July 15, 2022

Abbott Molecular, Inc.
Gina Sammarco
Senior Specialist Regulatory Affairs
1300 E. Touhy Ave
Des Plaines, Illinois 60018

Re: K212778
Trade/Device Name: Alinity m EBV AMP Kit (List No. 09N43-095), Alinity m EBV CTRL Kit (List No. 09N43-085), Alinity m EBV CAL Kit (List No. 09N43-075)
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: August 31, 2021
Received: September 1, 2021

Dear Gina Sammarco:

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 (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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 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 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 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,

Maria Garcia, Ph.D.
Assistant Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K212778

Device Name
Alinity m EBV (09N43)

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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Section 5: 510(k) Summary

Table of Contents

5.0 510(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).

5.1 Submitter

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

Contact Person: Gina Sammarco
Manager Regulatory Affairs
Abbott Molecular, Inc.
1300 E. Touhy Avenue
Des Plaines, IL 60018
Phone: 224-361-7627
Fax: 224-361-7646

Date Prepared: August 31, 2021

5.2 Device Information

Trade Name	Regulation Name	Product Code	Regulation Number	Class
Alinity m EBV	Quantitative viral nucleic acid test for transplant patient management	QLX	866.3183	II

Common Name: Nucleic acid test for quantitation of EBV DNA

5.3 Predicate Device

Device Name	Predicate Device	De Novo	Cleared
Alinity m EBV	cobas® EBV	DEN200015	July 30, 2020

5.4 Device Description

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

The steps of the Alinity m EBV assay 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 multi-well amplification trays (AMP Trays) containing lyophilized, unit-dose PCR amplification/detection reagents and multi-well activation trays (ACT Trays) containing liquid, unit-dose activation reagents ($MgCl_2$, TMAC, KCl, and ProClin). 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 a negative control, a low positive control, and a high positive control, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m EBV CTRL Kit is −15°C to −25°C.

- **Alinity m EBV CAL Kit (List No. 09N43-075)** consisting of two levels of calibrators (CAL A and CAL B), each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m EBV CAL Kit is −15°C to −25°C.

EBV DNA from specimens 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 the 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.

An EBV calibration curve is required for the quantitation of EBV targets. Two levels of calibrators are processed through sample preparation and real-time 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 remain satisfactory. During each control event, a negative control, a low-positive control, and a high-positive control are processed through sample preparation and real-time PCR procedures that are identical to those used for specimens.

At the beginning of the Alinity m EBV sample preparation process, a lyophilized unit -dose of Internal Control on the AMP Tray is rehydrated by the Alinity m System and delivered into each sample preparation reaction. The Internal Control 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 assay validity.

The Alinity m EBV amplification and detection reagents include primers and probes that amplify and detect dual targets in the EBV genome. Amplification and detection of the two EBV targets ensures sensitive detection of the viral genome even at low levels.

The Alinity m EBV assay also utilizes the following accessories:

- Alinity m EBV Application Specification File, List No. 09N43-05A
- 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 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
- 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

5.5 Intended Use

Alinity m EBV AMP Kit

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.

5.6 Similarities and Differences to Predicate Devices

The primary functional components of the Alinity m EBV assay are substantially equivalent to other legally marketed nucleic acid amplification tests (NAAT) intended for the quantitative detection of EBV DNA.

The Alinity m EBV assay has the same general intended use as the predicate device. Although there are some technological differences between the Alinity m EBV assay and the predicate device, these differences do 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 EBV assay and the predicate device are shown in **Table 1**.

Table 1. Similarities and *Differences* Between Alinity m EBV and Predicate Device		
Device & Predicate Device(s):		
	Alinity m EBV **K212778**	**cobas EBV test** **DEN200015**
General Device Characteristic Similarities		
Assay Type	Quantitative	Quantitative
Specimen Types	EDTA Plasma	EDTA Plasma
Sample Preparation Procedure	Automated liquid handling and robotic manipulation platform.	Automated liquid handling and robotic manipulation platform.
Amplification Technology	Real-time polymerase chain reaction (PCR)	PCR
Assay Controls	• Negative Control • Low Positive Control • High Positive Control • Internal Control	• Negative Control • Low Positive Control • High Positive Control • DNA Quantitation Standard (DNA-QS)
General Device Characteristic Differences		
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.	cobas EBV is an in vitro nucleic acid amplification test for the quantitation of Epstein-Barr virus (EBV) DNA in human EDTA plasma on the cobas 6800/8800 Systems.

	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.	cobas 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 response to treatment. The results from cobas EBV are intended to be read and analyzed by a qualified licensed healthcare professional in conjunction with clinical signs and symptoms and relevant laboratory findings. Negative test results do not preclude EBV infection or EBV disease. Test results must not be the sole basis for patient management decisions. cobas EBV is not intended for use as a screening test for donors of blood or blood products or human cells, tissues, and cellular and tissue-based products (HCT/Ps).
Assay Targets	2 highly conserved regions of the EBV genome	EBV EBNA-1 gene EBV *BMRF* gene

5.7 Performance Data

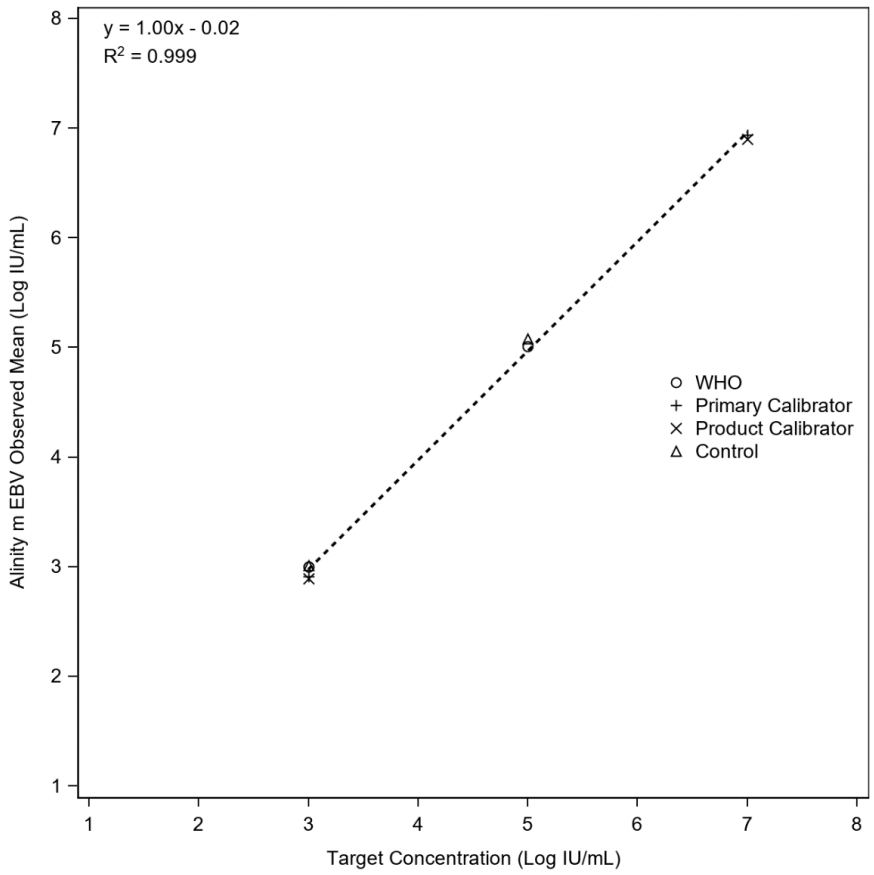
The following performance data were provided in support of the safety, effectiveness and substantial equivalence determination of the device.

