



**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION  
DECISION SUMMARY  
ASSAY AND INSTRUMENT**

**I Background Information:**

**A 510(k) Number**

K241921

**B Applicant**

Abbott Molecular Inc.

**C Proprietary and Established Names**

Alinity m BKV

**D Regulatory Information**

Product Code(s)	Classification	Regulation Section	Panel
QMI	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 clearance for the Alinity m BKV assay.

**B Measurand:**

BK virus (BKV) DNA

**C Type of Test:**

The Alinity m BKV assay is a quantitative Polymerase Chain Reaction (PCR) performed on the automated Alinity m System, for the detection of BKV DNA in transplant patients.

**III Intended Use/Indications for Use:**

#### **A Intended Use(s):**

Alinity m BKV is an in vitro nucleic acid amplification test for the quantitation of BK virus (BKV) DNA in human EDTA plasma (K2 EDTA, K3 EDTA, and PPT) and urine stabilized using the Alinity m Urine Transport Kit on the automated Alinity m System.

In EDTA plasma (K2EDTA, K3EDTA, and PPT) and urine stabilized using the Alinity m Urine Transport Kit, Alinity m BKV is intended for use as an aid in the diagnosis and management of BKV in transplant patients.

In patients undergoing monitoring of BKV in EDTA plasma, 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 BKV must be interpreted in conjunction with clinical signs and symptoms and other relevant laboratory findings. Alinity m BKV is not cleared as a screening test for blood or blood products or human cells, tissues, and cellular and tissue-based products.

#### **B Indication(s) for Use:**

Same as Intended Use

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

Rx - For Prescription Use Only

#### **D Special Instrument Requirements:**

For use with the Alinity m System.

### **IV Device/System Characteristics:**

#### **A Device Description:**

The Alinity m BKV assay is an automated assay for the quantitative detection of BKV genomic DNA in human plasma or urine specimens utilizing real-time polymerase chain reaction (PCR).

Alinity m BKV contain different components: Reagents (PCR amplification, detection, and internal control), Calibrator and Controls. The Alinity m BKV assay requires a transport kit for testing all urine specimens.

#### **B Principle of Operation:**

BKV DNA from human plasma or urine is extracted automatically on board the Alinity m System. The Alinity m System employs magnetic microparticle technology to facilitate nucleic acid capture, wash, and elution. The purified DNA is combined with the Alinity m BKV activation reagent and the Alinity m BKV 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 BKV DNA. In addition to the BKV primers and probes, the assay utilizes an IC primer/probe set for amplification and detection of the IC target sequence, which is not related to BKV. Manual dilutions may be performed for low-volume plasma specimens to

meet the minimum volume requirement. A BKV calibration curve is required for determination of BKV DNA concentration. Two levels of calibrators are processed through sample preparation and PCR to generate the calibration curve. The concentration of BKV DNA in specimens and controls is then calculated from the stored calibration curve. Assay controls (negative, low positive and high positive controls) are tested to ensure that instrument and reagent performance remains satisfactory.

### Interpretation of Results:

Table 1 shows results and interpretation for Alinity m BKV.

**Table 1.** Alinity m BKV Results Interpretation

Alinity m System Reported		
Result	Interpretation	Interpretation Additional Information
Not Detected	BKV DNA not detected	N/A
< LLoQ	BKV DNA detected but not quantified	BKV DNA concentration is below the Lower Limit of Quantitation (LLoQ) of the assay.
$\geq$ LLoQ to $\leq$ ULoQ	BKV DNA detected and quantified	BKV DNA concentration is within the linear range of the assay ( $\geq$ LLoQ to $\leq$ ULoQ).
> ULoQ	BKV DNA detected	BKV DNA concentration is above the Upper Limit of Quantitation (ULoQ) of the assay.

The Lower Limit of Quantitation (LLoQ) and Upper Limit of Quantitation (ULoQ) for both undiluted plasma and urine specimens is 50 IU/mL and 1,000,000,000 IU/mL, respectively. For plasma specimens tested with the dilution procedure, the lowest BKV DNA concentration that can be reported for a diluted plasma specimen is 125 IU/mL (2.10 Log IU/mL).

Urine specimens are tested as stabilized samples using the Alinity m Urine Transport Kit or stabilized samples prepared using the Low Volume Urine Procedure.

## C Instrument Description Information:

### 1. Instrument Name:

Alinity m System

### 2. Specimen Identification:

The following specimen types can be used:

Specimen Type	Collection Tubes
---------------	------------------

Plasma	K <sub>2</sub> EDTA K <sub>3</sub> EDTA Plasma Preparation Tube (PPT)
Urine	Urine specimens must be collected and transferred into the Alinity m Urine Transport Tube by following the instructions in the package insert.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):

cobas BKV

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

K203220

### C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K203220</u>	<u>K241921</u>
Device Trade Name	cobas BKV	Alinity m BKV
General Device Characteristic Similarities		
Intended Use/Indications For Use	<p>cobas BKV is an <i>in vitro</i> nucleic acid amplification test for the quantitation of BK virus (BKV) DNA in human EDTA plasma and urine stabilized in cobas PCR Media on the cobas 6800/8800 Systems.</p> <p>In EDTA plasma, cobas BKV is intended for use as an aid in the management of BKV in transplant patients. In patients undergoing monitoring of BKV in EDTA plasma, serial DNA measurements can be used to indicate the need for potential treatment changes and to assess viral response to treatment.</p> <p>In urine stabilized in cobas PCR Media, cobas BKV is intended for use as an aid in the management of BKV in transplant patients.</p> <p>The results from cobas BKV are intended to be read and analyzed by a qualified licensed healthcare professional in conjunction with clinical signs and symptoms and relevant laboratory findings. Test results must not be the sole basis for patient management decisions.</p> <p>cobas BKV is not intended for use as a screening test for blood or blood</p>	<p>Alinity m BKV is an <i>in vitro</i> nucleic acid amplification test for the quantitation of BK virus (BKV) DNA in human EDTA plasma (K<sub>2</sub> EDTA, K<sub>3</sub> EDTA, and PPT) and urine stabilized using the Alinity m Urine Transport Kit on the automated Alinity m System.</p> <p>In EDTA plasma (K<sub>2</sub>EDTA, K<sub>3</sub>EDTA, and PPT) and urine stabilized using the Alinity m Urine Transport Kit, Alinity m BKV is intended for use as an aid in the diagnosis and management of BKV in transplant patients. In patients undergoing monitoring of BKV in EDTA plasma, serial DNA measurements can be used to indicate the need for potential treatment changes and to assess viral response to treatment.</p> <p>The results from Alinity m BKV must be interpreted in conjunction with clinical signs and symptoms and other relevant laboratory findings. Alinity m BKV is not cleared as a screening test for blood or blood products or human cells,</p>

	products or human cells, tissues, and cellular and tissue-based products (HCT/Ps).	tissues, and cellular and tissue-based products.
Assay Type	Quantitative	Same
Specimen Types	EDTA Plasma, Stabilized Urine	Same
Sample Preparation Procedure	Automated liquid handling and robotic manipulation platform	Same
Amplification Technology	Real-Time polymerase chain reaction (PCR)	Same
Assay Controls	<ul style="list-style-type: none"> <li>• Negative Control</li> <li>• Low Positive Control</li> <li>• High Positive Control</li> <li>• DNA Quantitation Standard (DNA-QS)</li> </ul>	<ul style="list-style-type: none"> <li>• Negative Control</li> <li>• Low Positive Control</li> <li>• High Positive Control</li> <li>• Internal Control (IC)</li> </ul>
<b>General Device Characteristic Differences</b>		
Assay Targets	Dual targets in the BKV genome (small T-antigen and <u>VP2</u> regions)	Dual targets in the BKV genome (2 highly conserved regions of the BKV genome)

## VI Standards/Guidance Documents Referenced:

EP05-A3-Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition

EP06-Evaluation of Linearity of Quantitative Measurement Procedures – Second Edition

EP07-A2-Interference Testing in Clinical Chemistry; Approved Guideline – Second Edition

EP17-A2-Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures; Approved Guideline – Second Edition

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

### A Analytical Performance:

#### 1. Precision/Reproducibility:

##### a. Precision in Plasma (12 days):

Precision of Alinity m BKV was determined by analyzing a 7-member panel prepared in BKV-negative human plasma. 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 results were analyzed according to CLSI EP05-A3 for representative lot are provided in **Table 2**.

