

## Overview

### Useful For

A prospective and diagnostic marker for the development of nephropathy in renal transplant recipients

This test **should not be used** to screen healthy patients. Depending on the population, varying percentages of patients may be found to be positive.

### Method Name

Real-Time Polymerase Chain Reaction (PCR)/DNA Probe Hybridization

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma EDTA

### Advisory Information

This test is the preferred test for BK Virus detection. However, if qualitative results are requested, order LCBKP / BK Virus, Molecular Detection, PCR, Plasma.

### Specimen Required

**Container/Tube:** Lavender top (EDTA)

**Specimen Volume:** 1 mL

**Collection Instructions:** Centrifuge and aliquot plasma within 24 hours of collection.

### Forms

If not ordering electronically, complete, print, and send 1 of the following forms with the specimen:

[-Microbiology Test Request](#) (T244)

[-Renal Diagnostics Test Request](#) (T830)

[-General Request](#) (T239)

### Specimen Minimum Volume

0.3 mL

### Reject Due To

Gross hemolysis	Reject
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### Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Refrigerated (preferred)	14 days	
	Frozen	14 days	

## Clinical and Interpretive

### Clinical Information

Polyomaviruses are small (45 nm, approximately 5,000 bp), DNA-containing viruses and include 3 closely related viruses of clinical significance: Simian virus 40 (SV-40), JC virus (JCV), and BK virus (BKV). SV-40 naturally infects rhesus monkeys but can infect humans, while BKV and JCV cause productive infection only in humans.(1,2) Acquisition of BKV begins in infancy. Serological evidence of infection by BKV is present in 37% of individuals by 5 years of age and over 80% of adolescents.

BKV is an important cause of interstitial nephritis and BKV-associated nephropathy (BKVAN) in recipients of kidney transplants. Up to 5% of renal allograft recipients can be affected, and among those patients the average time from transplant to diagnosis is about 40 weeks (range 6-150).(3) Quantitative PCR analysis of BKV DNA in the plasma is the most widely used blood test for the laboratory diagnosis of BKV-associated nephropathy. Importantly, the presence of BKV DNA in blood reflects the dynamics of the disease: the conversion of plasma from negative to positive for BKV DNA after transplantation, the presence of DNA in plasma in conjunction with the persistence of nephropathy, and its disappearance from plasma after the reduction of immunosuppressive therapy.(4-8) The presence of BKV DNA in plasma at levels at or above 3,200 IU/mL may correlate with an increased risk of BKVAN with this assay. Furthermore, the trend of viral DNA quantitation (eg, increasing, decreasing) may be helpful in predicting the onset of BKVAN. Serial monitoring of viral loads may be indicated to assess changing levels of BKV DNA.

### Reference Values

None Detected

### Interpretation

Increasing copy levels of BK virus (BKV) DNA in serial specimens may indicate possible BKV- associated nephropathy (BKVAN) in kidney transplant patients.

Viral loads above 3,200 IU/mL BKV DNA in plasma may also indicate a risk for BKVAN.

This assay does not cross react with other polyomaviruses, including JC virus and Simian virus 40 (SV-40)

### Cautions

No significant cautionary statements.

### Supportive Data

The following validation supports the use of this assay for clinical testing.

Accuracy/Diagnostic Sensitivity and Specificity:

Results from this real-time PCR assay on the LightCycler (LC PCR) were compared to a previous PCR assay (directed to VP2 region of the polyoma virus based on a published method) on 112 plasma specimens and 108 urine specimens. Using the previous method as the gold standard, the diagnostic sensitivity and specificity is 94% and 90% for plasma and 100% and 100% for urine, respectively. The discrepant specimens had low viral DNA copy

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numbers (<5,000 copies/mL), which is associated with greater variability of quantitative results.

Supplemental Data (Spiking Studies):

To supplement the above data, 30 negative plasma and urine specimens were spiked with BK virus (BKV)-positive control plasmid at the approximate limit of detection (LoD). The 30-spiked specimens were run in a blinded manner along with 57 plasma and 58 urine negative (nonspiked) specimens. 100% of the spiked specimens were positive and 100% of the nonspiked specimens were negative.