5.7.1 Specific Performance Characteristics

5.7.1.1 Traceability to the WHO Standard

Primary calibrators and assay product calibrators with known concentrations were used throughout product development and product manufacturing to establish traceability to the 1st World Health Organization (WHO) International Standard for Epstein-Barr virus for Nucleic Acid Amplification Techniques (NIBSC code: 09/260). The concentrations tested for the WHO standard were 3.00 Log IU/mL and 5.00 Log IU/mL. The target concentrations tested for the primary calibrators were 3.00 Log IU/mL and 7.00 Log IU/mL. The Alinity m EBV product calibrators and controls were also tested along with the primary calibrators and the WHO standard. All of the tested material had observed EBV concentrations similar to the target concentrations, and were linear across the assay's quantitation range, as presented in **Figure 1**.

Figure 1. Traceability to the WHO Standard



5.7.1.2 Limit of Detection

The limit of detection (LoD) was determined for EBV type 1 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 4 lots of amplification reagents across multiple days. The results, representative of the analytical sensitivity performance of Alinity m EBV, are summarized in **Table 2** (Lot 1), **Table 3**, (Lot 2), **Table 4** (Lot 3), and **Table 5** (Lot 4) .

Probit analysis of the data using the least sensitive lot (Lot 3) determined that the concentration of EBV DNA in plasma detected with 95% probability (LoD by Probit) was 19.56 IU/mL with a 95% confidence interval (CI) of (13.09 IU/mL, 39.39 IU/mL) (**Table 4**).

Table 2. Alinity m EBV Limit of Detection (LoD) – Lot 1

EBV DNA (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
100.00	24	24	100.0
50.00	24	24	100.0
20.00	24	24	100.0
15.00	24	24	100.0
12.50	24	23	95.8
10.00	24	22	91.7
7.50	24	22	91.7
5.00	24	14	58.3
2.50	24	6	25.0
1.25	24	9	37.5

Table 3. Alinity m EBV Limit of Detection (LoD) – Lot 2

EBV DNA (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
100.00	24	24	100.0
50.00	24	24	100.0
20.00	24	23	95.8
15.00	24	24	100.0
12.50	24	24	100.0
10.00	24	23	95.8
7.50	24	21	87.5
5.00	24	17	70.8
2.50	24	13	54.2
1.25	24	9	37.5

Table 4. Alinity m EBV Limit of Detection (LoD) – Lot 3 (Least Sensitive Lot)			
EBV DNA (IU/mL)	**No. of Valid Replicates**	**No. of Detected Replicates**	**Detection Rate (%)**
100.00	24	24	100.0
50.00	24	24	100.0
20.00	24	24	100.0
15.00	23	22	95.7
12.50	23	20	87.0
10.00	24	21	87.5
7.50	24	19	79.2
5.00	24	16	66.7
2.50	24	9	37.5
1.25	24	7	29.2

Table 5. Alinity m EBV Limit of Detection (LoD) – Lot 4			
EBV DNA (IU/mL)	**No. of Valid Replicates**	**No. of Detected Replicates**	**Detection Rate (%)**
100.00	24	24	100.0
50.00	24	24	100.0
20.00	24	24	100.0
15.00	24	22	91.7
12.50	24	23	95.8
10.00	24	22	91.7
7.50	24	20	83.3
5.00	24	19	79.2
2.50	24	13	54.2
1.25	23	5	21.7

The claimed LoD of Alinity m EBV is 20 IU/mL (1.30 Log IU/mL) in plasma.

5.7.1.3 Limit of Detection for EBV Type 2

Cultured virus for EBV type 2 was diluted to 3 different concentrations in EBV negative human plasma. Testing was performed using one lot of amplification reagents across multiple days. The results, representative of the analytical sensitivity performance of Alinity m EBV for EBV type 2, are summarized in **Table 6**.

Alinity m EBV detected 95% or greater of EBV samples at and above 15 IU/mL (1.18 Log IU/mL) in plasma. These results demonstrate the ability of Alinity m EBV to detect EBV type 2 at the claimed LoD.

Table 6. Alinity m EBV Type 2 Limit of Detection (LoD)

EBV DNA (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
50.00	24	24	100.0
20.00	23	22	95.7
15.00	24	23	95.8