**Table 2.** Alinity m BKV Precision in Plasma

Panel Member	N <sup>a</sup>	Mean Concentration (Log IU/mL)	Within-Run		Between-Run		Between-Day		Within-Laboratory <sup>b</sup>		Between-Instrument <sup>c</sup>		Total <sup>d</sup>	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
07	288	7.99	0.047	0.6	0.028	0.3	0.000	0.0	0.054	0.7	0.028	0.4	0.061	0.8
06	286	5.95	0.054	0.9	0.007	0.1	0.019	0.3	0.057	1.0	0.014	0.2	0.059	1.0
05	288	4.89	0.054	1.1	0.024	0.5	0.015	0.3	0.061	1.2	0.015	0.3	0.063	1.3
04	288	3.87	0.070	1.8	0.020	0.5	0.015	0.4	0.075	1.9	0.015	0.4	0.076	2.0
03	287	2.83	0.066	2.3	0.026	0.9	0.000	0.0	0.071	2.5	0.029	1.0	0.077	2.7
02	287	2.32	0.100	4.3	0.027	1.2	0.029	1.2	0.107	4.6	0.035	1.5	0.113	4.9
01	96	1.81	0.103	5.7	0.025	1.4	0.000	0.0	0.106	5.9	0.000	0.0	0.106	5.9

<sup>a</sup> Valid replicates within the quantitation range.

<sup>b</sup> Within-Laboratory includes Within-Run, Between-Run, and Between-Day Components.

<sup>c</sup> Alinity m System (instrument), AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Between-Instrument Component.

<sup>d</sup> Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

b. Precision of Alinity m BKV Plasma Testing Using Dilution Procedure (12 days)

Precision of Alinity m BKV using the dilution procedure was determined by analyzing 3 plasma panel members. The results are summarized in **Table 3**.

**Table 3.** Precision of Alinity m BKV EDTA Plasma Testing Using Dilution Procedure

Panel Member	N <sup>a</sup>	Mean Concentration (Log IU/mL)	Within-Run		Between-Run		Between-Day		Within-Laboratory <sup>b</sup>		Between-Instrument <sup>c</sup>		Total <sup>d</sup>	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
01	287	3.50	0.054	1.5	0.050	1.4	0.038	1.1	0.083	2.4	0.000	0.0	0.083	2.4
02	286	4.82	0.112	2.3	0.067	1.4	0.065	1.3	0.146	3.0	0.000	0.0	0.146	3.0
03	287	7.98	0.049	0.6	0.030	0.4	0.000	0.0	0.057	0.7	0.021	0.3	0.061	0.8

<sup>a</sup> Valid replicates

<sup>b</sup> Within-Laboratory includes Within-Run, Between-Run, and Between-Day Components.

<sup>c</sup> Alinity m System (instrument), AMP Kit lot, Specimen Dilution Kit I lot, and Operator are confounded, and the confounding effect is represented by Between-Instrument Component.

<sup>d</sup> Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

c. Precision in Urine (12-days):

Precision of Alinity m BKV was determined by analyzing an 8-member panel prepared in BKV-negative stabilized human urine. All panel members were prepared using clinical specimens. 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 results were analyzed according to CLSI EP05-A3 for representative lot and are provided in **Table 4**.

**Table 4.** Alinity m BKV Precision in Urine

Panel Member	N <sup>a</sup>	Mean Concentration (Log IU/mL)	Within-Run		Between-Run		Between-Day		Within-Laboratory <sup>b</sup>		Between-Instrument <sup>c</sup>		Total <sup>d</sup>	
			SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV	SD	%CV
08	287	8.23	0.051	0.6	0.033	0.4	0.000	0.0	0.060	0.7	0.041	0.5	0.073	0.9
07	287	6.19	0.056	0.9	0.031	0.5	0.000	0.0	0.064	1.0	0.021	0.3	0.067	1.1
06	283	5.11	0.077	1.5	0.037	0.7	0.021	0.4	0.088	1.7	0.009	0.2	0.088	1.7
05	284	4.11	0.066	1.6	0.028	0.7	0.030	0.7	0.078	1.9	0.000	0.0	0.078	1.9
04	283	3.05	0.088	2.9	0.043	1.4	0.015	0.5	0.099	3.3	0.000	0.0	0.099	3.3
03	285	2.53	0.081	3.2	0.039	1.6	0.029	1.1	0.094	3.7	0.001	0.1	0.094	3.7
02	177	1.83	0.085	4.6	0.027	1.5	0.019	1.0	0.091	5.0	0.021	1.1	0.093	5.1
01	54	1.79	0.054	3.0	0.040	2.2	0.000	0.0	0.067	3.8	0.000	0.0	0.067	3.8

<sup>a</sup> Valid replicates within the quantitation range.

<sup>b</sup> Within-Laboratory includes Within-Run, Between-Run, and Between-Day Components.

<sup>c</sup> Alinity m System (instrument), AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Between-Instrument Component.

<sup>d</sup> Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

d. Reproducibility in Plasma:

Reproducibility performance of Alinity m BKV was evaluated by testing a 9-member reproducibility panel, including 8 positive panel members and 1 negative panel member at 3 clinical sites on 5 days. Six replicates of each panel member were tested on each of the 5 days. The reproducibility results for positive panel members are summarized in **Table 5**.

**Table 5.** Reproducibility for Positive Panel Members – EDTA Plasma

Panel	N <sup>a</sup>	Mean Concentration (Log IU/mL)	Within-Run/Day		Between-Run/Day		Within Laboratory <sup>c</sup>		Between-Lot		Between-Site/Instrument <sup>c</sup>		Total <sup>d</sup>	
			SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV
1	178	8.13	0.06	0.7	0.03	0.3	0.06	0.8	0.07	0.9	0.00	0.0	0.09	1.2
2	180	7.40	0.05	0.7	0.02	0.3	0.06	0.8	0.08	1.1	0.00	0.0	0.10	1.3
3	177	5.87	0.06	1.0	0.03	0.5	0.07	1.1	0.05	0.8	0.00	0.0	0.08	1.4
4	179	4.91	0.06	1.2	0.02	0.5	0.07	1.3	0.03	0.6	0.00	0.0	0.07	1.5
5	178	3.94	0.07	1.7	0.06	1.4	0.09	2.2	0.01	0.3	0.06	1.5	0.11	2.7
6	178	3.03	0.09	2.9	0.03	0.8	0.09	3.0	0.02	0.6	0.06	2.1	0.11	3.7
7	167	1.95	0.11	5.5	0.05	2.5	0.12	6.1	0.00	0.0	0.06	3.1	0.13	6.8
8	47	1.77	0.07	4.2	0.00	0.0	0.07	4.2	0.02	0.9	0.02	1.2	0.08	4.4

<sup>a</sup> Number of valid replicates within the quantitation range.

