# 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
# DECISION SUMMARY
ASSAY ONLY

## I Background Information:

### A 510(k) Number

K212778

### B Applicant

Abbott Molecular, Inc.

### C Proprietary and Established Names

Alinity m EBV AMP Kit

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| QLX | Class II | 21 CFR 866.3183 - Quantitative Viral Nucleic Acid Test For Transplant Patient Management | MI - Microbiology |

## II Submission/Device Overview:

### A Purpose for Submission:

To obtain 510k clearance for the Alinity m EBV 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.

### B Measurand:

EBV DNA

### C Type of Test:

Quantitative polymerase chain reaction (PCR)

## III Intended Use

### A Intended Use(s):

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.

### B Indication(s) for Use:

NA

### C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

### D Special Instrument Requirements:

Alinity m System

## IV Device/System Characteristics:

### A 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.

### B Principle of Operation:

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. EBV DNA from human plasma 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 DNA is

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.

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 possibility of nucleic acid contamination on the Alinity m System is minimized because:

- Aerosol barrier pipette tips are used for all pipetting. The pipette tips are discarded after use.
- PCR amplification and detection is carried out automatically in a sealed reaction vessel.
- Disposal of the reaction vessel is performed automatically by the Alinity m System.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):

cobas EBV, cobas EBV/BKV Control Kit, cobas Buffer Negative Control Kit

### B Predicate 510(k) Number(s):

DEN200015

### C Comparison with Predicate(s):

**Table 1. Alinity m EBV and Predicate Device**

| Feature | Current Application | Predicate Device |
|---|---|---|
| | **Alinity m EBV Assay** | **Cobas EBV** |
| 510(k) / De Novo Number | K212778 | DEN200015 |
| Regulation No. and Product Code | 866.3183 / QLX | 866.3183 / QLX |

| | | |
|---|---|---|
| Device Class | II | II |
| Technology/ Detection | Real-time polymerase chain reaction (PCR) | PCR |
| Instrument System | Alinity m System | cobas 6800 System<br>cobas 8800 System |

**Table 2**. Similarities and *Differences* Between

| **Device & Predicate Device(s):** | **Alinity m EBV Assay**<br>**K212778** | **cobas EBV**<br>**DEN** |
|---|---|---|
| | | |
| **General Device Characteristic Similarities** | | |
| **Assay Type** | Same | Quantitative |
| **Specimen Types** | Same | EDTA Plasma |
| **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.<br>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.<br>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 | 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.<br>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.<br>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.<br>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 |

| | | |
|---|---|---|
| | tissue-based products (HCT/Ps) for EBV. | 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 (*Gp350* and EBNA1) | EBNA 1gene, EBV BMRF gene |

## VI Standards/Guidance Documents Referenced:

ISO 17511: "In vitro diagnostic medical devices – Measurement of quantities in biological samples – Metrological traceability of values assigned to calibrators and control materials.

Clinical Laboratory Standards Institute (CLSI). *Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition*. CLSI Guideline EP17-A2, CLSI: Wayne, PA, 2012.

Clinical Laboratory Standards Institute (CLSI). *Evaluation of Linearity of Quantitative Measurement Procedures – Second Edition*. CLSI Guideline EP06 CLSI: Wayne, PA, 2020

Clinical Laboratory Standards Institute (CLSI). *Evaluation of the Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition*. CLSI Guideline EP05-A3, CLSI: Wayne, PA, 2014.

Clinical Laboratory Standards Institute (CLSI). *Interference Testing in Clinical Chemistry – Third Edition*. CLSI Guideline EP07, CLSI: Wayne, PA, 2018.

Clinical Laboratory Standards Institute (CLSI). *Supplemental Tables for Interference Testing in Clinical Chemistry – First Edition*. CLSI Guideline EP07, Supplement EP37, CLSI: Wayne, PA, 2018.

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

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 (one operator per instrument), using 3 AMP kit lots (one lot per instrument), for a total of 288 replicates per panel member.

The precision study results in **Table 3** and **Table 4** 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 3. Precision | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | 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 |
| 9 | 287 | 8.2 | 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 | 8.0 | 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 | 7.0 | 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 | 6.0 | 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 | 5.0 | 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 | 4.0 | 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 | 2.7 | 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 | 2.2 | 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 | 1.4 | 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 4. 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 | 169046883 | 10.0 | 9.5 | 0.0 | 10.9 | 17.7 |
| 8 | 287 | 111475841 | 10.7 | 8.2 | 0.0 | 14.9 | 20.2 |
| 7 | 288 | 11275291 | 10.8 | 4.3 | 0.0 | 5.7 | 13.0 |
| 6 | 284 | 1231685 | 11.4 | 6.1 | 0.0 | 9.4 | 16.0 |
| 5 | 287 | 112523 | 10.7 | 6.6 | 1.2 | 10.9 | 16.8 |
| 4 | 287 | 11596 | 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^2)*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.