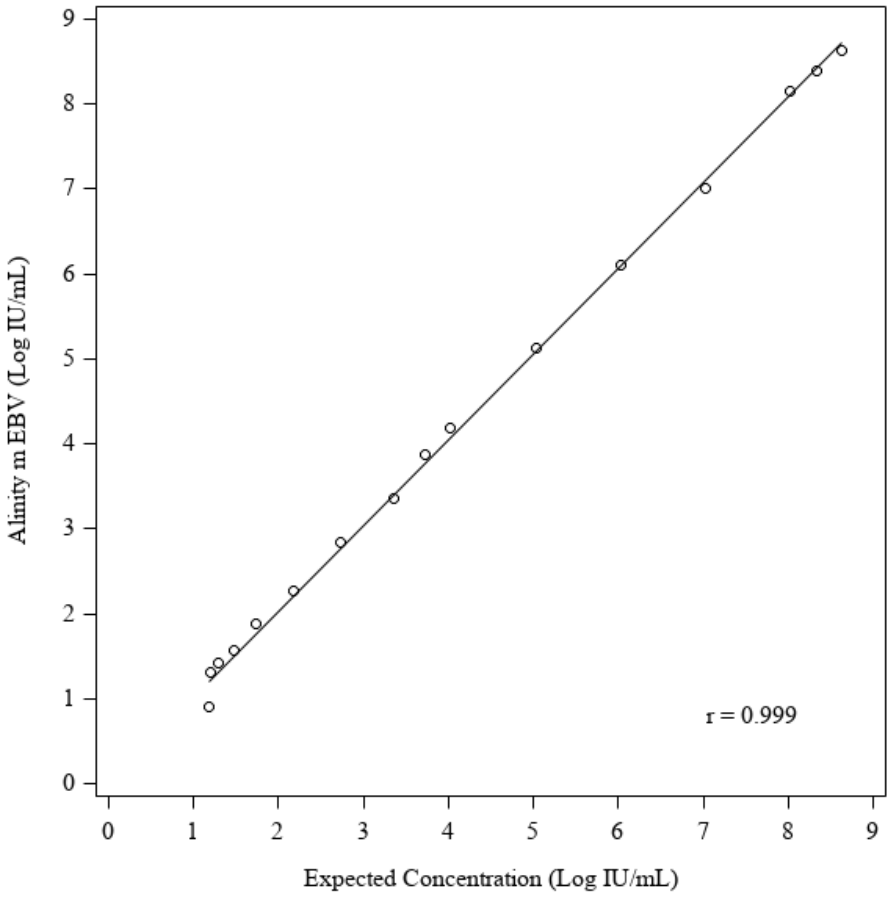
5.7.1.4 Linear Range

The quantitation range of Alinity m EBV is from the lower limit of quantitation (LLoQ) of 50 IU/mL (1.70 Log IU/mL) to the upper limit of quantitation (ULoQ) of 200,000,000 IU/mL (8.30 Log IU/mL).

Linearity of Alinity m EBV was assessed by testing a dilution series of EBV type 1 in negative human plasma, consisting of 16 panel levels targeted in the range of 10 IU/mL to 400,000,000 IU/mL (1.00 Log IU/mL to 8.60 Log IU/mL). Panel levels with concentrations from 10 IU/mL to 1,500 IU/mL (1.00 Log IU/mL to 3.18 Log IU/mL) were prepared using clinical specimen, while panel levels with concentrations from 15 IU/mL to 400,000,000 IU/mL (1.18 Log IU/mL to 8.60 Log IU/mL) were prepared using synthetic DNA. Panel quantitation values were traceable to the 1st World Health Organization (WHO) International Standard for Epstein-Barr Virus for Nucleic Acid Amplification Techniques (NIBSC code: 09/260).

Alinity m EBV was linear across the quantitation range from 50 IU/mL to 200,000,000 IU/mL (1.70 Log IU/mL to 8.30 Log IU/mL). Representative results for Alinity m EBV linearity performance are shown in **Figure 2**.

Figure 2. Linearity [a]



[a] The markers in the plot represent the mean Alinity m EBV concentration (in Log IU/mL) for each panel level.

5.7.1.5 Linearity of EBV Type 2

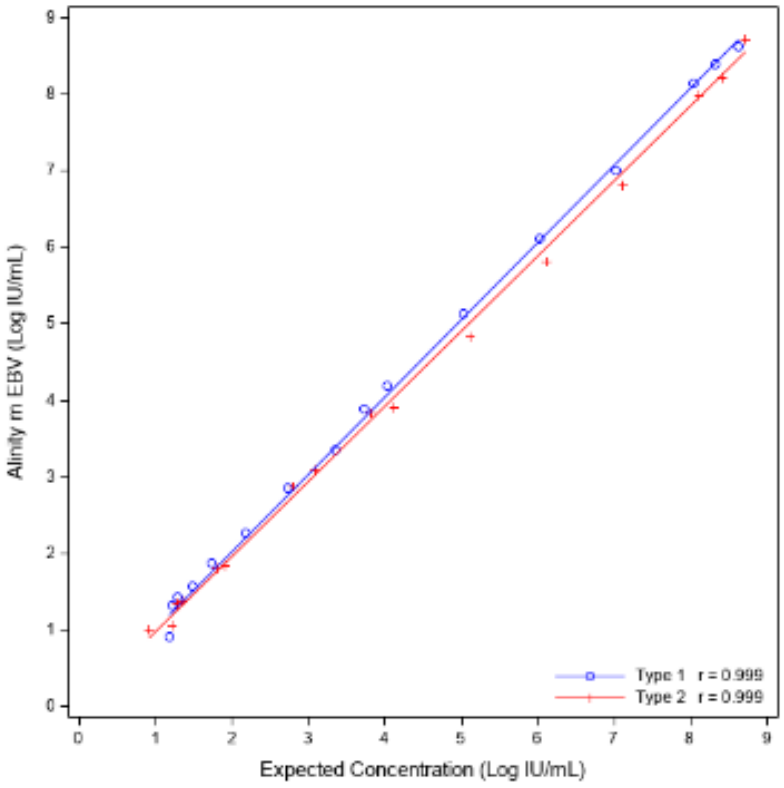
Linearity of Alinity m EBV for EBV type 2 was confirmed by testing a dilution series in negative human plasma, consisting of 16 panel levels targeted in the range of 10 IU/mL to 400,000,000 IU/mL (1.00 Log IU/mL to 8.60 Log IU/mL). Panel levels with concentrations from 10 IU/mL to 1,500 IU/mL (1.00 Log IU/mL to 3.18 Log IU/mL) were prepared using a cultured virus, while panel levels with concentrations from

15 IU/mL to 400,000,000 IU/mL (1.18 Log IU/mL to 8.60 Log IU/mL) were prepared using synthetic DNA. Panel quantitation values were traceable to the 1st World Health Organization (WHO) International Standard for Epstein-Barr Virus for Nucleic Acid Amplification Techniques (NIBSC code: 09/260).

Alinity m EBV was linear across the quantitation range from 50 IU/mL to 200,000,000 IU/mL (1.70 Log IU/mL to 8.30 Log IU/mL) for EBV type 2.

