March 24, 2025

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

Re: K241921
Trade/Device Name: Alinity m BKV
Regulation Number: 21 CFR 866.3183
Regulation Name: Quantitative Viral Nucleic Acid Test For Transplant Patient Management
Regulatory Class: Class II
Product Code: QMI
Dated: February 21, 2025
Received: February 21, 2025

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 (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

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

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

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

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

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

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

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

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

Sincerely,

MARIA I. GARCIA -S

Maria Garcia, Ph.D.
Assistant Director
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

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

510(k) Number *(if known)*
K241921

Device Name
Alinity m BKV

Indications for Use *(Describe)*
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 (K2 EDTA, K3 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.
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.

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

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

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

Table of Contents

1.0 510(k) Summary

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

1.1 Submitter

Applicant Name and Address:	Abbott Molecular Inc. 1300 E. Touhy Avenue Des Plaines, IL 60018
Contact Person:	Gina Sammarco Associate Director Regulatory Affairs Abbott Molecular, Inc. 1300 E. Touhy Avenue Des Plaines, IL 60018 Phone: 224-361-7627 Fax: 224-361-7269
Date Prepared:	March 21, 2025

1.2 Device Information

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

1.3 Predicate Device

Device Name	Predicate Device	510(k)	Cleared
Alinity m BKV	cobas® BKV	K203220	01/29/2021

1.4 Device Description

The Alinity m BKV assay utilizes real-time polymerase chain reaction (PCR) to amplify and detect BKV genomic DNA sequences that have been extracted from human EDTA plasma or urine specimens. The steps of the Alinity m BKV assay consist of sample preparation, real-time PCR assembly, amplification/detection, result calculation, and reporting. One transfer step of urine specimens into the Alinity m Urine Transport Kit by the user is required prior to placing urine specimens on the Alinity m System. Remaining steps of the Alinity m BKV assay procedure are executed automatically by the Alinity m System. Manual dilutions may be performed for low-volume plasma specimens to meet the minimum volume requirement. The Alinity m System is designed to be a random-access analyzer that can perform the Alinity m BKV assay in parallel with other Alinity m assays on the same instrument.

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

- **Alinity m BKV AMP Kit (List No. 09N85-095)**, consisting of 2 types of multi-well assay trays. The amplification tray (AMP TRAY 1) contains liquid, unit-dose PCR amplification/detection reagents and liquid, unit-dose Internal Control (IC) in separate wells; and the activation tray (ACT TRAY 2) contains liquid, unit-dose activation reagent. The intended storage condition for the Alinity m BKV AMP Kit is –25°C to –15°C.
- **Alinity m BKV CTRL Kit (List No. 09N85-085)**, consisting of negative controls, low positive controls, and high positive controls, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m BKV CTRL Kit is –25°C to –15°C.
- **Alinity m BKV CAL Kit (List No. 09N85-075)**, consisting of 2 calibrator levels, each supplied as liquid in single-use tubes. The intended storage condition for the Alinity m BKV CAL Kit is –25°C to –15°C.

The Alinity m BKV assay requires a transport kit for testing all urine specimens:

- **Alinity m Urine Transport Kit (List No. 09N85-001)** consisting of a transport tube and transfer pipette. The transport tube contains transport buffer. The intended storage condition for the Alinity m Urine Transport Kit is 15°C to 30°C.

BKV DNA from human plasma or urine is extracted automatically on board 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 DNA is then combined with liquid unit-dose Alinity m BKV activation reagent and liquid unit-dose 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.

At the beginning of the Alinity m BKV sample preparation process, a liquid unit-dose IC on the AMP Tray is transferred 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 BKV amplification/detection reagents consist of enzymes, primers, probes, and activation reagents that enable amplification and detection of dual targets in the BKV genome. Amplification and detection of the two BKV targets ensures sensitive detection of the viral genome even at low levels. 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. The IC probe is labeled with a different fluorophore than the BKV probes. This allows for simultaneous detection and discrimination of both the BKV and IC amplified products within the same reaction vessel.

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 are tested at or above an established minimum frequency to help ensure that instrument and reagent performance remains satisfactory. During each control event, a negative control, a low-positive control, and a high positive control are processed through sample preparation and PCR procedures that are identical to those used for specimens.

The Alinity m BKV assay also utilizes the following:

- Alinity m BKV Application Specification File (List No. 09N85-05A)
- 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 System Solutions, (List No. 09N20):
    - Alinity m Lysis Solution (List No. 09N20-001)
    - Alinity m Diluent Solution (List No. 09N20-003)
    - Alinity m Vapor Barrier Solution, (List No. 09N20-004)
- Alinity m Tubes and Caps (List No. 09N49):
    - Alinity m LRV Tube (List No. 09N49-001)
    - Alinity m Transport Tubes Pierceable Capped (List No. 09N49-010)
    - Alinity m Transport Tube (List No. 09N49-011)
    - Alinity m Pierceable Cap (List No. 09N49-012)
    - Alinity m Aliquot Tube (List No. 09N49-013)

1.5 Intended Use

Alinity m BKV AMP Kit:

Alinity m BKV is an in vitro nucleic acid amplification test for the quantitation of BK virus (BKV) DNA in human EDTA plasma (K_2 EDTA, K_3 EDTA, and PPT) and urine stabilized using the Alinity m Urine Transport Kit on the automated Alinity m System.

In EDTA plasma (K_2 EDTA, K_3 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.

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.

Alinity m Urine Transport Kit:

The Alinity m Urine Transport Kit is intended for the transportation and storage of urine specimens to stabilize nucleic acid in these specimens. The collected specimens are intended to be tested on the automated Alinity m System. Refer to the appropriate Alinity m assay package insert for additional information.

1.6 Similarities and Differences to Predicate Devices

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

The Alinity m BKV assay has the same general intended use as the predicate device. Although there are some technological differences between the Alinity m BKV 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 BKV DNA sequences, detect the amplified products, and report quantitative results.