<sup>b</sup> Standard deviations (SD) are in Log IU/mL.

<sup>c</sup> Within-Laboratory includes Within-Run/Day and Between-Run/Day Components.

<sup>d</sup> Total includes Within-Run/Day, Between-Run/Day, Between-Lot, and Between-Site/Instrument Components.

e. Reproducibility in Urine:

Reproducibility performance of Alinity m BKV was evaluated by testing a 9-member reproducibility panel, including 8 positive panel members and 1 negative panel member in urine stabilized in Alinity m Urine Transport Kit at 3 clinical sites on 5 days. Six replicates of each panel member were tested on each of the 5 days. The reproducibility results are summarized in **Table 6** for the positive panel members.

**Table 6.** Reproducibility for Positive Panel Members – Urine

Panel	N <sup>a</sup>	Mean Concentration (Log IU/mL)	Within-Run/Day		Between-Run/Day		Within Laboratory <sup>c</sup>		Between-Lot		Between-Site/Instrument		Total <sup>d</sup>	
			SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV	SD <sup>b</sup>	%CV
1	178	8.69	0.05	0.5	0.02	0.3	0.05	0.6	0.01	0.1	0.11	1.3	0.12	1.4
2	180	7.29	0.05	0.7	0.02	0.3	0.06	0.8	0.02	0.3	0.08	1.1	0.10	1.4
3	179	5.91	0.05	0.9	0.02	0.4	0.06	1.0	0.01	0.2	0.06	1.0	0.08	1.4
4	178	5.45	0.06	1.1	0.04	0.7	0.07	1.3	0.01	0.3	0.07	1.3	0.10	1.9
5	177	4.47	0.06	1.4	0.03	0.8	0.07	1.6	0.04	0.8	0.07	1.6	0.11	2.4
6	179	3.00	0.17	5.6	0.05	1.7	0.18	5.9	0.00	0.0	0.04	1.3	0.18	6.0
7	175	2.29	0.08	3.6	0.02	1.0	0.08	3.7	0.01	0.6	0.06	2.4	0.10	4.4
8	169	1.95	0.23	11.6	0.00	0.0	0.23	11.6	0.03	1.7	0.00	0.0	0.23	11.7

<sup>a</sup> Number of valid replicates within the quantitation range.

<sup>b</sup> Standard deviations (SD) are in Log IU/mL.

<sup>c</sup> Within-Laboratory includes Within-Run/Day and Between-Run/Day Components.

<sup>d</sup> Total includes Within-Run/Day, Between-Run/Day, Between-Lot, and Between-Site/Instrument Components.

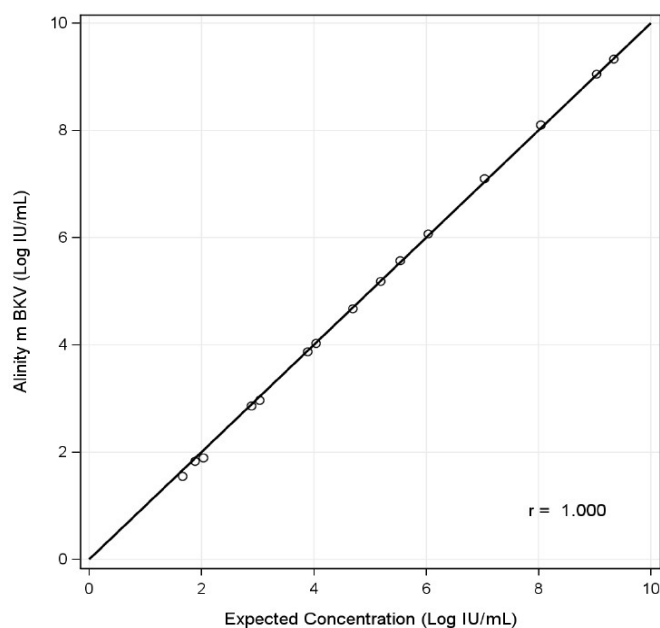
## 2. Linearity

### a. Linearity in Plasma:

The quantitation range of Alinity m BKV for plasma 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 1,000,000,000 IU/mL (9.00 Log IU/mL). Linearity of Alinity m BKV was assessed by testing a dilution series of BKV subgroup Ib in BKV-negative human plasma, consisting of 15 panel levels targeted in the range of 30 IU/mL to 2,000,000,000 IU/mL (1.48 Log IU/mL to 9.30 Log IU/mL). Plasma panel was prepared either using the international standard material for BK virus (NIBSC code: 14/212, subgroup Ib) for multiple levels ranging from 30 IU/mL to 100,000 IU/mL (1.48 Log IU/mL to 5.00 Log IU/mL) or using armored DNA for the remaining levels ranging from 100 IU/mL to 2,000,000,000 IU/mL (2.00 Log IU/mL to 9.30 Log IU/mL). Results were analyzed according to CLSI EP06, 2<sup>nd</sup> Edition. Alinity m BKV was linear across the quantitation range from 50 IU/mL (1.70 Log IU/mL) to 1,000,000,000 IU/mL (9.00 Log IU/mL) in plasma. Representative results for Alinity m BKV linearity performance are shown in **Figure 1**.



**Figure 1. Alinity m BKV Linearity in Plasma<sup>a</sup>**



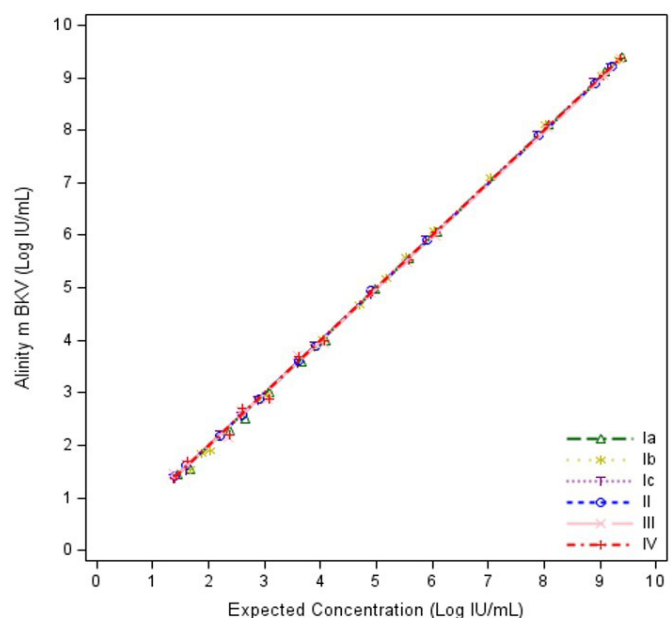
<sup>a</sup> Note: The markers in the plot represent the mean Alinity m BKV concentration (in Log IU/mL) for each panel level.

b. Linearity for Genotypes in Plasma:

Linearity of Alinity m BKV for subgroups/subtypes Ia, Ic, II, III, and IV was confirmed by testing a dilution series in BKV-negative human plasma, consisting of 13 panel levels for subgroup/subtypes Ia, III, and IV and 12 panel levels for subgroup/subtype Ic and II, targeted in the range of 30 IU/mL to 2,000,000,000 IU/mL (1.48 Log IU/mL to 9.30 Log IU/mL). For subgroup/subtypes Ia, III, and IV, plasma panel was prepared either using clinical specimens for multiple levels ranging from 30 IU/mL to 100,000 IU/mL (1.48 Log IU/mL to 5.00 Log IU/mL) or using armored DNA for the remaining levels ranging from 200 IU/mL to 2,000,000,000 IU/mL (2.30 Log IU/mL to 9.30 Log IU/mL). For subgroup/subtype Ic and II, plasma panel was prepared using armored DNA for all levels ranging from 30 IU/mL to 2,000,000,000 IU/mL (1.48 Log IU/mL to 9.30 Log IU/mL).