Representative results for Alinity m EBV linearity performance for type 2 and for type 1 (**Section 5.7.1.4**) are shown in **Figure 3**.

Figure 3. Linearity for EBV Type 1 and Type 2 [a]



[a] The markers in the plot represent the mean Alinity m EBV concentration (in Log IU/mL) for each panel level.

Alinity m EBV was demonstrated to be linear across the quantitation range for EBV type 1 and type 2 from 50 IU/mL to 200,000,000 IU/mL (1.70 Log IU/mL to 8.30 Log IU/mL).

5.7.1.6 Precision

Precision of Alinity m EBV was determined by analyzing a 9-member plasma panel. Panel members with concentrations targeted to 1.30 Log IU/mL and 2.00 Log IU/mL (20 IU/mL and 100 IU/mL) were prepared with positive clinical sample, panel members targeted in the range of 2.70 Log IU/mL to 5.00 Log IU/mL (500 IU/mL to 100,000 IU/mL) were prepared using cultured virus, and panel members with targeted concentrations greater than 5.00 Log IU/mL were prepared using synthetic DNA. Each panel member was tested in 4 replicates, twice each day for 12 days, on 3 Alinity m Systems operated by 3 operators (1 operator per instrument), using 3 AMP kit lots (1 lot per instrument), for a total of 288 replicates per panel member.

The representative precision study results in **Table 7** and **Table 8** demonstrated that Alinity m EBV within-laboratory standard deviation (SD) was less than or equal to 0.25 Log IU/mL for EBV DNA panels targeted in the range of 2.70 Log IU/mL to 8.30 Log IU/mL (500 IU/mL to 200,000,000 IU/mL), and less than or equal to 0.50 Log IU/mL for EBV DNA panels targeted in the range of 1.30 Log IU/mL to less than 2.70 Log IU/mL (20 IU/mL to less than 500 IU/mL).

Table 7. Precision

		Mean Concentration (Log IU/mL)	Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory [c]		Between-Instrument Component [d]		Total [e]	
Panel	N [a]		SD [b]	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
9	287	8.22	0.04	0.5	0.04	0.5	0.00	0.0	0.06	0.7	0.05	0.6	0.08	0.9
8	287	8.04	0.05	0.6	0.04	0.4	0.00	0.0	0.06	0.7	0.06	0.8	0.09	1.1
7	288	7.05	0.05	0.7	0.02	0.3	0.00	0.0	0.05	0.7	0.02	0.4	0.06	0.8
6	284	6.09	0.05	0.8	0.03	0.4	0.00	0.0	0.06	0.9	0.04	0.7	0.07	1.1
5	287	5.05	0.05	0.9	0.03	0.6	0.01	0.1	0.05	1.1	0.05	0.9	0.07	1.4
4	287	4.06	0.04	1.1	0.03	0.7	0.02	0.4	0.05	1.3	0.06	1.4	0.08	1.9
3	288	2.77	0.07	2.7	0.07	2.7	0.00	0.0	0.11	3.8	0.08	3.0	0.13	4.9
2	286	2.20	0.13	5.7	0.13	6.1	0.00	0.0	0.18	8.3	0.07	3.1	0.20	8.9
1	283	1.43	0.25	17.2	0.07	5.2	0.01	0.6	0.26	18.0	0.05	3.7	0.26	18.4

[a] Number of valid replicates with detectable viral load
[b] Standard deviations (SD) are in Log IU/mL.
[c] Within-Laboratory includes Within-Run, Between-Run, and Between-Day components.
[d] Alinity m System, AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Instrument.
[e] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

Table 8. Precision										
				CV(%) [c]						
Panel	**N** [a]	**Mean Concentration** [b] **(IU/mL)**		**Within-Run Component**		**Between-Run Component**		**Between-Day Component**	**Between-Instrument Component** [d]	**Total** [e]
9	287	169,046,883		10.0		9.5		0.0	10.9	17.7
8	287	111,475,841		10.7		8.2		0.0	14.9	20.2
7	288	11,275,291		10.8		4.3		0.0	5.7	13.0
6	284	1,231,685		11.4		6.1		0.0	9.4	16.0
5	287	112,523		10.7		6.6		1.2	10.9	16.8
4	287	11,596		10.0		6.3		3.5	13.3	18.2
3	288	620		17.4		17.2		0.0	19.5	31.8
2	286	176		29.5		31.5		0.0	16.0	47.5
1	283	32		61.3		17.2		2.0	12.3	66.2

[a] Number of valid replicates with detectable viral load

[b] Titer data are considered to be log-normally distributed and the mean values for titer data are calculated as exp(mean * ln(10) + [SD * ln(10)]^2/2).

[c] Titer data are considered to be log-normally distributed and %CV values are calculated as CV (%) = sqrt(10^[SD^2 * ln(10)] – 1) * 100.

[d] Alinity m System, AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Instrument.

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

5.7.1.7 Lower Limit of Quantitation

The lower limit of quantitation (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 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 World Health Organization (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 50.00 IU/mL (1.70 Log IU/mL) for Alinity m EBV, with an acceptable level of accuracy and precision, ie, TAE and TE less than or equal to 1.00 Log IU/mL.

Table 9. Total Error

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)
1.30	1.34	0.04	0.27	0.59	0.78
1.70	1.77	0.07	0.22	0.51	0.62
2.00	2.12	0.12	0.14	0.40	0.40

[a] Mean concentration – target concentration

5.7.1.8 Analytical Specificity – Potential Cross-Reactants

The analytical specificity of Alinity m EBV was evaluated with a panel of microorganisms (see **Table 10**) in EBV negative plasma, positive plasma targeted to 60 IU/mL EBV DNA, and positive plasma targeted to 10,000 IU/mL EBV DNA. Microorganisms were tested at a final concentration of 10^5 Units/mL for viruses and fungi or 10^6 Units/mL for bacteria. No cross-reactivity or interference in the performance of the Alinity m EBV assay was observed in the presence of the tested microorganisms.