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

Table 1. Similarities Between Alinity m BKV and Predicate Device

Description	Subject Device	Predicate Device
	Alinity m BKV	**cobas® BKV (K203220)**
Intended Use	Alinity m BKV is an in vitro nucleic acid amplification test for the quantitation of BK virus (BKV) DNA in human EDTA plasma (K_2 EDTA, K_3 EDTA, and PPT) and urine stabilized using the Alinity m Urine Transport Kit on the automated Alinity m System. In EDTA plasma (K_2 EDTA, K_3 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. 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.	cobas® BKV is an *in vitro* 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. 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. In urine stabilized in cobas® PCR Media, cobas® BKV is intended for use as an aid in the management of BKV in transplant patients. 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. cobas® BKV is not intended for use as a screening test for blood or blood products or human cells, tissues, and cellular and tissue-based products (HCT/Ps).
Assay Type	Quantitative	Quantitative
Specimen Types	EDTA Plasma, Stabilized Urine	EDTA Plasma, Stabilized Urine
Sample Preparation Procedure	Automated liquid handling and robotic manipulation platform	Automated liquid handling and robotic manipulation platform
Amplification Technology	Real-time polymerase chain reaction	Real-time polymerase chain reaction
Assay Controls	• Negative Control • Low Positive Control • High Positive Control • Internal Control (IC)	• Negative Control • Low Positive Control • High Positive Control • DNA Quantitation Standard (DNA-QS)

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

Description	Subject Device	Predicate Device
	Alinity m BKV	**cobas® BKV (K203220)**
Assay Targets	Dual targets in the BKV genome (2 highly conserved regions of the BKV genome)	Dual targets in the BKV genome (small T-antigen and *VP2* regions)

1.7 Results and Interpretation

The Alinity m System will report a result and interpretation for each specimen (refer to **Table 3**). If applicable message codes or flags will also be displayed.

Table 3. Alinity m BKV Results and 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.
≥ LLoQ to ≤ ULoQ	BKV DNA detected and quantified	BKV DNA concentration is within the linear range of the assay (≥ LLoQ to ≤ ULoQ).
> ULoQ	BKV DNA detected	BKV DNA concentration is above the Upper Limit of Quantitation (ULoQ) of the assay.

1.8 Performance Data

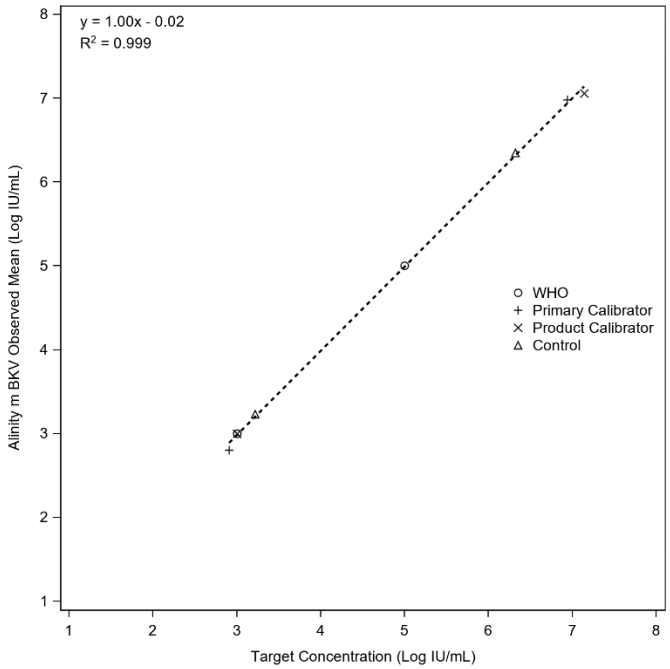
The following performance data were provided in support of safety, effectiveness, and substantial equivalence determination of the device.

1.8.1 Specific Performance Characteristics

1.8.1.1 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 BK virus for Nucleic Acid Amplification Techniques (NIBSC code: 14/212). 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 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 WHO standard. 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 1**.

Figure 1. Traceability to the WHO Standard



1.8.1.2 Performance Characteristics for Plasma Sample Type

1.8.1.2.1 Limit of Detection

The Limit of Detection (LoD) was determined by testing dilutions of the 1st WHO International Standard for BK virus for Nucleic Acid Amplification Techniques (NIBSC code: 14/212, subgroup Ib) prepared in BKV-negative human EDTA plasma. Testing for each BKV DNA concentration was performed with 3 lots of amplification reagents across multiple days. The results, representative of the analytical sensitivity performance of Alinity m BKV in plasma, are summarized in **Table 4** (Lot 1), **Table 5** (Lot 2), and **Table 6** (Lot 3). The claimed LoD of Alinity m BKV is 50 IU/mL (1.70 Log IU/mL) in plasma.

Probit analysis of the data for Lot 2 (least sensitive lot) determined that the concentration of BKV DNA in plasma detected with 95% probability (LoD by Probit) was 18.13 IU/mL (95% CI: 11.82 to 41.99 IU/mL).

Table 4. Alinity m BKV LoD in EDTA Plasma, Lot 1

BKV DNA (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
60.000	30	30	100.0
50.000	30	30	100.0
40.000	30	30	100.0
30.000	30	30	100.0
15.000	30	29	96.7
7.500	30	27	90.0
3.750	30	16	53.3
1.875	30	9	30.0

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Table 5. Alinity m BKV LoD in EDTA Plasma, Lot 2 (Least Sensitive Lot)

BKV DNA (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
60.000	30	30	100.0
50.000	30	30	100.0
40.000	30	30	100.0
30.000	30	29	96.7
15.000	30	29	96.7
7.500	30	23	76.7
3.750	30	11	36.7
1.875	29	10	34.5

Table 6. Alinity m BKV LoD in EDTA Plasma, Lot 3

BKV DNA (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
60.000	30	30	100.0
50.000	30	30	100.0
40.000	30	30	100.0
30.000	30	30	100.0
15.000	30	29	96.7
7.500	30	25	83.3
3.750	30	18	60.0
1.875	30	9	30.0

1.8.1.2.2 Limit of Detection for Genotypes

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 in BKV-negative human EDTA plasma. Testing was performed using one lot of amplification reagents across multiple days. The results, representative of the analytical sensitivity performance of Alinity m BKV for BKV subgroups Ia and Ic and subtypes II, III, and IV, are summarized in **Table 7** for plasma. Alinity m BKV detected 95% or greater of BKV samples at and above 30 IU/mL (1.48 Log IU/mL) in plasma. These results demonstrate the ability of Alinity m BKV to detect BKV subgroups Ia and Ic and subtypes II, III, and IV at the claimed LoD in plasma.