Alinity m BKV was linear in plasma across the quantitation range from 50 IU/mL (1.70 Log IU/mL) to 1,000,000,000 IU/mL (9.00 Log IU/mL) for subgroups/subtypes Ia, Ic, II, III, and IV. Representative results for Alinity m BKV linearity performance for subgroups/subtypes Ia, Ic, II, III, and IV, along with results for subgroup Ib (**Figure 1**), are shown in **Figure 2**.

**Figure 2. Alinity m BKV Linearity for Genotypes in Plasma<sup>a</sup>**



<sup>a</sup> Note: The markers in the plot represent the mean Alinity m BKV concentration (in Log IU/mL) for each panel level.

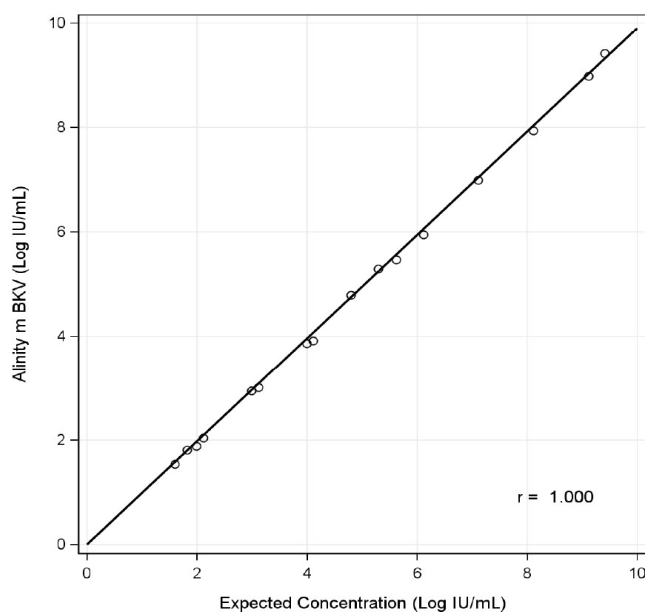
c. Linearity for Urine:

The quantitation range of Alinity m BKV for urine 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 1,000,000,000 IU/mL (9.00 Log IU/mL). Linearity of Alinity m BKV was assessed by testing a dilution series of BKV subgroup Ib in BKV-negative stabilized urine, consisting of 16 panel levels targeted in the range of 30 IU/mL to 3,000,000,000 IU/mL (1.48 Log IU/mL to 9.48 Log IU/mL).

Urine panel was prepared either using international standard material for BK virus (NIBSC code: 14/212, subgroup Ib) for multiple levels ranging from 30 IU/mL to 150,000 IU/mL (1.48 Log IU/mL to 5.18 Log IU/mL) or using armored DNA for the remaining levels ranging from 150 IU/mL to 3,000,000,000 IU/mL (2.18 Log IU/mL to 9.48 Log IU/mL).

Alinity m BKV was linear across the quantitation range from 50 IU/mL (1.70 Log IU/mL) to 1,000,000,000 IU/mL (9.00 Log IU/mL). Representative results for Alinity m BKV linearity performance are shown in **Figure 3**.

**Figure 3.** Alinity m BKV Linearity in Urine <sup>a</sup>



<sup>a</sup> Note: The markers in the plot represent the mean Alinity m BKV concentration (in Log IU/mL) for each panel level.

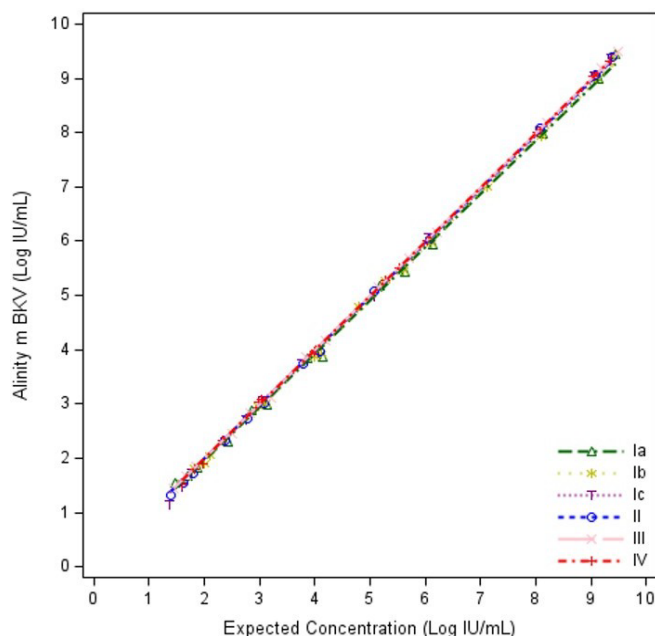
d. Linearity for Genotypes in Urine:

Linearity of Alinity m BKV for subgroups/subtypes Ia, Ic, II, III, and IV was confirmed by testing a dilution series in BKV-negative stabilized urine, consisting of 14 panel levels for subgroup/subtypes Ia, III, and IV and 13 panel levels for subgroup/subtype Ic and II, targeted in the range of 30 IU/mL to 3,000,000,000 IU/mL (1.48 Log IU/mL to 9.48 Log IU/mL).

For subgroup/subtypes Ia, III, and IV, urine panel was prepared either using clinical specimens for multiple levels ranging from 30 IU/mL to 150,000 IU/mL (1.48 Log IU/mL to 5.18 Log IU/mL) or using armored DNA for the remaining levels ranging from 300 IU/mL to 3,000,000,000 IU/mL (2.48 Log IU/mL to 9.48 Log IU/mL). For subgroup/subtype Ic and II, urine panel was prepared using armored DNA for all levels ranging from 30 IU/mL to 3,000,000,000 IU/mL (1.48 Log IU/mL to 9.48 Log IU/mL).

Alinity m BKV was linear in urine across the quantitation range from 50 IU/mL (1.70 Log IU/mL) to 1,000,000,000 IU/mL (9.00 Log IU/mL) for subgroups/subtypes Ia, Ic, II, III, and IV. Representative results for Alinity m BKV linearity performance for subgroups/subtypes Ia, Ic, II, III, and IV, along with results for subgroup Ib (**Figure 3**), are shown in **Figure 4**.

**Figure 4.** Alinity m BKV Linearity for Genotypes in Urine <sup>a</sup>



<sup>a</sup> Note: The markers in the plot represent the mean Alinity m BKV concentration (in Log IU/mL) for each panel level.