Table 10. Potential Cross-Reactants		
Viruses	**Bacteria**	**Fungi**
Adenovirus 2	*Actinomyces israelii*	*Aspergillus niger*
BK polyomavirus	*Clostridium perfringens*	*Candida albicans (CA)*
Cytomegalovirus (CMV)	*Enterococcus faecalis*	*Cryptococcus neoformans*
Enterovirus Type 71	*Escherichia coli*	
Hepatitis A Virus (HAV)	*Klebsiella pneumoniae*	
Hepatitis B Virus (HBV)	*Listeria monocytogenes*	
Hepatitis C Virus (HCV)	*Morganella morganii*	
Herpesvirus 6A	*Mycobacterium smegmatis*	
Herpesvirus 6B	*Mycoplasma pneumoniae*	
Herpesvirus 7	*Pseudomonas aeruginosa*	
Herpesvirus 8 (Kaposi's sarcoma associated virus)	*Salmonella enterica*	
Human immunodeficiency virus 1 (HIV-1)	*Staphylococcus aureus (SA)*	
Human immunodeficiency virus 2 (HIV-2)	*Staphylococcus epidermidis*	
Human papilloma virus 16 (HPV-16)	*Streptococcus pneumoniae*	
Human papilloma virus 18 (HPV-18)		
Herpes Simplex Virus-1 (HSV-1)		
Human T-lymphotropic virus type 1 (HTLV-1)		
Mumps orthorubulavirus		
Parvo virus B19		
Simian Virus 40		
Vaccinia virus (VACV)		
Varicella-Zoster virus (VZV)		

5.7.1.9 Analytical Specificity - Potentially Interfering Substances

The effects of endogenous substances and the presence of high levels of therapeutic drugs commonly prescribed in transplant patients were evaluated. Potential interference on Alinity m EBV performance in plasma was assessed by testing 8 negative samples, 8 positive samples targeted to 60 IU/mL and 8 positive samples targeted to 10,000 IU/mL EBV DNA.

No interference was observed in the presence of albumin (60 g/L), hemoglobin (10 g/L), triglycerides (16.94 mmol/L), conjugated bilirubin (475 µmol/L), unconjugated bilirubin (684 µmol/L), or human genomic DNA (2 µg/mL) that were introduced in the sample.

No interference was observed in the presence of drug compounds tested in pools or individually that are listed in **Table 11**, at a concentration of 3 times the reported C_{max} or higher.

Table 11. Drug Compounds

Pools Tested	**Drug Compounds**
1	Mycophenolic acid
2	Amoxicillin Clavulanate Foscarnet Piperacillin Tazobactam sodium Vancomycin
3	Acyclovir Amlodipine besylate Atenolol Azathioprine Cefotetan Cyclosporine Everolimus Famotidine Fluconazole Lisinopril Mycophenolate mofetil Prednisone Rabeprazole Sirolimus Sulfamethoxazole Tacrolimus Trimethoprim Valacyclovir Valsartan

5.7.1.10 Carryover

The carryover rate for Alinity m EBV was determined by analyzing 648 valid replicates of EBV negative samples processed from alternating positions with 647 valid replicates of high concentrated EBV positive samples greater than or equal to 20,000,000 IU/mL, across a minimum of 27 runs. The carryover resulting in a detectable concentration greater than or equal to LoD was 0.3% (95% CI: 0.1% to 1.1%). The carryover resulting in EBV detection was 1.2% (95% CI: 0.6% to 2.4%).

5.7.1.11 Alinity m EBV Testing Using Dilution Procedure

The 1:2.5 dilution procedure was evaluated by comparing quantitation of neat samples and samples tested using the Alinity m EBV dilution procedure. Five plasma panel members with EBV levels targeted in the range of 150 IU/mL to 100,000,000 IU/mL (2.18 Log IU/mL to 8.00 Log IU/mL) were tested. Each panel member was tested, neat or using the dilution procedures, in multiple replicates. For the 5 panel members, the differences in mean, ie, diluted minus neat, ranged from −0.01 Log IU/mL to 0.23 Log IU/mL.

5.7.1.12 Precision of Alinity m EBV Using Dilution Procedure

Precision of Alinity m EBV, using the dilution procedure, was determined by analyzing 3 plasma panel members. Panel members 1 and 2 were prepared by spiking cultured virus in EBV negative sample, and panel member 3 was prepared by spiking synthetic DNA in EBV negative sample. Each panel member was tested in at least 3 replicates, twice each day for 12 days, on 3 Alinity m Systems with 3 Alinity m Specimen Dilution Kit I lots and 3 Alinity m EBV AMP Kit lots by 3 operators (1 Specimen Diluent lot, 1 AMP kit lot and 1 operator per instrument), for a total of at least 216 replicates.

The results, representative of the precision of Alinity m EBV using dilution procedures, are summarized in **Table 12** and **Table 13**.

Table 12. Precision Using Dilution Procedure

		Mean Concentration	Within-Run Component		Between-Run Component		Between-Day Component		Within-Laboratory [c]		Between-Instrument Component [d]		Total [e]	
Panel	**N [a]**	**(Log IU/mL)**	**SD [b]**	**% CV**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**	**SD**	**% CV**
1	274	3.50	0.07	2.1	0.06	1.6	0.06	1.7	0.11	3.2	0.04	1.2	0.12	3.4
2	273	4.89	0.05	1.1	0.09	1.9	0.00	0.0	0.11	2.2	0.06	1.1	0.12	2.5
3	274	7.69	0.06	0.8	0.09	1.2	0.00	0.0	0.11	1.4	0.04	0.5	0.12	1.5

[a] Number of valid replicates with detectable viral load.
[b] Standard deviations (SD) are in Log IU/mL.
[c] Within-Laboratory includes Within-Run, Between-Run and Between-Day Components.
[d] Alinity m System, AMP Kit lot, Specimen Diluent lot, and Operator are confounded, and the confounding effect is represented by Instrument.
[e] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

Table 13. Precision Using Dilution Procedure

			CV(%) [c]				
Panel	**N [a]**	**Mean Concentration [b] (IU/mL)**	**Within-Run Component**	**Between-Run Component**	**Between-Day Component**	**Between-Instrument Component [d]**	**Total [e]**
1	274	3,263	17.0	13.3	13.7	9.7	27.7
2	273	81,253	12.6	21.7	0.0	12.9	28.5
3	274	51,057,729	14.4	21.2	0.0	9.6	27.6

[a] Number of valid replicates with detectable viral load
[b] Titer data are considered to be log-normally distributed and the mean values for titer data are calculated as exp(mean * ln(10) + [SD * ln(10)]^2/2).
[c] Titer data are considered to be log-normally distributed and %CV values are calculated as CV (%) = sqrt(10^[SD^2 * ln(10)] – 1) * 100.
[d] Alinity m System, AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Instrument.
[e] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

5.7.1.13 Confirmation of the LLoQ Using Dilution Procedure

Confirmation testing for Alinity m EBV LLoQ using the dilution procedure was performed by testing 2 panel members at 50 IU/mL (LLoQ) and 60 IU/mL (near LLoQ) with a dilution factor of 1:2.5. The EBV concentrations in the panel members were targeted at 20 IU/mL and 24 IU/mL (1.30 Log IU/mL and 1.38 Log IU/mL) after dilution in Specimen Diluent. Panel members were dilutions of cultured virus spiked into EBV negative plasma.