Table 7. Alinity m BKV LoD for Genotypes in EDTA Plasma

Genotype	BKV DNA (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
Subgroup Ia	60	30	30	100.0
	50	30	30	100.0
	30	30	30	100.0
Subgroup Ic	60	28	28	100.0
	50	30	30	100.0
	30	30	30	100.0
Subtype II	60	30	30	100.0
	50	30	30	100.0
	30	29	29	100.0
Subtype III	60	30	30	100.0
	50	29	29	100.0
	30	30	30	100.0
Subtype IV	60	30	30	100.0
	50	30	30	100.0
	30	30	29	96.7

1.8.1.2.3 Linear Range

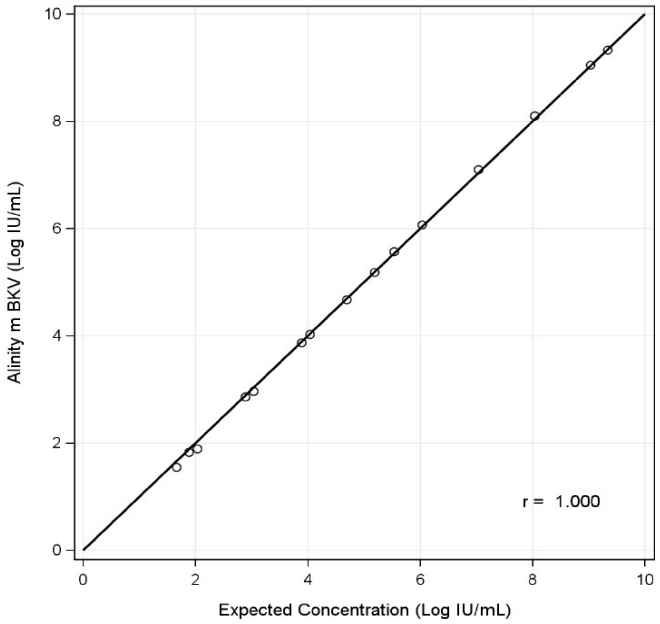
The quantitation range of Alinity m BKV for plasma is from the lower limit of quantitation (LLoQ) of 50 IU/mL (1.70 Log IU/mL) to the upper limit of quantitation (ULoQ) of 1,000,000,000 IU/mL (9.00 Log IU/mL). Linearity of Alinity m BKV was assessed by testing a dilution series of BKV subgroup Ib in BKV-negative

human EDTA 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 1st WHO International Standard 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).

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 2**.

Figure 2. Alinity m BKV Linearity in EDTA Plasma[a]



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

1.8.1.2.4 Linearity for Genotypes

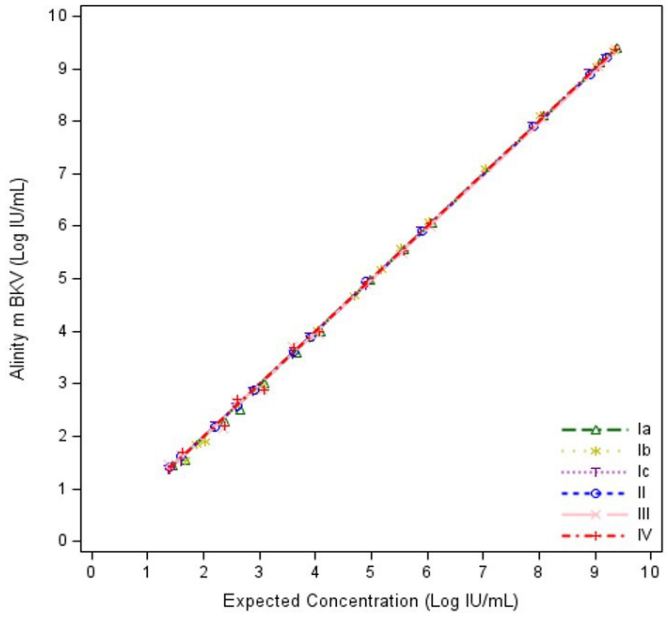
Linearity of Alinity m BKV for subgroups/subtypes Ia, Ic, II, III, and IV was confirmed by testing a dilution series in BKV-negative human EDTA plasma, consisting of 13 panel levels for subgroup/subtypes Ia, III, and IV and 12 panel levels for

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 (**Section 1.7.1.2.3**), are shown in **Figure 3**.

Figure 3. Alinity m BKV Linearity for Genotypes in EDTA Plasma[a]



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

1.8.1.2.5 Precision

Precision of Alinity m BKV was determined by analyzing an 7-member panel prepared in BKV-negative human plasma. 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 representative precision results in **Table 8** and **Table 9** demonstrated that Alinity m BKV within-laboratory standard deviation (SD) in plasma was less than or equal to 0.25 Log IU/mL for BKV DNA panels within the range of 2.70 Log IU/mL to 9.00 Log IU/mL (500 IU/mL to 1,000,000,000 IU/mL), and less than or equal to 0.50 Log IU/mL for BKV DNA panels within the range of 1.70 Log IU/mL to less than 2.70 Log IU/mL (50 IU/mL to less than 500 IU/mL).

Table 8. Alinity m BKV Precision in Plasma (Log IU/mL)

Panel Member	N[a]	Mean Concentration (Log IU/mL)	Within-Run		Between-Run		Between-Day		Within-Laboratory[b]		Between-Instrument[c]		Total[d]	
			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

[a] Valid replicates within the quantitation range.
[b] Within-Laboratory includes Within-Run, Between-Run, and Between-Day Components.
[c] Alinity m System (Instrument), AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Between-Instrument Component.
[d] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

Table 9. Alinity m BKV Precision in Plasma (IU/mL)

Panel Member	N[a]	Mean Concentration[b] (IU/mL)	%CV[c]				
			Within-Run	Between-Run	Between-Day	Between-Instrument[d]	Total[e]
07	288	98,734,723	10.7	6.4	0.0	6.5	14.1
06	286	897,345	12.4	1.5	4.4	3.2	13.6
05	288	78,731	12.5	5.5	3.4	3.4	14.5
04	288	7,609	16.3	4.5	3.6	3.6	17.7
03	287	679	15.2	6.1	0.0	6.8	17.8
02	287	218	23.3	6.3	6.6	8.1	26.5
01	96	66	24.1	5.7	0.0	0.0	24.8

[a] Valid replicates within the quantitation range.
[b] Titer data are considered to be log-normally distributed and the mean values for log-normal 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 the %CV values for log-normal titer data are calculated as sqrt(10^[SD^2 * ln(10)] – 1) * 100.
[d] Alinity m System (Instrument), AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Between-Instrument Component.
[e] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

1.8.1.2.6 Lower Limit of Quantitation (LLoQ)

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

Total error was estimated for detected plasma 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 10**.

Panel members were dilutions of the 1st WHO International Standard for BK Virus (NIBSC code: 14/212, subgroup Ib) prepared in BKV-negative plasma.