### 3. Lower Limit of Quantitation (LLoQ)

#### a. LLoQ in Plasma

The LLoQ is defined as the lowest concentration at which BKV DNA is reliably quantitated within an acceptable total error of  $\leq 1.00$  Log IU/mL. Total error was estimated for detected plasma samples from the LoD study by 2 methods:

Total Analytical Error (TAE) =  $|\text{bias}| + 2 \times \text{SD}$ , and

Total Error (TE) =  $\text{SQRT}(2) \times 2 \times \text{SD}$ .

Panel members were dilutions of the international standard material for BK Virus (NIBSC code: 14/212, subgroup Ib) prepared in BKV-negative plasma. The results of the calculations are shown in **Table 7** and support a claimed LLoQ for Alinity m BKV of 50 IU/mL (1.70 Log IU/mL) in plasma.

**Table 7.** TAE and TE for Plasma

Target Concentration (Log IU/mL)	Mean Concentration (Log IU/mL)	Bias <sup>a</sup> (Log IU/mL)	SD (Log IU/mL)	TAE (Log IU/mL)	TE (Log IU/mL)
1.60	1.59	-0.01	0.22	0.45	0.63
1.70	1.71	0.01	0.22	0.44	0.61
1.78	1.79	0.01	0.21	0.43	0.59

<sup>a</sup> Bias = Mean Concentration – Target Concentration

#### b. Confirmation of LLoQ using Plasma Dilution Procedure

Confirmation testing for Alinity m BKV LLoQ using the dilution procedure was performed by testing 2 panel members at 125 IU/mL ( $2.5 \times \text{LLoQ}$ ) and 150 IU/mL ( $3 \times \text{LLoQ}$ ) with a dilution factor of 1:2.5. The BKV concentrations in the panel members were targeted at 50 IU/mL (LLoQ) and 60 IU/mL (near LLoQ). Panel members were dilutions of the international standard material for BK Virus (NIBSC code: 14/212, subgroup Ib) prepared in BKV-negative plasma.

Total error was estimated by TAE and TE, as shown in **Table 8**. The accuracy and precision at 50 IU/mL and 60 IU/mL were confirmed for Alinity m BKV testing using the 1:2.5 dilution procedure.

**Table 8.** Total Error Using Plasma Dilution Procedure

Panel Member	Target Concentration Neat (Log IU/mL)	Dilution Factor	Target Concentration in Specimen Diluent (Log IU/mL)	Mean Concentration <sup>a</sup> (Log IU/mL)	Bias <sup>b</sup> (Log IU/mL)	SD (Log IU/mL)	TAE (Log IU/mL)	TE (Log IU/mL)
1	2.10	2.5	1.70	2.04	-0.06	0.17	0.40	0.49
2	2.18	2.5	1.78	2.13	-0.05	0.15	0.35	0.44

<sup>a</sup> Reported concentration for neat samples

<sup>b</sup> Bias = Mean Concentration – Target Concentration Neat

c. LLoQ in Urine

The LLoQ is defined as the lowest concentration at which BKV DNA is reliably quantitated within an acceptable total error of  $\leq 1.00$  Log IU/mL.

Total error was estimated for detected urine samples from the LoD study by 2 methods:

Total Analytical Error (TAE) =  $|\text{bias}| + 2 \times \text{SD}$ , and

Total Error (TE) =  $\text{SQRT}(2) \times 2 \times \text{SD}$ .

Panel members were dilutions of the international standard material for BK Virus (NIBSC code: 14/212, subgroup Ib) prepared in BKV-negative urine stabilized in Alinity m Urine Transport Kit. The results of the calculations are shown in **Table 9** and support a claimed LLoQ for Alinity m BKV of 50 IU/mL (1.70 Log IU/mL) in urine.

**Table 9.** TAE and TE for Urine

Target Concentration (Log IU/mL)	Mean Concentration (Log IU/mL)	Bias <sup>a</sup> (Log IU/mL)	SD (Log IU/mL)	TAE (Log IU/mL)	TE (Log IU/mL)
1.35	1.39	0.04	0.25	0.54	0.70
1.65	1.70	0.05	0.18	0.40	0.50
1.78	1.84	0.06	0.14	0.34	0.41

<sup>a</sup> Bias = Mean Concentration – Target Concentration

4. Analytical Specificity/Interference:

a. Cross Reactivity in Plasma.

The analytical specificity of Alinity m BKV was evaluated with a panel of microorganisms (**Table 10**) in BKV-negative plasma, positive plasma targeted to 150 IU/mL BKV DNA, and positive plasma targeted to 10,000 IU/mL BKV DNA. Microorganisms were tested at a final concentration of at least 10<sup>5</sup> Units/mL for viruses and fungi, or at least 10<sup>6</sup> Units/mL for bacteria. No cross-reactivity or interference in the performance of the Alinity m BKV assay was observed in the presence of the tested microorganisms.

**Table 10. Microorganisms Tested in Plasma**

<b>Viruses</b>		
Adenovirus 5	Herpesvirus 8 (Kaposi's sarcoma associated virus)	Human T-cell Lymphotropic Virus (HTLV)
Cytomegalovirus (CMV)	Human Immunodeficiency Virus 1 (HIV-1)	Influenza A Virus
Epstein-Barr Virus (EBV)	Human Immunodeficiency Virus 2 (HIV-2)	JC Polyomavirus
Hepatitis B Virus (HBV)	Human Papillomavirus 16 (HPV-16)	Parvovirus B19
Hepatitis C Virus (HCV)	Human Papillomavirus 18 (HPV-18)	Simian Virus 40
Herpesvirus 6	Herpes Simplex Virus 1 (HSV-1)	Vaccinia Virus (VACV)
Herpesvirus 7	Herpes Simplex Virus 2 (HSV-2)	Varicella-Zoster Virus (VZV)
<b>Bacteria</b>		<b>Fungi</b>
<i>Actinomyces israelii</i>	<i>Mycoplasma pneumoniae</i>	<i>Aspergillus niger</i>
<i>Chlamydia trachomatis</i>	<i>Neisseria gonorrhoeae</i>	<i>Candida albicans</i>
<i>Clostridium perfringens</i>	<i>Salmonella enterica</i>	<i>Cryptococcus neoformans</i>
<i>Cutibacterium acnes</i>	<i>Salmonella typhimurium</i>	
<i>Enterococcus faecalis</i>	<i>Staphylococcus aureus</i>	
<i>Escherichia coli</i>	<i>Staphylococcus epidermidis</i>	
<i>Klebsiella pneumoniae</i>	<i>Streptococcus pneumoniae</i>	
<i>Listeria monocytogenes</i>	<i>Streptococcus pyogenes</i>	
<i>Mycobacterium avium</i>		

**b. Cross Reactivity in Urine.**

The analytical specificity of Alinity m BKV was evaluated with a panel of microorganisms (**Table 11**) in BKV-negative urine, positive urine targeted to 150 IU/mL BKV DNA, and positive urine targeted to 1,000,000 IU/mL BKV DNA. Microorganisms were tested at final concentrations of at least 10<sup>5</sup> Units/mL for viruses and fungi or at least 10<sup>6</sup> Units/mL for bacteria and protozoa. No cross-reactivity or interference in the performance of the Alinity m BKV assay was observed in the presence of the tested microorganisms.