Table 14. Total Error Using Dilution Procedure

Panel	Target Concentration Undiluted (Log IU/mL)	Dilution Factor	Target Concentration in Specimen Diluent (Log IU/mL)	Mean Concentration [a] (Log IU/mL)	Bias [b] (Log IU/mL)	SD (Log IU/mL)	TAE (Log IU/mL)	TE (Log IU/mL)
1	1.70	2.5	1.30	1.71	0.01	0.17	0.35	0.48
2	1.78	2.5	1.38	1.74	−0.04	0.23	0.50	0.65

[a] Reported concentration for undiluted samples.
[b] Mean concentration – target concentration for undiluted samples

A minimum of 14 replicates per day of each panel level were tested using the dilution procedure in 3 runs across 3 days (one run per day). The study was performed using 1 Alinity m EBV AMP Kit lot, 1 Specimen Diluent lot, and 1 Alinity m System. Total error was estimated by TAE and TE, as shown in **Table 14**. The accuracy and precision at 20 IU/mL and 24 IU/mL were confirmed for Alinity m EBV testing using the 1:2.5 dilution procedure.

5.7.2 Clinical Reproducibility

Reproducibility performance of Alinity m EBV was evaluated by testing a 9-member reproducibility panel, including 8 positive panel members and 1 negative panel member. The positive panel members were prepared using an EBV positive clinical specimen, cultured virus, or plasmid DNA diluted in human EDTA plasma. The concentration levels targeted for the reproducibility panels spanned the quantitation range of the assay. A total of 3 Alinity m EBV AMP Kit lots, 3 Alinity m EBV CAL Kit lots, 3 Alinity m EBV CTRL Kit lots and 3 Alinity m Sample Prep Kit 2 lots were used. Three clinical sites each tested 2 unique reagent lot combinations (consisting of 2 Alinity m EBV AMP Kit lots along with 1 lot of each Alinity m EBV CAL Kit, Alinity m EBV CTRL Kit and Alinity m Sample Prep Kit 2) on 5 non-consecutive days for each lot combination. Six replicates of each panel member were tested on each of 5 days to ensure a minimum of 5 valid replicates for analysis. The reproducibility results are summarized in **Table 15** and **Table 16** (for the positive panel members) and **Table 17** (for the negative panel member).

Table 15. Reproducibility for Positive Panel Members

Panel	N [a]	Target Concentration (Log IU/mL)	Mean Concentration (Log IU/mL)	Within-Run/Day Component		Between-Run/Day Component		Within-Laboratory [c]		Between-Lot Component		Between-Site/ Instrument Component		Total [d]	
				SD [b]	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV	SD	% CV
1	178	8.30	8.40	0.05	0.5	0.03	0.3	0.05	0.6	0.06	0.7	0.18	2.1	0.19	2.3
2	177	7.00	7.04	0.04	0.6	0.00	0.1	0.04	0.6	0.04	0.6	0.12	1.8	0.14	2.0
3	179	6.00	5.76	0.05	0.8	0.02	0.3	0.05	0.9	0.04	0.7	0.08	1.3	0.10	1.8
4	179	5.00	5.04	0.06	1.1	0.04	0.9	0.07	1.4	0.04	0.7	0.09	1.8	0.12	2.4
5	179	4.00	4.01	0.05	1.2	0.03	0.9	0.06	1.5	0.04	1.0	0.05	1.3	0.09	2.2
6	172	3.00	3.07	0.07	2.2	0.03	1.0	0.07	2.4	0.02	0.7	0.04	1.3	0.09	2.8
7	179	1.78	1.64	0.19	11.4	0.02	1.0	0.19	11.5	0.04	2.4	0.13	7.6	0.23	14.0
8	174	1.30	1.20	0.28	23.5	0.05	4.2	0.29	23.8	0.00	0.0	0.10	8.0	0.30	25.1

[a] Number of valid replicates with detectable viral load
[b] Standard deviations (SD) are in Log IU/mL.
[c] Within-Laboratory includes Within-Run/Day and Between-Run/Day components.
[d] Total includes Within-Run/Day, Between-Run/Day, Between-Lot, and Between-Site/Instrument Components.

Table 16. Reproducibility for Positive Panel Members

			CV(%) [c]			
Panel	**N [a]**	**Mean Concentration [b] (IU/mL)**	**Within-Run/Day Component**	**Between-Run/Day Component**	**Between-Lot Component**	**Between-Site/ Instrument Component**	**Total [d]**
1	178	279,192,220	10.6	6.4	13.0	42.8	47.1
2	177	11,407,341	9.5	1.1	9.3	29.3	32.5
3	179	586,126	11.3	3.9	9.4	18.0	23.7
4	179	112,772	13.1	10.1	8.2	21.4	28.6
5	179	10,572	11.6	8.0	9.7	11.7	20.8
6	172	1,187	15.3	6.9	4.9	9.3	19.9
7	179	51	45.4	3.9	9.0	29.4	56.8
8	174	20	72.1	11.5	0.0	22.3	78.6

[a] Number of valid replicates with detectable viral load

[b] Titer data are considered to be log-normally distributed and the mean values for titer data are calculated as exp(mean * ln(10) + [SD * ln(10)]^2/2).

[c] Titer data are considered to be log-normally distributed and %CV values are calculated as CV (%) = sqrt(10^[SD^2 * ln(10)] – 1) * 100.

[d] Total includes Within-Run/Day, Between-Run/Day, Between-Lot, and Between-Site/Instrument Components.