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

Table 10. TAE and TE for Plasma

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)
1.60	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

[a] Bias = Mean Concentration – Target Concentration

1.8.1.2.7 Alinity m BKV Plasma Testing Using Dilution Procedure

The 1:2.5 dilution procedure for plasma samples was evaluated by comparing quantitation of neat samples and samples tested using the Alinity m BKV dilution procedure. Five plasma panel members with BKV levels targeted in the range of 375 IU/mL to 1,000,000,000 IU/mL (2.57 Log IU/mL to 9.00 Log IU/mL) were tested. Each panel member was tested, neat and using the dilution procedure, in multiple replicates. The differences in mean (ie, diluted minus neat) ranged from –0.19 Log IU/mL to 0.27 Log IU/mL.

1.8.1.2.8 Precision of Alinity m BKV Plasma Testing Using Dilution Procedure

Precision of Alinity m BKV using the dilution procedure was determined by analyzing 3 EDTA plasma panel members. 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 with 3 Alinity m Specimen Dilution Kit I lots, and 3 Alinity m BKV AMP Kit lots by 3 operators (1 Specimen Diluent lot, 1 AMP kit lot, and 1 operator per instrument), for a total of 288 replicates. The results, representative of the precision of Alinity m BKV using the plasma dilution procedure, are summarized in **Table 11** and **Table 12**.

Table 11. Precision of Alinity m BKV EDTA Plasma Testing Using Dilution Procedure (Log IU/mL)

Panel Member	N[a]	Mean Concentration (Log IU/mL)	Within-Run		Between-Run		Between-Day		Within-Laboratory[b]		Between-Instrument[c]		Total[d]	
			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

[a] Valid replicates
[b] Within-Laboratory includes Within-Run, Between-Run, and Between-Day Components
[c] 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.
[d] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

Table 12. Precision of Alinity m BKV EDTA Plasma Testing Using Dilution Procedure (IU/mL)

Panel Member	N[a]	Mean Concentration[b] (IU/mL)	%CV[c]				
			Within-Run	Between-Run	Between-Day	Between-Instrument[d]	Total[e]
01	287	3,218	12.5	11.5	8.8	0.0	19.2
02	286	69,564	26.2	15.5	15.0	0.0	34.5
03	287	96,200,926	11.2	7.0	0.0	4.8	14.1

[a] Valid replicates
[b] Titer data are considered to be log-normally distributed and the mean values for log-normal 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 the %CV values for log-normal titer data are calculated as sqrt(10^[SD^2 * ln(10)] – 1) * 100.
[d] 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.
[e] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

1.8.1.2.9 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 × LLoQ) and 150 IU/mL (3 × 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) after dilution in Specimen Diluent. Panel members were dilutions of the 1st WHO International Standard for BK Virus (NIBSC code: 14/212, subgroup Ib) prepared in BKV-negative EDTA 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 BKV AMP Kit lot, 1 Alinity m Specimen Dilution Kit I lot, and 1 Alinity m System. Total error was estimated by TAE and TE, as shown in **Table 13**. 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 13. 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[a] (Log IU/mL)	Bias[b] (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

[a] Reported concentration for neat samples
[b] Bias = Mean Concentration – Target Concentration Neat

1.8.1.2.10 Analytical Specificity – Potential Cross-Reactants

The analytical specificity of Alinity m BKV was evaluated with a panel of microorganisms (**Table 14**) in BKV-negative K_2 EDTA 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 10^5 Units/mL for viruses and fungi, or at least 10^6 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 14. Microorganisms Tested in Plasma

Viruses		
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)
Bacteria		**Fungi**
Actinomyces israelii	*Mycoplasma pneumoniae*	*Aspergillus niger*
Chlamydia trachomatis	*Neisseria gonorrhoeae*	*Candida albicans*
Clostridium perfringens	*Salmonella enterica*	*Cryptococcus neoformans*
Cutibacterium acnes	*Salmonella typhimurium*	
Enterococcus faecalis	*Staphylococcus aureus*	
Escherichia coli	*Staphylococcus epidermidis*	
Klebsiella pneumoniae	*Streptococcus pneumoniae*	
Listeria monocytogenes	*Streptococcus pyogenes*	
Mycobacterium avium		

1.8.1.2.11 Analytical Specificity – Potentially Interfering Substances

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 EDTA 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 15** at a concentration of 3 times the reported C_{max} or higher.

Table 15. Drug Compounds Tested in Plasma

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

1.8.1.2.12 Carryover in Plasma

The carryover rate for Alinity m BKV plasma protocol was determined by analyzing 360 valid replicates of BKV-negative samples processed from alternating positions with 360 valid replicates of high concentrated BKV-positive plasma samples targeted at 20,000,000 IU/mL, across a total of 15 runs (15 AMP Trays). BKV DNA was not detected in any of the BKV-negative samples, resulting in an overall carryover rate of 0.0% (95% CI: 0.0% to 1.1%).

1.8.1.3 Performance Characteristics for Urine Sample Type

1.8.1.3.1 Limit of Detection

The LoD was determined by testing dilutions of the 1st WHO International Standard for BK virus (NIBSC code: 14/212, subgroup Ib) prepared in BKV negative urine stabilized in transport buffer (Alinity m Urine Transport Kit). Testing for each BKV DNA concentration was performed with 3 lots of amplification reagents across multiple days. The results, representative of the analytical sensitivity performance of Alinity m BKV in urine, are summarized in **Table 16** (Lot 1), **Table 17** (Lot 2) and **Table 18** (Lot 3). The claimed LoD of Alinity m BKV is 50 IU/mL (1.70 log IU/mL) in neat urine.

Probit analysis of the data for Lot 2 (least sensitive lot) determined that the concentration of BKV DNA in urine detected with 95% probability (LoD by Probit) was 16.97 IU/mL (95% CI: 11.42 to 39.14 IU/mL).

Table 16. Alinity m BKV LoD in Urine, Lot 1

BKV DNA[a] (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
330.00	30	30	100.0
300.00	30	30	100.0
75.00	30	30	100.0
60.00	30	30	100.0
45.00	30	30	100.0
22.50	30	30	100.0
11.25	30	28	93.3
5.63	30	22	73.3
2.81	30	17	56.7

[a] Urine samples tested stabilized in transport buffer. BKV concentration based on neat urine input.