**Table 11. Microorganisms Tested in Urine**

<b>Bacteria</b>		
<i>Bacillus cereus</i>	<i>Lactobacillus acidophilus</i>	<i>Staphylococcus aureus</i>
<i>Bacillus subtilis</i>	<i>Lactobacillus crispatus</i>	<i>Staphylococcus epidermidis</i>
<i>Chlamydia trachomatis</i>	<i>Lactobacillus jensenii</i>	<i>Staphylococcus saprophyticus</i>
<i>Corynebacterium diphtheriae</i>	<i>Lactobacillus vaginalis</i>	<i>Streptococcus agalactiae</i>
<i>Enterobacter cloacae</i>	<i>Morganella morganii</i>	<i>Streptococcus bovis</i>
<i>Enterococcus faecalis</i>	<i>Mycoplasma genitalium</i>	<i>Streptococcus oralis/viridans</i>
<i>Enterococcus faecium</i>	<i>Neisseria gonorrhoeae</i>	<i>Streptococcus pneumoniae</i>
<i>Escherichia coli</i>	<i>Proteus mirabilis</i>	<i>Treponema pallidum</i> <sup>a</sup>

<i>Klebsiella pneumoniae</i>	<i>Pseudomonas aeruginosa</i>	<i>Ureaplasma urealyticum</i>
<b>Fungi</b>	<b>Viruses</b>	<b>Protozoa</b>
<i>Candida albicans</i>	Herpes Simplex Virus-2 (HSV-2)	<i>Trichomonas vaginalis</i>
<i>Candida glabrata</i>	Human Papillomavirus 16 (HPV-16)	
<i>Candida parapsilosis</i>		
<i>Candida tropicalis</i>		

<sup>a</sup> *T. pallidum* was not a whole organism and was only attainable as synthetic partial genome.

c. Potentially Interfering Substances in Plasma

The effects of endogenous substances, the presence of autoimmune diseases, and the presence of high levels of therapeutic drugs commonly prescribed in transplant patients were evaluated. Potential interference on Alinity m BKV performance in plasma was assessed by testing a minimum of 8 samples at each BKV DNA level: negative, 150 IU/mL, and 10,000 IU/mL. No interference was observed in the presence of albumin (60 mg/mL), 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 for specimens collected from patients with the following disease states: systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and anti-nuclear antibodies (ANA).

No interference was observed in the presence of drug compounds tested in pools as listed in **Table 12** at a concentration of 3 times the reported  $C_{max}$  or higher.

**Table 12.** Drug Compounds Tested in Plasma

Drug Pool	Drug Compounds
1	Abacavir Sulfate, Acyclovir, Amoxicillin, Atenolol, Azathioprine, Cefotetan, Cidofovir, Cyclosporine, Everolimus, Fluconazole, Ganciclovir, Leflunomide, Letemovir, Miconazole, Mycophenolate Mofetil, Mycophenolic acid, Piperacillin, Prednisone, Sirolimus, Sulfamethoxazole, Tacrolimus, Tazobactam Sodium, Trimethoprim, Valacyclovir, Valganciclovir, Vancomycin
2	Clavulanate, Foscarnet

d. Potentially Interfering Substances in Urine

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 BKV performance in urine was assessed by testing a minimum of 8 samples at each BKV DNA level: negative, 150 IU/mL, and 1,000,000 IU/mL. No interference was observed in the presence of albumin (90 mg/mL), conjugated bilirubin (1000 mg/dL), glucose (1500 mg/dL), mucus (0.4% w/v), acidic pH (pH 4.0), basic pH (pH 9.0), semen (5.0% v/v), whole blood (10% v/v), sodium (450 mEq/L) or peripheral blood mononuclear cells (PBMCs) ( $1 \times 10^5$  cells/mL) that were introduced in the sample. Interference was observed with mucus at  $>0.4\%$  w/v and with PBMCs at  $>1 \times 10^5$  cells/mL.

No interference was observed in the presence of drug compounds tested in pools or individually at the concentrations shown in **Table 13**.

<b>Table 13. Drug Compounds Tested in Urine</b>		
<b>Drug Pool</b>	<b>Drug Compound</b>	<b>Tested Concentration</b>
1	Metronidazole	1079 µmol/L
	Phenazopyridine Hydrochloride	300 µg/mL
	Acetaminophen	1986 µmol/L
	Acetylsalicylic Acid (Aspirin)	5.43 mmol/L
	Naproxen	3255 µmol/L
	Ibuprofen	3638 µmol/L
	Talc	0.15% w/v
2	Clotrimazole	150 µg/mL
3	Propylene Glycol	1500 µg/mL
4	Beta Estradiol	6.62 nmol/L
5	Abacavir sulfate	0.014 mg/mL
	Amoxicillin	0.905 mg/mL
	Atenolol	0.050 mg/mL
	Azathioprine	0.337 mg/mL
	Cefotetan	5.36 mg/mL
	Cyclosporine	0.0002 mg/mL
	Everolimus	0.001 mg/mL
	Ganciclovir	0.137 mg/mL
	Leflunomide	0.1 mg/mL
	Micafungin	0.002 mg/mL
	Sirolimus	0.000088 mg/mL
	Sulfamethoxazole	2.88 mg/mL
	Tacrolimus	0.0003 mg/mL
	Trimethoprim	1.152 mg/mL
	Valacyclovir	4.095 mg/mL
	Valganciclovir HCl	0.1365 mg/mL
	Vancomycin	3 mg/mL
6	Cidofovir	6.75 mg/mL
	Fluconazole	2.24 mg/mL
	Piperacillin	19.20 mg/mL
	Tazobactam sodium	2.4 mg/mL
7	Clavulanate potassium	0.0343 mg/mL
	Foscarnet	12.83 mg/mL
8	Letermovir	0.019 mg/mL

5. Assay Reportable Range:

Based on the linearity study, the reportable range of the Alinity m BKV assay in plasma and urine is 50 IU/mL (1.70 Log IU/mL) to 1,000,000,000 IU/mL (9.00 Log IU/mL).

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

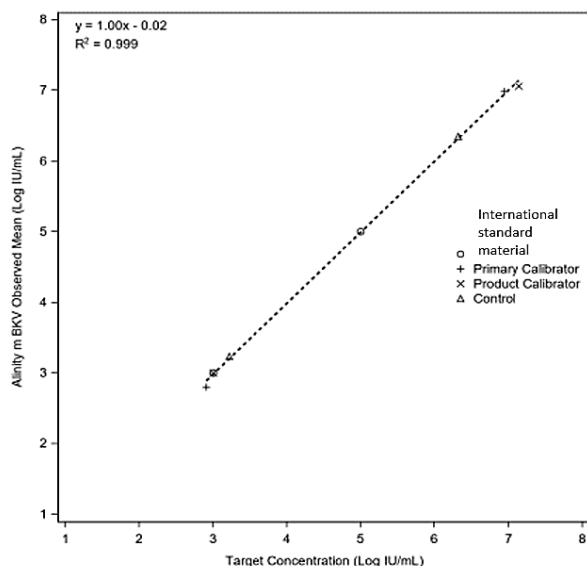
Traceability

Primary calibrators and assay product calibrators with known concentrations were used throughout product development and product manufacturing to establish traceability to the international standard material for BK virus (NIBSC code: 14/212, subgroup Ib). The



concentrations tested for the international standard material were 3.00 Log IU/mL and 5.00 Log IU/mL. The target concentrations tested for the primary calibrators were 2.91 Log IU/mL and 6.94 Log IU/mL. The Alinity m BKV product calibrators and controls were also tested along with the primary calibrators and the international standard material. All the tested material had observed BKV concentrations similar to the target concentrations and were linear across the assay's quantitation range, as presented in **Figure 5**.