**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 procedure, 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.

**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 are summarized in **Table 5 and Table 6.**

**Table 5. 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 represe Instrument.

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

**Table 6. Precision using Dilution Procedure**

| | | | CV % | | | | |
|---|---|---|---|---|---|---|---|
| **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 | 3263 | 17.0 | 13.3 | 13.7 | 9.7 | 27.7 |
| 2 | 273 | 81253 | 12.6 | 21.7 | 0.0 | 12.9 | 28.5 |
| 3 | 274 | 51057729 | 14.4 | 21.2 | 0.0 | 9.6 | 27.6 |

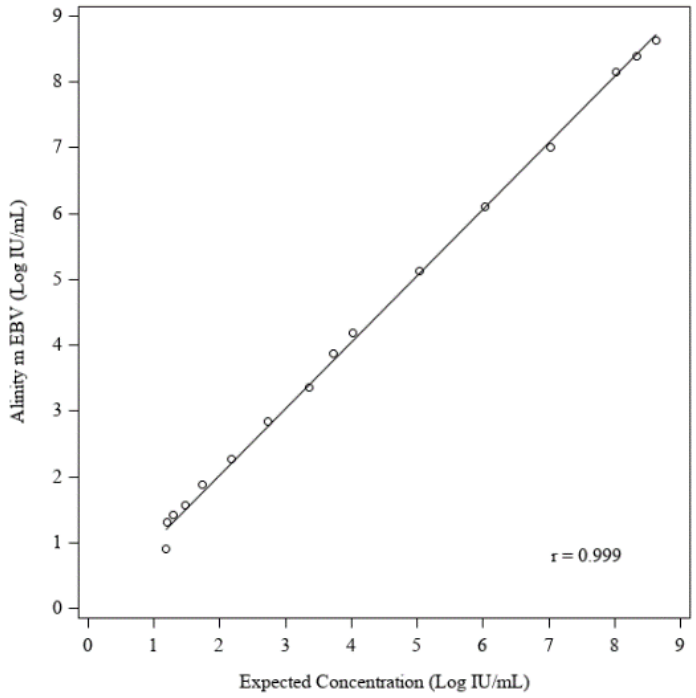
[a] Number of valid replicates with detectable viral load
[b] Titer data are considered to be log-normally distributed and the mean values for titer data are calculated as exp(mean*ln(10)+ (SD^2)*ln(10)^2/2).
[c] Titer data are considered to be log-normally distributed and %CV values are calculated as 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.

2. Linearity:

The quantitation range of Alinity m EBV is from the LLoQ of 50 IU/mL (1.70 Log IU/mL) to the 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). Results for Alinity m EBV linearity performance are shown in **Figure 1.**

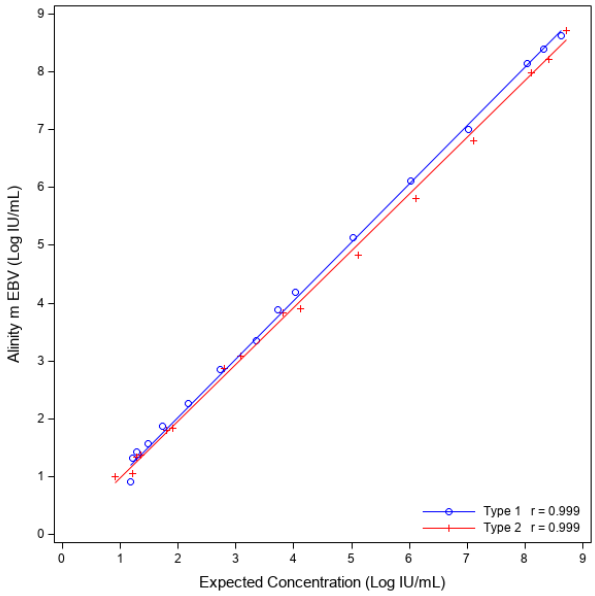
**Figure 1 Alinity m EBV linearity EBV type 1**




[a]Note: The markers in the plot represent the mean Alinity m EBV concentration (Log IU/ml) for each panel member.

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. Results for Alinity m EBV linearity performance for type 2 and for type 1 are shown in **Figure 2.**

**Figure 2. Alinity m EBV linearity EBV type 1 and 2**




3. Lower Limit of Quantitation

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 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 7**.