Table 17. Alinity m BKV LoD in Urine, Lot 2 (Least Sensitive Lot)

BKV DNA[a] (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
330.00	29	29	100.0
300.00	30	30	100.0
75.00	30	30	100.0
60.00	30	30	100.0
45.00	30	30	100.0
22.50	30	29	96.7
11.25	30	28	93.3
5.63	30	19	63.3
2.81	30	14	46.7

[a] Urine samples tested stabilized in transport buffer. BKV concentration based on neat urine input.

Table 18. Alinity m BKV LoD in Urine, Lot 3

BKV DNA[a] (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
330.00	30	30	100.0
300.00	30	30	100.0
75.00	30	30	100.0
60.00	30	30	100.0
45.00	30	30	100.0
22.50	29	27	93.1
11.25	29	28	96.6
5.63	30	24	80.0
2.81	29	14	48.3

[a] Urine samples tested stabilized in transport buffer. BKV concentration based on neat urine input.

1.8.1.3.2 Limit of Detection for Genotypes

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. Testing was performed using one lot of amplification reagents across multiple days. The results, representative of the analytical sensitivity performance of Alinity m BKV for BKV subgroups Ia and Ic and subtypes II, III, and IV, are

summarized in **Table 19** for urine. Alinity m BKV detected 95% or greater of BKV samples at and above 45 IU/mL (1.65 Log IU/mL) in urine. These results demonstrate the ability of Alinity m BKV to detect BKV subgroups Ia and Ic and subtypes II, III, and IV at the claimed LoD in urine.

Table 19. Alinity m BKV LoD for Genotypes in Urine

Genotype	BKV DNA (IU/mL)	No. of Valid Replicates	No. of Detected Replicates	Detection Rate (%)
Subgroup Ia	330	30	30	100.0
	300	30	30	100.0
	90	30	30	100.0
	75	29	29	100.0
	45	30	30	100.0
Subgroup Ic	330	30	30	100.0
	300	29	29	100.0
	90	30	30	100.0
	75	30	30	100.0
	45	29	29	100.0
Subtype II	330	30	30	100.0
	300	30	30	100.0
	90	30	30	100.0
	75	30	30	100.0
	45	30	30	100.0
Subtype III	330	30	30	100.0
	300	30	30	100.0
	90	29	29	100.0
	75	30	30	100.0
	45	30	30	100.0
Subtype IV	330	30	30	100.0
	300	30	30	100.0
	90	30	30	100.0
	75	29	29	100.0
	45	30	30	100.0

1.8.1.3.3 Linear Range

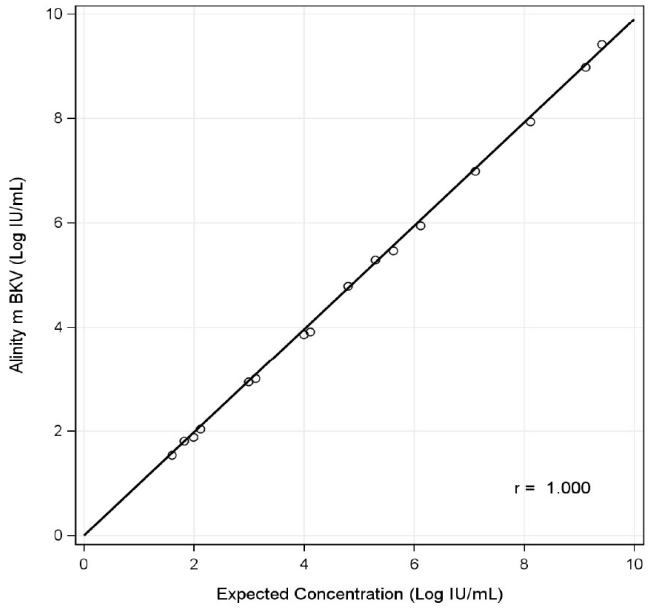
The quantitation range of Alinity m BKV for urine is from the lower limit of quantitation (LLoQ) of 50 IU/mL (1.70 Log IU/mL) to the upper limit of quantitation (ULoQ) of 1,000,000,000 IU/mL (9.00 Log IU/mL). Linearity of Alinity m BKV was assessed by testing a dilution series of BKV subgroup Ib in

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 the 1st WHO International Standard 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 4**.

Figure 4. Alinity m BKV Linearity in Urine[a]



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

1.8.1.3.4 Linearity for Genotypes

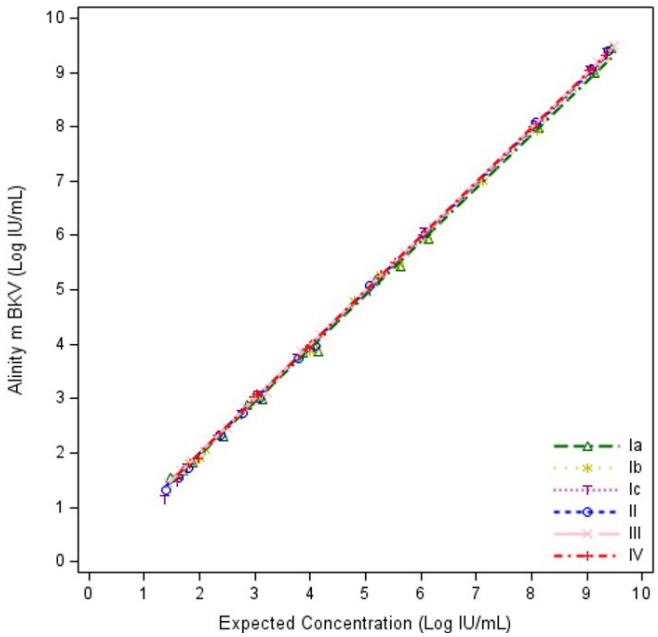
Linearity of Alinity m BKV for subgroups/subtypes Ia, Ic, II, III, and IV was confirmed by testing a dilution series in BKV-negative stabilized urine, consisting of 14 panel levels for subgroup/subtypes Ia, III, and IV and 13 panel levels for subgroup/subtype Ic and II,

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 (**Section 1.7.1.3.3**), are shown in **Figure 5**.

Figure 5. Alinity m BKV Linearity for Genotypes in Urine[a]



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

1.8.1.3.5 Precision

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 representative precision results in **Table 20** and **Table 21** demonstrated that Alinity m BKV within-laboratory standard deviation (SD) in urine was less than or equal to 0.25 Log IU/mL for BKV DNA panels within the range of 2.70 Log IU/mL to 9.00 Log IU/mL (500 IU/mL to 1,000,000,000 IU/mL) and less than or equal to 0.50 Log IU/mL for BKV DNA panels within the range of 1.70 Log IU/mL to less than 2.70 Log IU/mL (50 IU/mL to less than 500 IU/mL).