**Figure 5.** Traceability to international standard material



### Sample Stability

The data submitted support the following storage conditions:

**Table 14.** Specimen Storage

Specimen	Temperature	Maximum Storage Time
Whole Blood	2°C to 8°C	5 days
	15°C to 30°C	1 day
Plasma*	2°C to 8°C	5 days
	15°C to 30°C	1 day
Neat Urine	2°C to 30°C	1 day
Stabilized Urine	2°C to 30°C	90 days

\* Plasma can be subjected to at most 1 freeze-thaw cycle.

### Reagent Stability

The data submitted support the following storage condition for the Alinity m BKV:

**Table 15.** Alinity m BKV storage conditions

Stability Study	Kit	Expiration Dates
Reagent in-Use/Opened	Alinity m BKV AMP Kit	15 months
	Alinity m BKV CTRL Kit	15 months
	Alinity m BKV CAL Kit	15 months
	Alinity m Urine Transport Kit	15 months
Reagent On-Board	Alinity m BKV AMP Kit	15 days
	Alinity m BKV CTRL Kit	4 hours
	Alinity m BKV CAL Kit	4 hours

7. Detection Limit:

a. Detection Limit for Plasma Samples:

The Limit of Detection (LoD) was determined by testing dilutions of the international standard material for BK virus for Nucleic Acid Amplification Techniques (NIBSC code: 14/212, subgroup Ib) prepared in BKV-negative human plasma. Eight panel members with BKV concentration ranging from approximately 2.0 to 60.0 IU/mL were tested. Testing for each BKV DNA concentration was performed with 3 lots of amplification reagents across multiple days in a minimum of 30 replicates per each panel member. The LoD was estimated from the detection rate and probit analysis. The claimed LoD of Alinity m BKV is 50 IU/mL (1.70 Log IU/mL) in plasma.

b. Detection Limits for Genotypes in Plasma.

BKV armored DNA for subgroup Ic and subtype II and clinical specimens for BKV subgroup Ia and subtypes III and IV were diluted to 3 different concentrations (30, 50, and 60 IU/mL) in BKV-negative human plasma using one lot of amplification reagents. The results demonstrated the ability of Alinity m BKV to detect BKV subgroups Ia and Ic and subtypes II, III, and IV at the claimed LoD of 50 IU/mL (1.70 Log IU/mL) in plasma.

c. Detection Limit for Urine Samples.

The LoD was determined by testing dilutions of the international standard material for BK virus (NIBSC code: 14/212, subgroup Ib) prepared in BKV negative urine stabilized in transport buffer (Alinity m Urine Transport Kit). Nine panel members with BKV concentration ranging from approximately 3.0 to 330.0 IU/mL were tested. Testing for each BKV DNA concentration was performed with 3 lots of amplification reagents across multiple days. The claimed LoD of Alinity m BKV is 50 IU/mL (1.70 log IU/mL) in neat urine.

d. Detection Limits for Genotypes in Urine.

BKV armored DNA for subgroup Ic and subtype II and clinical specimens for BKV subgroup Ia and subtypes III and IV were diluted to 5 different concentrations in BKV-negative stabilized urine, ranging from approximately 45.0 to 330.0 IU/mL. Testing was performed using one lot of amplification reagents across multiple days. Alinity m BKV detected 95% or greater of BKV samples at and above 45 IU/mL (1.65 Log IU/mL) in urine. The results

demonstrated the ability of Alinity m BKV the ability of Alinity m BKV to detect BKV subgroups Ia and Ic and subtypes II, III, and IV at the claimed LoD of 50 IU/mL (1.70 Log IU/mL) in urine.

8. Assay Cut-Off:

Not applicable

9. Accuracy (Instrument):

Not applicable

10. Carry-Over:

The Alinity m BKV is not susceptible to sample carryover.

## B Comparison Studies:

1. Method Comparison with Predicate Device:

a. Performance for Plasma Sample Type.

Alinity m BKV results were compared to those of an FDA-cleared BKV nucleic acid test in a representative study. A total of 579 EDTA plasma clinical specimens (555 neat and 24 diluted clinical specimens from 556 subjects) collected from solid organ transplant (SOT) and hematopoietic stem cell transplant (HSCT) subjects were included in the analysis. The Alinity m BKV assay testing was performed at 4 clinical testing sites with 4 Alinity m BKV reagent lots. The agreement between Alinity m BKV and comparator results is shown in **Table 16**.

**Table 16.** Agreement Between Alinity m BKV and Comparator – Plasma

Alinity m BKV (Log IU/mL)	Comparator BKV (Log IU/mL)							Total
	Target not detected (TND)	<LLoQ <sup>a</sup> (<1.7)	1.7 to <2.3	2.3 to <3.0	3.0 to <3.7	3.7 to <4.4	≥ 4.4	
Target not detected (TND)	264	13	1	0	0	0	0	278
<LLoQ (<1.7)	6	16	10	1	0	0	0	33
1.7 to <2.3	0	0	4	19	0	0	0	23
2.3 to <3.0	0	0	0	63	21	0	0	84
3.0 to <3.7	0	0	0	3	76	10	0	89
3.7 to <4.4	0	0	0	1	5	33	3	42
≥ 4.4	0	0	0	0	0	3	27	30
Total	270	29	15	87	102	46	30	579
Agreement (%)	(270/270) 100%	(29/29) 100%	(14/15) 93.3%	(85/87) 97.7%	(102/102) 100%	(46/46) 100%	(30/30) 100%	
95% CI	98.6%, 100%	88.3%, 100%	70.2%, 98.8%	92.0%, 99.4%	96.4%, 100%	92.3%, 100%	88.6%, 100%	

<sup>a</sup> The LLoQ used here is the higher LLoQ between Alinity m BKV 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 BKV Target Not Detected and <LLoQ cells were combined. Agreement between Alinity m BKV assay and the comparator assay was also evaluated using different clinical thresholds (**Table 17**).

