# Test Definition: UBKQN

BK Virus DNA Detection and Quantification, Random, Urine

## Overview

### Useful For

Detection and serial monitoring of BK virus (BKV)-associated nephropathy in kidney transplant recipients using random urine specimens

Detection and serial monitoring of BKV-associated hemorrhagic cystitis in organ transplant recipients

### Highlights

This assay detects and quantifies the level of BK virus (BKV) DNA present in the urine of kidney transplant recipients who are at risk of developing BKV-associated nephropathy or hemorrhagic cystitis leading to decreasing kidney function and eventual kidney failure. The assay is calibrated to the First World Health Organization International Standard for BKV DNA.

### Method Name

Real-Time Polymerase Chain Reaction (RT-PCR)

### NY State Available

No

## Specimen

### Specimen Type

Urine

### Specimen Required

**Supplies:** COBAS PCR - Urine Sample Kit (T903)
**Container/Tube:** cobas PCR urine tube
**Specimen Volume:** 4.3 mL
**Collection Instructions:**
1. Collect random urine into a sterile, plastic, preservative-free container.
2. Transfer 4.3 mL of urine into the cobas PCR urine sample tube using the disposable pipette provided within 24 hours of collection. The correct volume of urine has been added when the fluid level is between the black fill lines on the urine transport tube. Place the labels on the transport tube so the black fill lines are still visible for volume confirmation at Mayo Clinic Laboratories.
3. Transport and store urine specimen transport container at 2 to 30 degrees C (refrigerate is preferred temperature).
**Additional Information:** cobas PCR media contains guanidine hydrochloride. Do not allow these tubes to come in direct contact with sodium hypochlorite (bleach) or other highly reactive reagents such as acids and bases. These mixtures can release a noxious gas.

### 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)
-Kidney Transplant Test Request

### Specimen Minimum Volume

See Specimen Required

### Reject Due To

All specimens will be evaluated at Mayo Clinic Laboratories for test suitability.

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Urine | Refrigerated (preferred) | 84 days | COBAS PCR URINE |
| | Ambient | 84 days | COBAS PCR URINE |

## Clinical & Interpretive

### Clinical Information

BK virus (BKV) is a circular, double-stranded DNA virus with an approximately 5 kilobase-size genome in the polyomavirus family, of which 13 members of the family are known, including the JC virus (JCV) and SV40. BKV shares about 75% of its DNA sequence with JCV. Nearly 80% of the adult population worldwide have antibodies to both viruses, indicating previous infection or exposure to these viruses.

Initial infection with BKV is usually acquired in childhood, mostly asymptomatic or manifesting as a mild flu-like illness. After primary infection, BKV establishes latency in the kidney and bladder of the infected individual. In the setting of immunosuppression, the virus reactivates and begins to replicate, triggering renal tubular cell lysis and viruria. As the reactivation progresses, the virus multiplies and crosses into the bloodstream, causing viremia and invading the kidney graft. In patients with kidney transplants, reactivation of BKV typically reaches peak incidence at 3 months post-transplantation with BK viral replication in the kidney graft, causing BKV-associated nephropathy (BKVAN), which manifests as kidney dysfunction that may result in eventual loss of the transplanted kidney. Reactivation of BKV in the bladder can lead to hemorrhagic cystitis. Currently, there are no US Food and Drug Administration-approved antiviral agents or treatments for BKVAN or BKV-associated hemorrhagic cystitis. The main treatment is to decrease the immunosuppression with risk of acute rejection of the kidney graft.

After BK reactivation, the virus is first detectable in the urine, with viremia developing several weeks later. Quantitative BKV DNA in the plasma is the most widely used and preferred test for the laboratory diagnosis of BKVAN and BKV-associated hemorrhagic cystitis, as BKV viremia has higher positive predictive value (50%-60%) than BKV viruria for the diagnosis of BKVAN. Serial monitoring of BKV DNA level in plasma is recommended to guide optimal immunosuppressant dosing regimen. In those with BKVAN, clearance of BK viremia is a sign of resolution of the nephropathy.

## Reference Values

Undetected

## Interpretation

The quantification range of this assay is 200 to 100,000,000 IU/mL (2.30 log to 8.00 log IU/mL), with a limit of detection (95% detection rate) at 12 IU/mL.

An "Undetected" test result indicates the absence of BK virus (BKV) DNA in the urine.

A test result of "<200 IU/mL (<2.30 log IU/mL)" indicates that BKV DNA is detected in the urine, but the assay cannot accurately quantify the BKV DNA present below this level.

A quantitative value (reported in IU/mL and log IU/mL) indicates the level of BKV DNA (ie, viral load) present in the urine.