Table 20. Alinity m BKV Precision in Urine (Log IU/mL)

Panel Member	N[a]	Mean Concentration (Log IU/mL)	Within-Run		Between-Run		Between-Day		Within-Laboratory[b]		Between-Instrument[c]		Total[d]	
			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

[a] Valid replicates within the quantitation range.
[b] Within-Laboratory includes Within-Run, Between-Run, and Between-Day Components.
[c] Alinity m System (Instrument), AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Between-Instrument Component.
[d] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

Table 21. Alinity m BKV Precision in Urine (IU/mL)

Panel Member	N[a]	Mean Concentration[b] (IU/mL)	%CV[c]				
			Within-Run	Between-Run	Between-Day	Between-Instrument[d]	Total[e]
08	287	170,547,602	11.7	7.5	0.0	9.6	17.0
07	287	1,572,305	12.8	7.2	0.0	4.8	15.5
06	283	131,873	17.9	8.5	4.8	2.1	20.6
05	284	13,156	15.2	6.5	6.9	0.0	18.0
04	283	1,160	20.5	9.9	3.5	0.0	23.2
03	285	348	18.8	9.1	6.6	0.3	22.0
02	177	69	19.7	6.1	4.3	4.8	21.7
01	54	62	12.5	9.2	0.0	0.0	15.5

[a] Valid replicates within the quantitation range.
[b] Titer data are considered to be log-normally distributed and the mean values for log-normal 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 the %CV values for log-normal titer data are calculated as sqrt(10^[SD^2 * ln(10)] – 1) * 100.
[d] Alinity m System (Instrument), AMP Kit lot, and Operator are confounded, and the confounding effect is represented by Between-Instrument Component.
[e] Total includes Within-Run, Between-Run, Between-Day, and Between-Instrument Components.

1.8.1.3.6 Lower Limit of Quantitation (LLoQ)

The LLoQ is defined as the lowest concentration at which BKV DNA is reliably quantitated within an acceptable total error of ≤ 1.00 Log IU/mL. Total error was estimated for detected urine 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 22**.

Panel members were dilutions of the 1st WHO International Standard for BK Virus (NIBSC code: 14/212, subgroup Ib) prepared in BKV-negative urine stabilized in transport buffer (Alinity m Urine Transport Kit).

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

Table 22. TAE and TE for Urine

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)
1.35	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

[a] Bias = Mean Concentration – Target Concentration

1.8.1.3.7 Analytical Specificity – Potential Cross-Reactants

The analytical specificity of Alinity m BKV was evaluated with a panel of microorganisms (**Table 23**) 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 10^5 Units/mL for viruses and fungi or at least 10^6 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 23. Microorganisms Tested in Urine

Bacteria		
Bacillus cereus	*Lactobacillus acidophilus*	*Staphylococcus aureus*
Bacillus subtilis	*Lactobacillus crispatus*	*Staphylococcus epidermidis*
Chlamydia trachomatis	*Lactobacillus jensenii*	*Staphylococcus saprophyticus*
Corynebacterium diphtheriae	*Lactobacillus vaginalis*	*Streptococcus agalactiae*
Enterobacter cloacae	*Morganella morganii*	*Streptococcus bovis*
Enterococcus faecalis	*Mycoplasma genitalium*	*Streptococcus oralis/viridans*
Enterococcus faecium	*Neisseria gonorrhoeae*	*Streptococcus pneumoniae*
Escherichia coli	*Proteus mirabilis*	*Treponema pallidum* [a]
Klebsiella pneumoniae	*Pseudomonas aeruginosa*	*Ureaplasma urealyticum*
Fungi	**Viruses**	**Protozoa**
Candida albicans	Herpes Simplex Virus-2 (HSV-2)	*Trichomonas vaginalis*
Candida glabrata	Human Papillomavirus 16 (HPV-16)	
Candida parapsilosis		
Candida tropicalis		

[a] *T. pallidum* was not a whole organism and was only attainable as synthetic partial genome

1.8.1.3.8 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 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) (1×10^5 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 24**.

Table 24. Drug Compounds Tested in Urine

Drug Pool	Drug Compound	Tested Concentration
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

Table 24. Drug Compounds Tested in Urine

Drug Pool	Drug Compound	Tested Concentration
5 *(continued)*	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

1.8.1.3.1 Carryover in Urine

The carryover rate for Alinity m BKV urine protocol was determined by analyzing 360 valid replicates of BKV-negative samples processed from alternating positions with 360 valid replicates of high concentrated BKV-positive stabilized urine samples targeted at 1,500,000,000 IU/mL, across a total of 15 runs (15 AMP Trays). BKV DNA was not detected in any of the BKV-negative samples, resulting in an overall carryover rate of 0.0% (95% CI: 0.0% to 1.1%).

1.8.2 Clinical Performance Characteristics

1.8.2.1 Clinical Reproducibility for Plasma Sample Type

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. The positive panel members were prepared using a BKV positive clinical specimen or cultured virus diluted in human EDTA plasma. A total of 3 Alinity m BKV AMP Kit lots, 3 Alinity m BKV CAL Kit lots, 3 Alinity m BKV CTRL Kit lots, and 3 Alinity m Sample Prep Kit 2 lots were used. Three clinical sites each tested 2 Alinity m BKV AMP Kit lots on 5 non-consecutive days for each lot. Six replicates of each panel member were tested on each of the 5 days. Each of the 3 clinical sites used different lots of Alinity m BKV CAL Kit, Alinity m BKV CTRL Kit, and Alinity m Sample Prep Kit 2. The reproducibility results are summarized in **Table 25** and **Table 26** (for the positive panel members) and **Table 27** (for the negative panel member).