Table 17. Reproducibility for Negative Panel Member				
Expected EBV DNA Concentration	**No. of Replicates**		**Negative Rate (%)**	**95% Confidence Interval**
	Valid	**Negative**		
Negative	180	176	97.8 (176/180)	(94.4, 99.1)

5.7.3 Clinical Performance

Alinity m EBV results were compared to those of an FDA-cleared EBV nucleic acid test in a representative study. A total of 558 EDTA plasma samples were tested (neat or diluted), including 542 clinical specimens from hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) subjects, and 16 contrived samples prepared by spiking inactivated EBV virus into the individual clinical specimens. The Alinity m EBV assay testing was performed at 3 clinical testing sites with 3 Alinity m EBV reagent kit lots.

Of the 558 clinical samples, 550 produced valid results with Alinity m EBV and the comparator assay, including 388 samples detected by Alinity m EBV and 162 samples not detected by Alinity m EBV. Out of 550 valid samples, 168 were from HSCT subjects, 379 were from SOT subjects, and 3 were from dual-transplant (HSCT/SOT) subjects. The agreement between Alinity m EBV and comparator results is shown in **Table 18** (HSCT samples), **Table 19** (SOT samples), and **Table 20** (HSCT and SOT samples combined).

Table 18. HSCT Samples – Agreement Between Alinity m EBV and Comparator [a]								
	Comparator EBV (Log IU/mL)							
Alinity m EBV (Log IU/mL)	**Target Not Detected**	**<LLoQ [b]**	**LLoQ [b] to <2.70**	**2.70 to <3.00**	**3.00 to <3.70**	**3.70 to <4.00**	**≥4.00**	**Total**
Target Not Detected	44	0	0	0	0	0	0	44
<LLoQ [b]	4	20	6	0	0	0	0	30
LLoQ [b] to <2.70	0	6	24	1	0	0	0	31
2.70 to <3.00	0	0	4	4	1	0	0	9
3.00 to <3.70	0	0	0	5	13	2	0	20
3.70 to <4.00	0	0	0	0	2	4	2	8
≥4.00	0	0	0	0	0	1	28	29
Total	48	26	34	10	16	7	30	171
Column Agreement (%)	(48/48) 100.0%	(26/26) 100.0%	(34/34) 100.0%	(10/10) 100.0%	(16/16) 100.0%	(7/7) 100.0%	(30/30) 100.0%	
95% Score CI	(92.6%, 100.0%)	(87.1%, 100.0%)	(89.8%, 100.0%)	(72.2%, 100.0%)	(80.6%, 100.0%)	64.6%, 100.0%)	(88.6%, 100.0%)	

[a] Three dual-transplant specimens were included in both HSCT and SOT agreement analyses.
[b] The LLoQ used here is the higher LLoQ between Alinity m EBV and comparator.

Table 19. SOT Samples – Agreement Between Alinity m EBV and Comparator [a]								
	Comparator EBV (Log IU/mL)							
Alinity m EBV (Log IU/mL)	**Target Not Detected**	**<LLoQ [b]**	**LLoQ [b] to <2.70**	**2.70 to <3.00**	**3.00 to <3.70**	**3.70 to <4.00**	**≥4.00**	**Total**
Target Not Detected	110	7	1	0	0	0	0	118
<LLoQ [b]	28	61	8	0	0	0	0	97
LLoQ [b] to <2.70	1	16	61	4	1	0	0	83
2.70 to <3.00	0	0	5	9	0	0	0	14
3.00 to <3.70	0	0	0	6	20	0	0	26
3.70 to <4.00	0	0	0	0	4	2	2	8
≥4.00	0	0	0	0	0	4	32	36
Total	139	84	75	19	25	6	34	382
Column Agreement (%)	(138/139) 99.3%	(84/84) 100.0%	(74/75) 98.7%	(19/19) 100.0%	(24/25) 96.0%	(6/6) 100.0%	(34/34) 100.0%	
95% Score CI	(96.0%, 99.9%)	(95.6%, 100.0%)	(92.8%, 99.8%)	(83.2%, 100.0%)	(80.5%, 99.3%)	61.0%, 100.0%)	(89.8%, 100.0%)	

[a] Three dual-transplant specimens were included in both HSCT and SOT agreement analyses.
[b] The LLoQ used here is the higher LLoQ between Alinity m EBV and comparator.

Table 20. HSCT and SOT Samples Combined – Agreement Between Alinity m EBV and Comparator								
	Comparator EBV (Log IU/mL)							
Alinity m EBV (Log IU/mL)	**Target Not Detected**	**<LLoQ [a]**	**LLoQ [a] to <2.70**	**2.70 to <3.00**	**3.00 to <3.70**	**3.70 to <4.00**	**≥4.00**	**Total**
Target Not Detected	154	7	1	0	0	0	0	162
<LLoQ [a]	32	80	14	0	0	0	0	126
LLoQ [a] to <2.70	1	22	83	5	1	0	0	112
2.70 to <3.00	0	0	9	13	1	0	0	23
3.00 to <3.70	0	0	0	11	33	2	0	46
3.70 to <4.00	0	0	0	0	6	6	4	16
≥4.00	0	0	0	0	0	5	60	65
Total	187	109	107	29	41	13	64	550
Column Agreement (%)	(186/187) 99.5%	(109/109) 100.0%	(106/107)9 9.1%	(29/29) 100.0%	(40/41) 97.6%	(13/13) 100.0%	(64/64) 100.0%	
95% Score CI	(97.0%, 99.9%)	(96.6%, 100.0%)	(94.9%, 99.8%)	(88.3%, 100.0%)	(87.4%, 99.6%)	77.2%, 100.0%)	(94.3%, 100.0%)	

[a] The LLoQ used here is the higher LLoQ between Alinity m EBV and comparator.

Discordant results were defined as those that are more than one box away from the diagonal (indicated by shading). For Target Not Detected (TND) by Comparator Column Agreement, the Alinity m EBV Target Not Detected and < LLoQ cells were combined. The rationale for adding the adjacent <LLoQ and TND cells for the TND column was that the difference between a TND and <LLoQ were not clinically meaningful and that these were analytically at the lower end of the quantitation range, which may be impacted by random error.

Of the 550 samples, 44 were collected for the estimation of Negative Percent Agreement (NPA) and were confirmed as EBV DNA negative. For this subset of confirmed EBV DNA negative clinical specimens, the NPA with the Comparator assay was 100.0% (44/44) with a 95% confidence interval of (92.0%, 100.0%).

Agreement between Alinity m EBV assay and the comparator assay was also evaluated using different clinical thresholds and is shown in **Table 21** (HSCT samples), **Table 22** (SOT samples), and **Table 23** (HSCT and SOT samples combined).