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 demonstrated that Alinity m EBV can determine the concentration of EBV DNA at 50.00 IU/mL with an acceptable level of accuracy and precision, ie, TAE and TE less than or equal to 1.00 Log IU/mL. In combination with the linearity data this supports a claimed LLoQ of 50.00 IU/mL (1.7 Log IU/mL) for Alinity m EBV.

| Table 7. Total Error | | | | | |
|---|---|---|---|---|---|
| **Target Conc. (Log IU/mL)** | **Mean Conc. (Log IU/mL)** | **Bias[a] (Log IU/mL)** | **SD (Log IU/mL)** | **TAE (Log IU/mL)** | **TE (Log IU/mL)** |
| 1.00 | 1.04 | 0.04 | 0.33 | 0.70 | 0.94 |
| 1.10 | 1.13 | 0.03 | 0.33 | 0.68 | 0.93 |
| 1.18 | 1.18 | -0.00 | 0.30 | 0.61 | 0.85 |
| 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

**Confirmation of the LLoQ Using Dilution Procedure**

LLoQ for Alinity m EBV using the dilution procedure was confirmed by testing 2 panel members 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.

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 8**. 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.

**Table 8. 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

4. Analytical Specificity/Interference:

The analytical specificity of Alinity m EBV was evaluated with a panel of microorganisms (**Table 9)** 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 9. Microorganisms**

| ***Viruses*** | ***Bacteria*** |
|---|---|
| Adenovirus 2 | *Actinomyces israelii* |
| BK polyomavirus | *Clostridium perfringens* |
| Cytomegalovirus (CMV) | *Enterococcus faecalis* |
| 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 | ***Fungus*** |
| Parvo virus B19 | *Aspergillus niger* |
| Simian Virus 40 | *Candida albicans (CA)* |
| Vaccinia virus (VACV) | *Cryptococcus neoformans* |
| Varicella-Zoster virus (VZV) | |

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 10**, at a concentration of 3 times the reported $C_{max}$ or higher.

| Table 10 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. Assay Reportable Range:

   See linearity section #2 above.

6. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   The Alinity m EBV Assay (List No. 09N43) was standardized against the 1st World Health Organization (WHO) International Standard for Epstein-Bar Working Reference Calibrators are prepared from the WHO International Standard r virus for Nucleic Acid Amplification Techniques (NIBSC code: 09/260). Primary Calibrators are prepared by diluting linearized EBV dual target plasmid (pEBV) and EBV DNA concentrations are assigned based on the results of Alinity m EBV testing against the Working Reference Calibrators.

   Stability was established for the Alinity m EBV AMP kit, CTRL Kit, and CAL kit using real time stability studies

**Table 11**. Alinity m EBV assay Proposed Dating at Estimated Time of Premarket Notification Clearance[a]

| Kit | Proposed Expiration Dating |
|---|---|
| Alinity m EBV AMP Kit | 9 months |
| Alinity m EBV CTRL Kit | 9 months |
| Alinity m EBV CAL Kit | 9 months |

[a] AM intends to conduct stability studies in order achieve final dating of 24 months.

7. Detection Limit:

   EBV Type 1: 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 12**.
   Probit analysis of the data determined that the concentration of EBV DNA in plasma detected with 95% probability (LoD by Probit) was 20 IU/mL with a 95% confidence interval (CI) of (11.81 IU/mL, 18.22 IU/mL

| Table 12. EBV type 1 LoD for Each Lot in Plasma | | |
|---|---|---|
| **Lot** | **LoD (IU/mL)** | **95% CI of LoD** |
| 1 | 15.23 | (7.33, 915.12) |
| 2 | 13.70 | (8.56, 37.30) |
| 3 | 19.56 | (13.09, 39.39) |
| 4 | 13.23 | (9.71, 21.39) |

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 13**. 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 limit of detection, 20 IU/ml.

| **Table 13. EBV type 2 LoD for Each Lot in Plasma** | | | |
|---|---|---|---|
| EBV DNA (IU/ml) | No. of Valid Replicates | No. of Detected Replicates | Detection Rate (%) |
| 50 | 24 | 24 | 100 |
| 20 | 23 | 22 | 95.7 |
| 15 | 24 | 23 | 95.8 |

8. Result Reporting and Interpretation

Assay results are reported according to their relationship to LoD, LLoQ and ULoQ as in **Table 14**.

| **Table 14 Results and Interpretation** | | |
|---|---|---|
| **Alinity m System Reported** | | |
| **Result** | **Interpretation** | **Interpretation Additional Information** |
| Not Detected | EBV DNA not detected | |
| <LLoQ | EBV DNA detected but not quantified | EBV DNA concentration is below the Lower Limit of Quantitation (LLoQ) of the assay |
| LLoQ to ≤ULoQ | EBV DNA detected and quantified | EBV DNA concentration is within the linear range of the assay (≥ LLoQ to ≤ ULoQ) |
| >ULoQ | EBV DNA detected | EBV DNA concentration is above the Upper Limit of Quantitation (ULoQ) of the assay. |

9. Carry over

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%).