Table 25. Reproducibility for Positive Panel Members – EDTA Plasma (Log IU/mL)

Panel Member	N[a]	Mean Concentration (Log IU/mL)	Within-Run/Day		Between-Run/Day		Within-Laboratory[c]		Between-Lot		Between-Site/ Instrument		Total[d]	
			SD[b]	%CV	SD[b]	%CV	SD[b]	%CV	SD[b]	%CV	SD[b]	%CV	SD[b]	%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

[a] Number of valid replicates within the quantitation range.
[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 26. Reproducibility for Positive Panel Members – EDTA Plasma (IU/mL)

Panel Member	N[a]	Mean Concentration[b] (IU/mL)	%CV[c] Within-Run/Day	Between-Run/Day	Between-Lot	Between-Site/ Instrument	Total[d]
1	178	138,532,920	12.8	6.2	16.4	0.0	21.8
2	180	25,521,653	12.2	4.8	18.2	0.0	22.6
3	177	759,793	13.5	6.6	11.5	0.0	19.1
4	179	82,823	14.1	5.7	6.4	0.0	16.5
5	178	9,024	15.6	13.0	2.8	13.7	24.9
6	178	1,103	20.2	5.9	4.3	14.6	26.2
7	167	94	25.2	11.3	0.0	14.2	31.4
8	47	60	17.1	0.0	3.6	5.1	18.3

[a] Number of valid replicates within the quantitation range.
[b] Titer data are considered to be log-normally distributed and the mean values for log-normal 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 the %CV values for log-normal titer data are calculated as sqrt(10^[SD^2 * ln(10)] – 1) * 100.
[d] Total includes Within-Run/Day, Between-Run/Day, Between-Reagent Lot,, and Between-Site/Instrument Components.

Table 27. Reproducibility for Negative Panel Member – EDTA Plasma

Expected BKV DNA Concentration	No. of Replicates Total	Negative	Negative Rate (%)	95% Confidence Interval
Negative	176	176	100.0 % (176/176)	(97.9%, 100.0%)

1.8.2.2 Clinical Reproducibility for Urine Sample Type

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 transport buffer (Alinity m Urine Transport Kit). The positive panel members were prepared using a BKV positive clinical specimen, cultured virus, or plasmid DNA diluted with urine stabilized in transport buffer. A total of 3 Alinity m BKV AMP Kit lots, 3 Alinity m BKV CAL Kit lots, 3 Alinity m BKV CTRL Kit lots, and 3 Alinity m Sample Prep Kit 2 lots were used. Three clinical sites each tested 2 Alinity m BKV AMP Kit lots on 5 non-consecutive days for each lot. Six replicates of each panel member were tested on each of the 5 days. Each of the 3 clinical sites used different lots of Alinity m BKV CAL Kit, Alinity m BKV CTRL Kit, and Alinity m Sample Prep Kit 2. The reproducibility results are summarized in **Table 28** and **Table 29** (for the positive panel members) and **Table 30** (for the negative panel member).

Table 28. Reproducibility for Positive Panel Members – Urine (Log IU/mL)

Panel Member	N[a]	Mean Concentration (Log IU/mL)	Within-Run/Day		Between-Run/Day		Within-Laboratory[c]		Between-Lot		Between-Site/ Instrument		Total[d]	
			SD[b]	%CV	SD[b]	%CV	SD[b]	%CV	SD[b]	%CV	SD[b]	%CV	SD[b]	%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

[a] Number of valid replicates within the quantitation range.
[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 29. Reproducibility for Positive Panel Members – Urine (IU/mL)

Panel Member	N[a]	Mean Concentration[b] (IU/mL)	%CV[c] Within-Run/Day	Between-Run/Day	Between-Lot	Between-Site/ Instrument	Total[d]
1	178	512,317,248	10.9	5.5	1.3	26.3	29.2
2	180	20,177,082	11.8	5.3	5.0	18.3	23.1
3	179	828,919	12.4	5.5	2.1	13.1	19.0
4	178	291,864	13.8	8.9	3.4	17.0	24.0
5	177	30,237	14.9	8.0	8.2	16.0	25.0
6	179	1,090	40.3	11.7	0.0	9.2	43.4
7	175	202	18.9	5.2	3.0	12.8	23.8
8	169	102	55.5	0.0	7.8	0.0	56.2

[a] Number of valid replicates within the quantitation range.
[b] Titer data are considered to be log-normally distributed and the mean values for log-normal 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 the %CV values for log-normal titer data are calculated as sqrt(10^[SD^2 * ln(10)] – 1) * 100.
[d] Total includes Within-Run/Day, Between-Run/Day, Between-Reagent Lot,, and Between-Site/Instrument Components.

Table 30. Reproducibility for Negative Panel Member – Urine

Expected BKV DNA Concentration	No. of Replicates Total	Negative	Negative Rate (%)	95% Confidence Interval
Negative	174	173	99.4% (173/174)	(96.8%, 99.9%)

1.8.2.3 Clinical 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 31**.

Table 31. Agreement between Alinity m BKV and Comparator – Plasma

	Comparator BKV (Log IU/mL)							
Alinity m BKV (Log IU/mL)	**Target not detected (TND)**	**< LLoQ[a] (< 1.70)**	**1.70 to < 2.30**	**2.30 to < 3.00**	**3.00 to < 3.70**	**3.70 to < 4.40**	**≥ 4.40**	**Total**
Target not detected (TND)	264	13	1	0	0	0	0	278
< LLoQ (< 1.70)	6	16	10	1	0	0	0	33
1.70 to < 2.30	0	0	4	19	0	0	0	23
2.30 to < 3.00	0	0	0	63	21	0	0	84
3.00 to < 3.70	0	0	0	3	76	10	0	89
3.70 to < 4.40	0	0	0	1	5	33	3	42
≥ 4.40	0	0	0	0	0	3	27	30
Total	270	29	15	87	102	46	30	579
Column Agreement (%)	(270/270) 100.0%	(29/29) 100.0%	(14/15) 93.3%	(85/87) 97.7%	(102/102) 100.0%	(46/46) 100.0%	(30/30) 100.0%	
95% CI	(98.6%, 100.0%)	(88.3%, 100.0%)	(70.2%, 98.8%)	(92.0%, 99.4%)	(96.4%, 100.0%)	(92.3%, 100.0%)	(88.6%, 100.0%)	

[a] 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. 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.

Agreement between Alinity m BKV assay and the comparator assay was also evaluated using different clinical thresholds (**Table 32**).