Table 21. HSCT Samples – Agreement between Alinity m EBV and Comparator EBV using Different Thresholds

Threshold	Percent Agreement < Threshold (%) 95% Score CI (n/N)	Percent Agreement ≥ Threshold (%) 95% Score CI (n/N)
Not Detected	100.0 (92.6, 100.0) (48/48)	100.0 (97.0, 100.0) (123/123)
< LLoQ [a]	91.9 (83.4, 96.2) (68/74)	93.8 (87.2, 97.1) (91/97)
< 3.00 Log IU/mL	95.8 (90.5, 98.2) (113/118)	98.1 (90.1, 99.7) (52/53)
< 4.00 Log IU/mL	99.3 (96.1, 99.9) (140/141)	93.3 (78.7, 98.2) (28/30)

[a] The LLoQ used here is the higher LLoQ between Alinity m EBV and comparator.

Table 22. SOT Samples – Agreement between Alinity m EBV and Comparator EBV using Different Thresholds

Threshold	Percent Agreement < Threshold (%) 95% Score CI (n/N)	Percent Agreement ≥ Threshold (%) 95% Score CI (n/N)
Not Detected	99.3 (96.0, 99.9) (138/139)	96.7 (93.6, 98.3) (235/243)
< LLoQ [a]	92.4 (88.1, 95.2) (206/223)	94.3 (89.6, 97.0) (150/159)
< 3.00 Log IU/mL	98.1 (95.9, 99.1) (311/317)	98.5 (91.8, 99.7) (64/65)
< 4.00 Log IU/mL	98.9 (97.1, 99.6) (344/348)	94.1 (80.9, 98.4) (32/34)

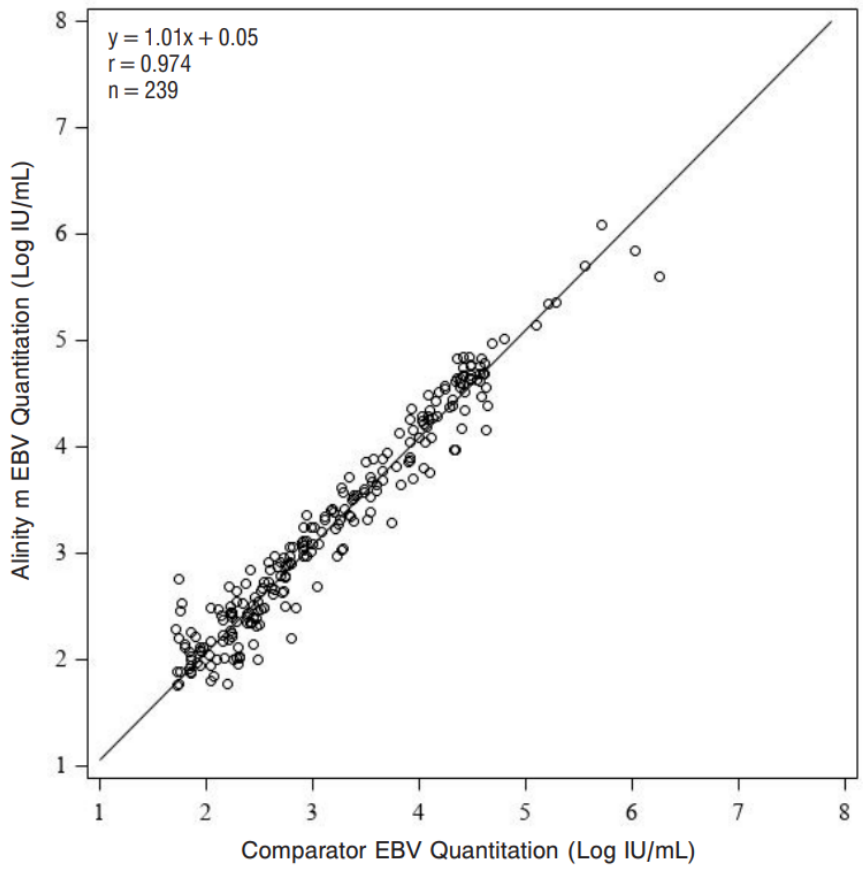
[a] The LLoQ used here is the higher LLoQ between Alinity m EBV and comparator.

Table 23. HSCT and SOT Samples Combined – Agreement between Alinity m EBV and Comparator EBV using Different Thresholds		
Threshold	**Percent Agreement < Threshold (%) 95% Score CI (n/N)**	**Percent Agreement ≥ Threshold (%) 95% Score CI (n/N)**
Not Detected	99.5 (97.0, 99.9) (186/187)	97.8 (95.7, 98.9) (355/363)
< LLoQ [a]	92.2 (88.6, 94.8) (273/296)	94.1 (90.5, 96.4) (239/254)
< 3.00 Log IU/mL	97.5 (95.5, 98.6) (421/432)	98.3 (94.0, 99.5) (116/118)
< 4.00 Log IU/mL	99.0 (97.6, 99.6) (481/486)	93.8 (85.0, 97.5) (60/64)

[a] The LLoQ used here is the higher LLoQ between Alinity m EBV and comparator.

Regression and bias analysis included a total of 239 samples with results that were within the common quantitation range of both Alinity m EBV and the comparator assay. **Figure 4** shows the results of the Deming regression analysis with a slope of 1.01, intercept of 0.05, and correlation coefficient of 0.974. The mean bias between Alinity m EBV and the comparator (Alinity m EBV minus comparator) was 0.09 Log IU/mL with a 95% CI of (0.06, 0.12).

Figure 4. Deming Regression Analysis



Systematic difference between Alinity m EBV and the comparator at 4 selected viral load levels is shown in **Table 24**.

Table 24. Systematic Difference at Selected Viral Load Levels

Target Viral Load Level (based on comparator)	**Systematic Difference**
LLoQ	0.07 Log IU/mL
3.00 Log IU/mL	0.09 Log IU/mL
4.00 Log IU/mL	0.10 Log IU/mL
5.00 Log IU/mL	0.11 Log IU/mL

5.8 Conclusions Drawn from the Studies

The analytical and clinical study results demonstrate that the Alinity m EBV assay for use on the Alinity m System is safe, effective, and performs comparably to the predicate device. The results support a substantial equivalence decision for Alinity m EBV.