Analytical Sensitivity/LoD:

The lower LoD of this assay is 244 DNA target copies per mL in urine and plasma (78 IU/mL).

Analytical Specificity:

No PCR signal was obtained from the extracts of a variety of human viruses that can be found in urine or plasma, including cytomegalovirus, Epstein-Barr virus, human herpesvirus-6, enterovirus, adenovirus, and mumps virus.

Precision:

Qualitative interassay and intra-assay precision were 100%. Quantitative values had a standard deviation of <0.25 log<sub>10</sub> across the analytical measuring range.

Reference Range:

The reference range of BKV in plasma is "None Detected." This test is not to be used to screen healthy patients. It is to be used for patients with a clinical history or risk factors for BKV-associated nephropathy.

Reportable Range (lower and upper limits of quantification, analytical measurement range):

Reportable range is from 1,600 to 16,000,000 IU/mL.

### Clinical Reference

1. Kazory A, Ducloux D: Renal transplantation and polyomavirus infection: recent clinical facts and controversies. *Transplant Infect Dis* 2003;5(2):65
2. Vilchez RA, Arrington AS, Butel JS: Polyomaviruses in kidney transplant recipients. *Am J Transplantation* 2002;2(5):481
3. Hirsch HH: Polyomavirus BK nephropathy: a (re-)emerging complication in renal transplantation. *Am J Transplantation* 2002;2(1):25-30
4. Randhawa PS, Demetris AJ: Nephropathy due to polyomavirus type BK. *N Engl J Med* 2000;342:1361-1363
5. Volker NT, Klimkait IF, Binet P, et al: Testing for polyomavirus type BK DNA in plasma to identify renal-allograft recipients with viral nephropathy. *N Engl J Med* 2000;342:1309-1315
6. Hariharan S: BK virus nephritis after renal transplantation. *Kidney Int* 2006;69:655-662
7. Blanckaert K, De Vriese AS: Current recommendations for diagnosis and management of polyoma BK virus nephropathy in renal transplant recipients. *Nephrol Dial Transplant* 2006;21(12):3364-3367

8. Viscount HB, Eid AJ, Espy MJ, et al: Polyomavirus polymerase chain reaction as a surrogate marker of polyomavirus-associated nephropathy. *Transplantation* 2007;84(3):340-345

## Performance

### Method Description

Viral nucleic acid is extracted by the MagNA Pure automated instrument (Roche Applied Science) from clinical specimens. Primers are directed to the large T antigen gene, which is a conserved sequence specific for BK virus (BKV). This assay detects only BKV; it does not detect JC virus or Simian virus 40 (SV-40) (other polyoma viruses). The LightCycler instrument (Roche Applied Science) amplifies and monitors the development of target nucleic acid sequences after the annealing step during PCR cycling. This automated PCR system can rapidly detect (30-40 minutes) amplicon development through stringent air-controlled temperature cycling and capillary cuvettes. The detection of amplified products is based on the fluorescence resonance energy transfer (FRET) principle. For FRET product detection, a hybridization probe with a donor fluorophore, fluorescein, on the 3'-end is excited by an external light source and emits light that is absorbed by a second hybridization probe with an acceptor fluorophore, LC-Red 640, at the 5'-end. The acceptor fluorophore then emits a light of a different wavelength that can be measured with a signal that is proportional to the amount of specific PCR product. Quantitative standards are used to develop a standard curve. Specimens with unknown levels of BKV DNA are then compared to the standard curve to determine the copy level of the virus. Reportable range is from 1,600 IU/mL to 16,000,000 IU/mL. (Unpublished Mayo method)

### PDF Report

No

### Day(s) and Time(s) Test Performed

Monday through Saturday; Varies

### Analytic Time

2 days

### Maximum Laboratory Time

5 days

### Specimen Retention Time

1 week

### Performing Laboratory Location

Rochester

## Fees and Codes

### Fees

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

### Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

### CPT Code Information

87799

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
QBK	BK Virus PCR, Quant, P	32362-6

Result ID	Test Result Name	Result LOINC Value
83187	BK Virus PCR, Quant, P	32362-6
606459	BK Quant, P, IU/mL	32284-2