Table 32. Agreement between Alinity m BKV and Comparator Using Different Thresholds – Plasma

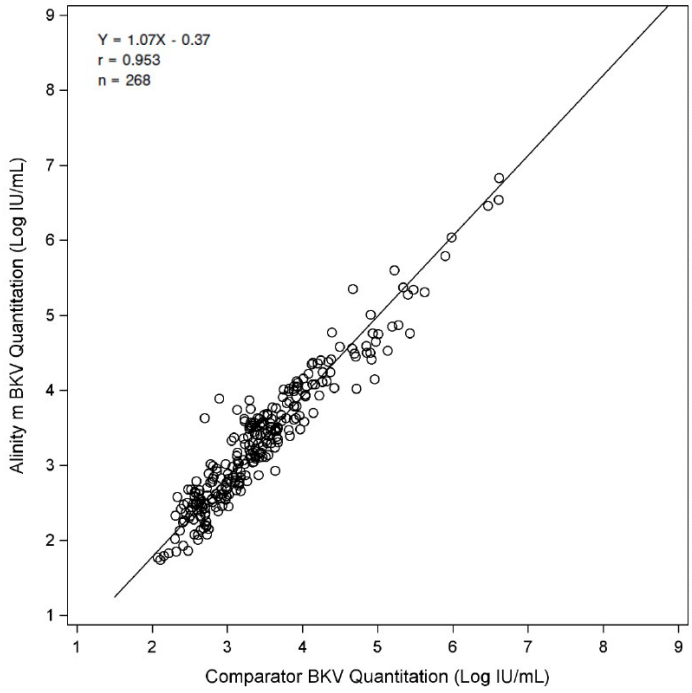
Threshold	% Agreement < Threshold (n/N) 95% CI	% Agreement ≥ Threshold (n/N) 95% CI
Target Not Detected	100.0% (270/270) (98.6%, 100.0%)	95.5% (295/309) (92.5%, 97.3%)
LLoQ[a] (1.70 Log IU/mL)	100.0% (299/299) (98.7%, 100.0%)	95.7% (268/280) (92.7%, 97.5%)
3.00 Log IU/mL	99.0% (397/401) (97.5%, 99.6%)	88.2% (157/178) (82.6%, 92.2%)
4.00 Log IU/mL	98.7% (521/528) (97.3%, 99.4%)	90.2% (46/51) (79.0%, 95.7%)

[a] 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 100.0% (29/29) (95% CI: 88.3% to 100.0%).

Regression and bias analysis included a total of 268 samples 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).

Figure 6. Deming Regression Analysis for Plasma



Systematic difference between Alinity m BKV and the comparator at 2 selected viral load levels is shown in **Table 33**.

Table 33. Systematic Difference at Selected Viral Load Levels – Plasma

Viral Load Level (per comparator)	Systematic Difference
3.00 Log IU/mL	–0.15 Log IU/mL
4.00 Log IU/mL	–0.08 Log IU/mL

1.8.2.4 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 34**.

Table 34. Agreement between Alinity m BKV and Comparator – Urine

	Comparator BKV (Log IU/mL)						
Alinity m BKV (Log IU/mL)	**Target not detected (TND)**	**< LLoQ[a] (< 2.30)**	**2.30 to < 4.00**	**4.00 to < 5.00**	**5.00 to < 7.00**	**≥ 7.00**	**Total**
Target not detected (TND)	165	9	0	0	0	0	174
< LLoQ (< 2.30)	12	20	7	0	1	0	40
2.30 to < 4.00	0	0	45	7	1	0	53
4.00 to < 5.00	0	0	1	21	8	0	30
5.00 to < 7.00	0	0	1	7	37	4	49
≥ 7.00	0	0	0	0	1	33	34
Total	177	29	54	35	48	37	380
Column Agreement (%)	(177/177) 100.0%	(29/29) 100.0%	(53/54) 98.1%	(35/35) 100.0%	(46/48) 95.8%	(37/37) 100.0%	
95% CI	(97.9%, 100.0%)	(88.3%, 100.0%)	(90.2%, 99.7%)	(90.1%, 100.0%)	(86.0%, 98.8%)	(90.6%, 100.0%)	

[a] 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. 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.

Agreement between Alinity m BKV assay and the comparator assay was also evaluated using different clinical thresholds and is shown in **Table 35**.

Table 35. Agreement between Alinity m BKV and Comparator Using Different Thresholds – Urine

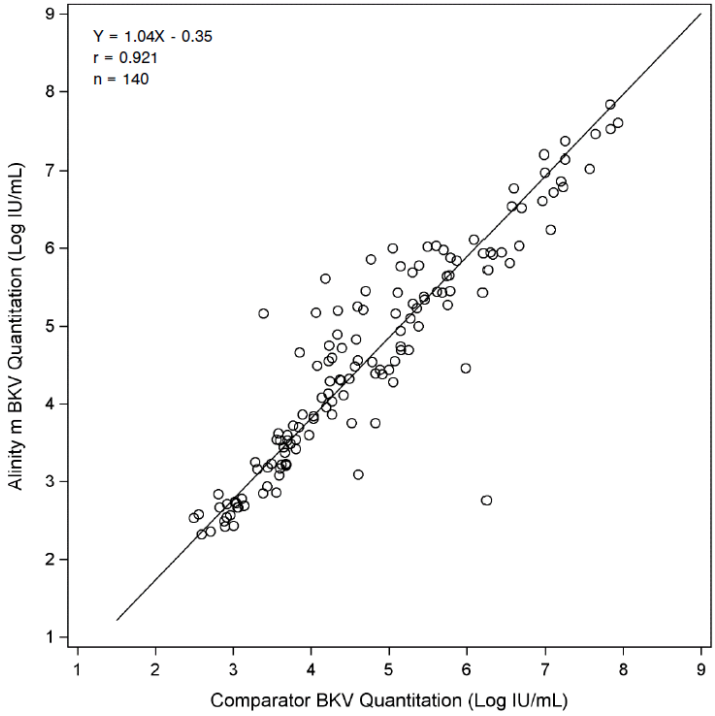
Threshold	% Agreement < Threshold (n/N) 95% CI	% Agreement ≥ Threshold (n/N) 95% CI
Target Not Detected	100.0% (177/177) (97.9%, 100.0%)	95.6% (194/203) (91.8%, 97.7%)
LLoQ[a] (2.30 Log IU/mL)	100.0% (206/206) (98.2%, 100.0%)	95.4% (166/174) (91.2%, 97.7%)
4.00 Log IU/mL	99.2% (258/260) (97.2%, 99.8%)	92.5% (111/120) (86.4%, 96.0%)
7.00 Log IU/mL	99.7% (342/343) (98.4%, 99.9%)	89.2% (33/37) (75.3%, 95.7%)

[a] 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).

Figure 7. Deming Regression Analysis for Urine



Systematic difference between Alinity m BKV and the comparator at 2 selected viral load levels is shown in **Table 36**.

Table 36. Systematic Difference at Selected Viral Load Levels – Urine

Viral Load Level (per comparator)	Systematic Difference
4.00 Log IU/mL	–0.19 Log IU/mL
7.00 Log IU/mL	–0.07 Log IU/mL

1.9 Conclusions Drawn from the Studies

The analytical and clinical study results demonstrate that the Alinity m BKV 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 BKV.