**Table 17.** Agreement Between Alinity m BKV and Comparator Using Different Thresholds – Plasma

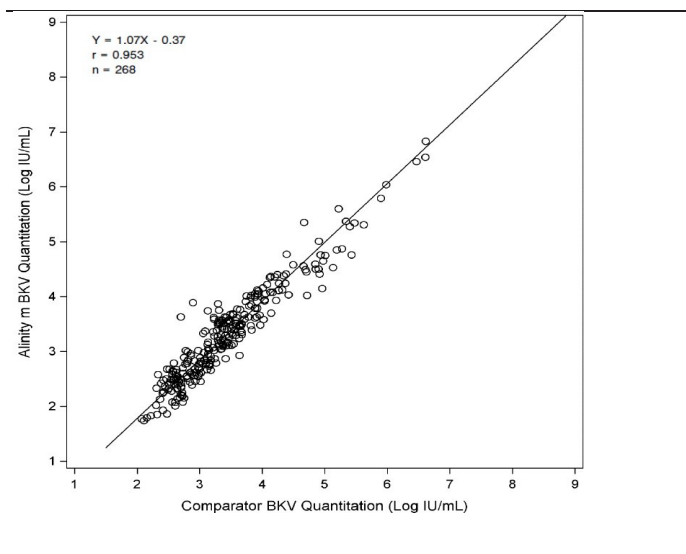
Threshold	Percent Agreement < Threshold (n/N) 95% CI	Percent Agreement ≥ Threshold (n/N) 95% CI
Target Not Detected	100% (270/270) (98.6%, 100%)	95.5% (295/309) (92.5%, 97.3%)
LLoQ <sup>a</sup> (1.7 Log IU/mL)	100% (299/299) (98.7%, 100%)	95.7% (268/280) (92.7%, 97.5%)
3.0 Log IU/mL	99.0% (397/401) (97.5%, 99.6%)	88.2% (157/178) (82.6%, 92.2%)
4.0 Log IU/mL	98.7% (521/528) (97.3%, 99.4%)	90.2% (46/51) (79.0%, 95.7%)

<sup>a</sup> The LLoQ used here is the higher LLoQ between Alinity m BKV and comparator.

Of the 579 specimens, 29 confirmed BKV DNA negative clinical specimens were used for the estimation of Negative Percent Agreement (NPA). For this subset of BKV DNA negative clinical specimens, the NPA with the comparator assay was 100% (29/29) (95% CI: 88.3% to 100%).

Regression and bias analysis included a total of 268 specimens with results that were within the common quantitation range of both Alinity m BKV and the comparator. **Figure 6** shows the results of the Deming regression analysis with a slope of 1.07, intercept of -0.37, and correlation coefficient of 0.953. The mean bias between Alinity m BKV and the comparator (Alinity m BKV minus comparator) was -0.12 Log IU/mL (95% CI: -0.16 to -0.09 Log IU/mL) and the systematic difference between both assays was -0.15 log<sub>10</sub> IU/mL and -0.08 log<sub>10</sub> IU/mL for samples with DNA levels at 3 and 4 log<sub>10</sub> IU/mL, respectively.

**Figure 6.** Deming Regression Analysis for Plasma



b. Clinical Performance for Urine Sample Type.

Alinity m BKV results were compared to those of an FDA-cleared BKV nucleic acid test in a representative study. Alinity m testing was performed using urine specimens stabilized using Alinity m Urine Transport Kit. A total of 380 urine specimens collected from solid organ transplant (SOT) and hematopoietic stem cell transplant (HSCT) subjects (1 specimen per subject) were included in the analysis. The Alinity m BKV assay testing was performed at 3 clinical testing sites with 3 Alinity m BKV reagent lots. The agreement between Alinity m BKV and comparator results is shown in **Table 18**.

**Table 18.** Agreement Between Alinity m BKV and Comparator – Urine

Alinity m BKV (Log IU/mL)	Comparator BKV (Log IU/mL)						Total
	Target not detected (TND)	<LLOQ <sup>a</sup> (<2.3)	2.3 to <4.0	4.0 to <5.0	5.0 to <7.0	≥7.0	
Target not detected (TND)	165	9	0	0	0	0	174
<LLOQ (<2.3)	12	20	7	0	1	0	40
2.3 to <4.0	0	0	45	7	1	0	53
4.0 to <5.0	0	0	1	21	8	0	30
5.0 to <7.0	0	0	1	7	37	4	49
≥7.0	0	0	0	0	1	33	34
Total	177	29	54	35	48	37	380
Agreement (%)	(177/177) 100%	(29/29) 100%	(53/54) 98.1%	(35/35) 100%	(46/48) 95.8%	(37/37) 100%	
95% CI	(97.9%, 100%)	(88.3%, 100%)	(90.2%, 99.7%)	(90.1%, 100%)	(86.0%, 98.8%)	(90.6%, 100%)	

<sup>a</sup> The LLOQ used here is the higher LLOQ between Alinity m BKV 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 BKV Target Not Detected and <LLOQ cells were combined. Agreement between Alinity m BKV assay and the comparator assay was also evaluated using different clinical thresholds and is shown in **Table 19**.

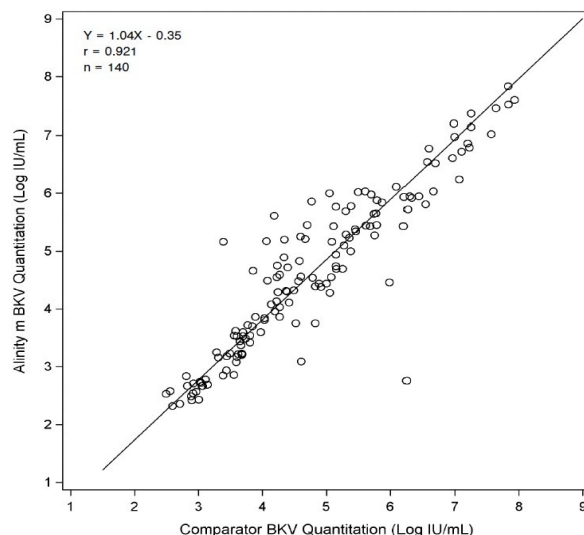
**Table 19.** Agreement Between Alinity m BKV and Comparator Using Different Thresholds – Urine

Threshold	Percent Agreement < Threshold (n/N) 95% CI	Percent Agreement ≥ Threshold (n/N) 95% CI
Target Not Detected	100% (177/177) (97.9%, 100%)	95.6% (194/203) (91.8%, 97.7%)
LLoQ <sup>a</sup> (2.3 Log IU/mL)	100% (206/206) (98.2%, 100%)	95.4% (166/174) (91.2%, 97.7%)
4.0 Log IU/mL	99.2% (258/260) (97.2%, 99.8%)	92.5% (111/120) (86.4%, 96.0%)
7.0 Log IU/mL	99.7% (342/343) (98.4%, 99.9%)	89.2% (33/37) (75.3%, 95.7%)

<sup>a</sup> The LLoQ used here is the higher LLoQ between Alinity m BKV and comparator.

Of the 380 specimens, 67 confirmed BKV DNA negative specimens were used for the estimation of Negative Percent Agreement (NPA). For this subset of BKV DNA negative clinical specimens, the NPA with the comparator assay was 95.5% (64/67) (95% CI: 87.6% to 98.5%). Regression and bias analysis included a total of 140 specimens with results that were within the common quantitation range of both Alinity m BKV and the comparator assay. **Figure 7** shows the results of the Deming regression analysis with a slope of 1.04, intercept of -0.35, and correlation coefficient of 0.921. The mean bias between Alinity m BKV and the comparator (Alinity m BKV minus comparator) was -0.16 Log IU/mL (95% CI: -0.25 to -0.07 Log IU/mL) and the systematic difference between both assays was -0.19 log<sub>10</sub> IU/mL and -0.07 log<sub>10</sub> IU/mL for samples with DNA levels at 4 and 7 log<sub>10</sub> IU/mL, respectively.

**Figure 7.** Deming Regression Analysis for Urine



2. Matrix Comparison:

Not applicable

**C Clinical Studies:**

1. Clinical Sensitivity:

Not applicable

2. Clinical Specificity:

Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not Applicable

**D Clinical Cut-Off:**

Not Applicable.

**E Expected Values/Reference Range:**

Not applicable

**F Other Supportive Instrument Performance Characteristics Data:**

Not applicable

**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.