**B Comparison Studies:**

1. Method Comparison with Predicate Device:

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 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 15** (HSCT samples), **Table 16** (SOT samples) and **Table 17** (HSCT and SOT samples combined).

| Table 15. HSCT - 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** | 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) | (26/26) | (34/34) | (10/10) | (16/16) | (7/7) | (30/30) | |
| **(%)** | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 100.0% | 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 16. SOT Samples - 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** | 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) | (84/84) | (74/75) | (19/19) | (24/25) | (6/6) | (34/34) | |
| **(%)** | 99.3% | 100.0% | 98.7% | 100.0% | 96.0% | 100.0% | 100.0% | 99.3% |
| **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%) | (96.0%, 99.9%) |

[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 17. HSCT and SOT Samples Combined - Agreement Between Alinity m EBV and | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | 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 [b]** | 32 | 80 | 14 | 0 | 0 | 0 | 0 | 126 |
| **LLoQ [b] 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) | (109/109) | (106/107) | (29/29) | (40/41) | (13/13) | (64/64) | |
| **(%)** | 99.5% | 100.0% | 99.1% | 100.0% | 97.6% | 100.0% | 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% CI 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 18** (HSCT samples). and **Table 19** (SOT samples) **Table 20** (HSCT and SOT samples combined).

| Table 18. HSCT Samples - Agreement between Alinity m EBV and Comparator EBV using Different Thresholds | | |
|---|---|---|
| **Threshold** | **Percent Agreement < Threshold (%)** | **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) |

| Table 19. SOT Samples - Agreement between Alinity m EBV and Comparator EBV using Different Thresholds | | |
|---|---|---|
| **Threshold** | **Percent Agreement < Threshold (%)** | **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) |

| Table 20. HSCT and SOT Samples Combined - Agreement between Alinity m EBV and Comparator EBV using Different Thresholds | | |
|---|---|---|
| **Threshold** | **Percent Agreement < Threshold (%)** | **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) |

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. Systematic difference between Alinity m EBV and the comparator at 4 selected viral load levels is shown in **Table 21**.

| **Table 21**. 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 |

2. Matrix Comparison:

Compatibility of Alinity m EBV with specimens collected as plasma in Di-potassium Ethylenediaminetetraacetic Acid ($K_2$ EDTA) tubes, Tri-potassium EDTA ($K_3$ EDTA) tubes, and Plasma Preparation Tubes (PPT) was evaluated.

The acceptance criteria for each sample collection tube type at each EBV positive level tested was met. All valid EBV positive samples targeted at 60-150 IU/mL reported a "Detected" interpretation (100% "Detected" result). The mean difference between the test condition and the control condition across tube types ranged from 0.03 to 0.05 Log IU/mL.

3. Other Clinical Supportive Data:

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 22** and **Table 23** (for the positive panel members) and **Table 24** (for the negative panel member).

**Table 22 Reproducibility for Positive Panel Members**

| | | | Mean Concentration | Within-Run/Day Component | | Between-Run/Day Component | | Within-Laboratory [c] | | Between-Lot Component | | Between-Site/ Instrument Component | | Total [d] | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Panel | N[a] | Target (Log IU/mL) | (Log IU/mL) | 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 23. Reproducibility for Positive Panel Members**

| | | | %CV | | | | |
|---|---|---|---|---|---|---|---|
| **Panel** | **N[a]** | **Mean Concentration[b] (IU/mL)** | **Within-Run/Day Component** | **Between-Run/Day Component** | **Between-Lot Component** | **Between-Site/Instr Component** | **Total[d]** |
| 1 | 178 | 279192220 | 10.6 | 6.4 | 13.0 | 42.8 | 47.1 |
| 2 | 177 | 11407341 | 9.5 | 1.1 | 9.3 | 29.3 | 32.5 |
| 3 | 179 | 586126 | 11.3 | 3.9 | 9.4 | 18.0 | 23.7 |
| 4 | 179 | 112772 | 13.1 | 10.1 | 8.2 | 21.4 | 28.6 |
| 5 | 179 | 10572 | 11.6 | 8.0 | 9.7 | 11.7 | 20.8 |
| 6 | 172 | 1187 | 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^2)*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 24. Overall Agreement for the Negative Reproducibility Panel Member | | | | | |
|---|---|---|---|---|---|
| | Numbers of Replicates | | | | |
| **Panel Member** | **Valid** | **Negative** | **Negative Rate (%)** | **95% Confidence Interval** | **Acceptance Criteria** |
| Negative | 180 | 176 | 97.8 (176/180) | (94.4, 99.1) | Met |

## VIII. Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

## IX. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.