

**Overview****Useful For**

As an adjunct in the rapid diagnosis of human herpesvirus-6 infection in plasma specimens

**Method Name**

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

**NY State Available**

Yes

**Specimen****Specimen Type**

Plasma EDTA

**Specimen Required**

**Supplies:** Aliquot Tube, 5 mL (T465)

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

**Submission Container/Tube:**

**Preferred:** Aliquot Tube, 5 mL (T465)

**Acceptable:** Screw-capped, sterile container

**Specimen Volume:** 1 mL

**Collection Instructions:** Spin down promptly.

**Forms**

If not ordering electronically, complete, print, and send a [Microbiology Test Request](#) (T244) with the specimen.

**Specimen Minimum Volume**

0.3 mL

**Reject Due To**

Gross hemolysis	Reject
Gross lipemia	OK

**Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Refrigerated (preferred)	7 days	
	Frozen	7 days	

## Clinical and Interpretive

### Clinical Information

Herpesvirus-6 (HHV-6) is a member of the Herpesviridae family. These viruses contain DNA surrounded by a lipid envelope. Among members of this group, this virus is most closely related to cytomegalovirus (CMV) and HHV-7. As with other members of the herpesvirus group (herpes simplex virus [HSV] 1, HSV 2, varicella zoster virus [VZV], CMV, Epstein-Barr virus [EBV], HHV-7, HHV-8), HHV-6 may cause primary and reactivated infections subsequent to latent association with cells.(1) Infection with HHV-6 occurs early in childhood. Most adults (80%-90%) have been infected with this virus.

HHV-6 was first linked with exanthem subitum (roseola infantum) in 1998; since then, the virus has been associated with central nervous system disease almost exclusively in immunocompromised patients.(1) HHV-6 is commonly detected in patients posttransplantation. Clinical symptoms associated with this viral infection include febrile illness, pneumonitis, hepatitis, encephalitis, and bone marrow suppression. However, the majority of HHV-6 infections are asymptomatic.(2) The incidence of HHV-7 infection and its clinical manifestations posttransplantation are less well characterized.

HHV-6 is designated as variant A (HHV-6A) or variant B (HHV-6B) depending on restriction enzyme digestion patterns and on its reaction with monoclonal antibodies. Generally, variant B has been associated with exanthem subitum, whereas variant A has been found in many immunosuppressed patients.(3)

### Reference Values

Negative

### Interpretation

A positive result indicates the presence of specific DNA from human herpesvirus-6 (HHV-6) and supports the diagnosis of infection with this virus.

A negative result indicates the absence of detectable DNA from HHV-6 in the specimen, but it does not negate the presence of the virus or active or recent disease.

### Cautions

The sensitivity of the assay is very dependent upon the quality of the specimen submitted.

A negative test does not exclude infection with human herpesvirus-6 (HHV-6) virus. Therefore, the results obtained should be used in conjunction with clinical findings to make an accurate diagnosis.

This assay detects nucleic acid, and therefore, cannot distinguish between viable and nonviable virus. Test performance depends on viral load in the specimen and may not correlate with cell culture performed on the same specimen.

### Supportive Data

Accuracy:

A total of 32 plasma specimens and 30 cerebrospinal fluid (CSF) specimens were spiked with human herpesvirus-6 (HHV-6) plasmid control at the limit of detection (LoD) (25-50 copies/mL). The 62 spiked specimens were run in a blinded manner along with 28 negative (nonspiked) plasma and 30 negative (nonspiked) CSF specimens. Of the spiked specimens, 100% were positive; of the nonspiked specimens, 100% were negative.

Analytical Sensitivity/LoD:

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The lower LoD of this assay is 25 to 50 DNA target copies per mL (in plasma).

**Analytical Specificity:**

No PCR signal was obtained from extracts of 25 viral, bacterial, and fungal isolates that can cause similar symptoms as HHV-6 infection.

**Precision:**

Interassay precision was 100% and intra-assay precision was 100%.

**Reference Range:**

Although the reference range is typically "negative" for this assay, this assay may detect viremia in asymptomatic individuals. However, this assay is only to be used for patients with a clinical history and symptoms consistent with HHV-6 infection, and must be interpreted in the context of the clinical picture. This test should not be used to screen asymptomatic patients.

**Reportable Range:**

This is a qualitative assay and results are reported either as negative or positive for targeted HHV-6 DNA.

**Clinical Reference**

1. De Bolle L, Naesens L, De Clercq E: Update on human herpesvirus 6 biology, clinical features, and therapy. Clin Microbiol Rev 2005 Jan;18(1):217-245
2. Dockrell DH, Paya CV: Human herpesvirus-6 and -7 in transplantation. Rev Med Virol 2001 Jan-Feb;11(1):23-36
3. Abdel-Haq NM, Asmar BI: Human herpesvirus 6 (HHV6) infection. Indian J Pediatr 2004 Jan;71(1):89-96
4. Dockrell DH, Smith TF, Paya CV: Human herpesvirus 6. Mayo Clin Proc 1999 Feb;74(2):163-170

**Performance****Method Description**

Viral nucleic acid is extracted by the MagNA Pure automated instrument (Roche Applied Science) from clinical specimens. Primers directed to the immediate early gene of human herpesvirus-6 (HHV-6), produce a 195-bp amplicon. 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 (1 hour) detect 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 light of a different wavelength that can be measured with a signal that is proportional to the amount of specific PCR product. LightCycler hybridization probes are designed for exact homology to HHV-6.(Cockerill FR III, Uhl JR: Applications and challenges of real-time PCR for the clinical microbiology laboratory. In Rapid Cycle Real-Time PCR Methods and Applications. Edited by U Reischel, C Wittwer, F Cockerill. Berlin, Germany, Springer-Verlag, 2002, pp 3-30)

**PDF Report**

No

**Day(s) Performed**

Monday through Friday

**Report Available**

2 to 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 US Food and Drug Administration.

**CPT Code Information**

87532

**LOINC® Information**

Test ID	Test Order Name	Order LOINC Value
HHV6	HHV-6 PCR, P	29495-9

Result ID	Test Result Name	Result LOINC Value
87532	HHV-6 PCR, P	29495-9