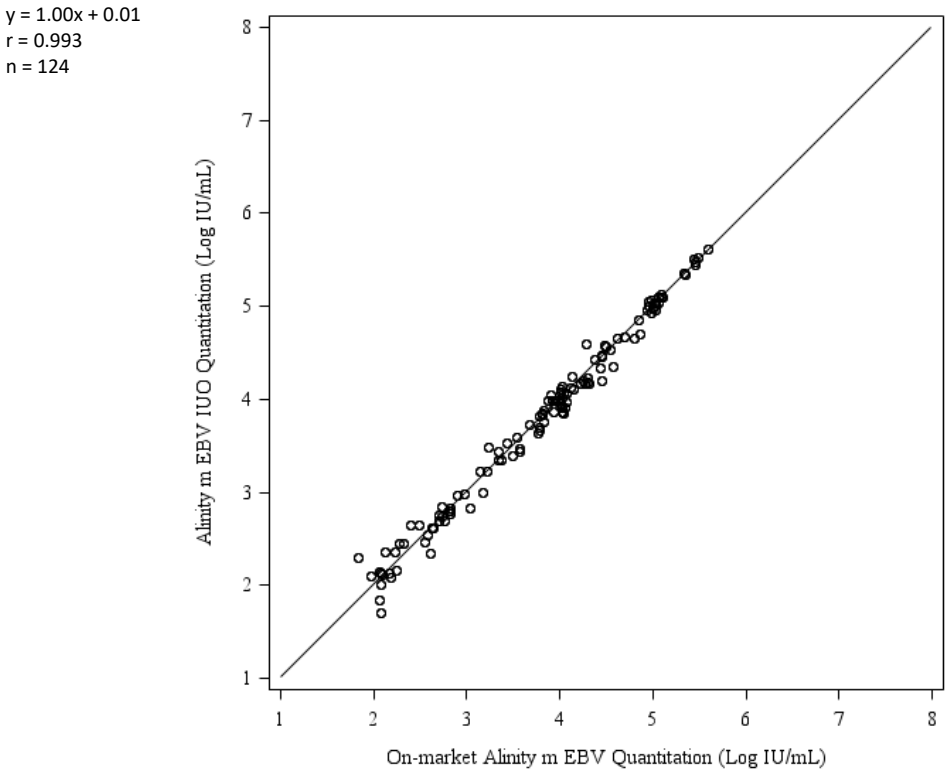
[c] Reproducibility results were effectively equivalent if the 95% confidence interval for the ratio of SD or ratio of %CVs between the MomentaTaq DNA Polymerase ("New") and KAPA2G DNA Polymerase ("Original") contained 1.00 or the ratio of SD or ratio of %CV is <1.00; these results were therefore considered "Clinically Acceptable."

1.7.1.2 Clinical Performance

A method comparison study was conducted with the Alinity m EBV assay formulated with MomentaTaq DNA Polymerase to demonstrate equivalence to the FDA-cleared (on-market) Alinity m EBV assay formulated with KAPA2G DNA Polymerase (K212778)

Regression and bias analysis included a total of 124 samples with results that were within the common quantitation range of both the Alinity m EBV assay formulated with MomentaTaq (Alinity m EBV IUO) and the comparator assay (on-market Alinity m EBV). **Figure 2** shows the results of the Deming regression analysis with a slope of 1.00, an intercept of 0.01, and a correlation coefficient of 0.993. The mean bias between Alinity m EBV IUO and the comparator (Alinity m EBV IUO minus comparator) was –0.01 Log IU/mL with a 95% Confidence Interval of (–0.03, –0.01).

Figure 2. Deming Regression Analysis



Systematic difference between Alinity m EBV assay formulated with MomentaTaq and the on-market Alinity m EBV assay (comparator) at 4 selected viral load levels is shown in **Table 13**.

Table 13. Systematic Difference at Selected Viral Load Levels

Target Viral Load Level (based on comparator) (Log IU/mL)	**Systematic Difference (Log IU/mL)**
1.70 (LLoQ)	0.02
3.00	0.01
4.00	0.01
5.00	0.00

1.8 Conclusions Drawn from the Studies

The additional analytical and clinical study results demonstrate that the Alinity m EBV assay formulated with MomentaTaq DNA Polymerase performs comparably to the FDA-cleared Alinity m EBV assay formulated with KAPA2G DNA Polymerase.

The results support a substantial equivalence decision for Alinity m EBV formulated with MomentaTaq DNA Polymerase.