A test result of ">100,000,000 IU/mL (>8.00 log IU/mL)" indicates that BKV DNA level present in urine is above 100,000,000 IU/mL (8.00 log IU/mL), and the assay cannot accurately quantify BKV DNA present above this level.

An "Inconclusive" result indicates that the presence or absence of BKV DNA in the urine specimen could not be determined with certainty after repeat testing in the laboratory, possibly due to polymerase chain reaction inhibition or presence of interfering substance. Submission of a new specimen for testing is recommended if clinically indicated.

## Cautions

On average, quantitative BK virus (BKV) DNA results in urine tested with this assay can be up to 3.5-fold (about 0.54 log IU/mL) higher than those generated from the previous laboratory-developed BKV DNA quantification assay performed at Mayo Clinic Laboratories, due to differences in the specimen extraction method and design in the amplification primers and probes for the viral target sequences.

A single "Undetected" test result does not necessarily rule out the presence BKV infection or reactivation. Serial measurement (eg, once weekly) of BKV DNA in urine or plasma is recommended to determine the BKV replication status in a given transplant recipient.

While unlikely to be present in urine specimens, vaginal lubricants, speculum jellies, creams, and gels containing carbomers may interfere with the test and should not be used during or prior to sample collection. Urogenital specimens from patients who have used carbomer-containing products such as Replens Long-Lasting Vaginal Moisturizer, RepHresh Odor Eliminating Vaginal Gel, and RepHresh Clean Balance or used metronidazole vaginal gel may generate invalid or false-negative results.

## Clinical Reference

1. Bechert CJ, Schnadig VJ, Payne DA, Dong J. Monitoring of BK viral load in renal allograft recipients by real-time PCR assays. Am J Clin Pathol. 2010;133(2):242-250. doi:10.1309/AJCP63VDFCKCRUUL
2. Hirsch HH, Randhawa P, AST Infectious Diseases Community of Practice. BK polyomavirus in solid organ transplantation. Am J Transplant. 2013;13(Suppl 4):179-188. doi:10.1111/ajt.12110
3. Hirsch HH, Randhawa PS, AST Infectious Diseases Community of Practice. BK polyomavirus in solid organ transplantation-Guidelines from the American Society of Transplantation Infectious Diseases Community of Practice. Clin Transplant. 2019;33(9):e13528. doi:10.1111/ctr.13528

4. Muhsin SA, Wojciechowski D. BK virus in transplant recipients: current perspectives. Transplant Research and Risk Management. 2019;11:47-58. doi:10.2147/TRRM.S188021

## Performance

### Method Description

The cobas BK virus (BKV) assay is an FDA-approved, in vitro nucleic acid amplification test for the quantification of BKV DNA using either the cobas 6800 or 8800 system for fully automated viral nucleic acid extraction (generic silica-based capture technique) and automated amplification and detection of the viral RNA. This dual-target polymerase chain reaction (PCR) assay amplifies 2 highly conserved target regions within the BKV genome (small t-antigen and VP2 regions) for real-time detection and quantification by 2 target-specific TaqMan probes. A non-BKV armored DNA quantitation standard (DNA-QS) is introduced into each specimen during sample preparation to serve as internal control for nucleic acid extraction and PCR amplification and detection processes. Fluorescent reporter dye-labeled TaqMan probes hybridized to the complementary BKV target sequences and DNA-QS sequence undergo hydrolysis during PCR amplification step to generate fluorescent signal detected in 3 different dye channels. Concentration of the BKV DNA in a patient's sample is determined by a ratio of the intensity of the fluorescent dye from the cleaved BKV target sequence probes to that of the DNA-QS target probe detected throughout the PCR process.(Package insert: cobas BKV - Quantitative nucleic acid test for use on the cobas 6800/8800 Systems; Roche Molecular Systems; Doc rev 2.0, 02/2021)

### PDF Report

No

### Day(s) Performed

Monday through Saturday

### Report Available

1 to 3 days

### Specimen Retention Time

14 days

### Performing Laboratory Location

Mayo Clinic Jacksonville Clinical Lab

## Fees & 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 account representative. For assistance, contact Customer Service.

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## Test Classification

This test has been cleared, approved, or is exempt by the US Food and Drug Administration and is used per manufacturer's instructions. Performance characteristics were verified by Mayo Clinic in a manner consistent with CLIA requirements.

## CPT Code Information

87799

## LOINC® Information

| Test ID | Test Order Name | Order LOINC® Value |
|---|---|---|
| UBKQN | BKV DNA Detect/Quant, U | 32285-9 |

| Result ID | Test Result Name | Result LOINC® Value |
|---|---|---|
| 614568 | BKV DNA Detect/Quant, U | 32285-9 |