PREMERA HMO

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ROUTINE TEST MANAGEMENT POLICY – 15.01.016

Identification of Microorganisms using Nucleic Acid Probes

Ref. Policy:	M2097
Effective Date:	Feb. 6, 2026
Last Revised:	Oct. 14, 2025
Replaces:	N/A

RELATED POLICIES:

15.01.008	Lyme Disease
15.01.043	Pathogen Panel Testing
15.01.026	Testing for Vector-Borne Infections

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Policy Description

Nucleic acid hybridization technologies utilize complementary properties of the DNA double-helix structures to anneal together DNA fragments from different sources. These techniques are utilized in polymerase chain reaction (PCR) and fluorescent resonance energy transfer (FRET) techniques to identify microorganisms (Khan, 2014).

A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy. Many probes have been combined into panels of tests. For the purposes of this policy, only individual probes are reviewed.

Indications

1. The coverage status of nucleic acid identification using direct probe, amplified probe, or quantification for the microorganism's procedure codes is summarized in Table 1 below. "MCC" in the table below indicates that the test is considered **reimbursable**; while "DNMCC" tests indicates that the test is **not reimbursable**.

Microorganism	Direct Probe	Amplified Probe	Quantification
Bartonella henselae or quintana			87472 (DNMCC)
Chlamydia pneumoniae			87487 (DNMCC)
Cytomegalovirus	87495 (MCC)	87496 (MCC)	
Hepatitis G	87525 (DNMCC)	87526 (DNMCC)	87527 (DNMCC)
Herpes virus-6		87532 (DNMCC)	
Legionella pneumophila	87540 (MCC)	87541 (MCC)	87542 (DNMCC)
Mycoplasma pneumoniae	87580 (MCC)	87581 (MCC)	87582 (DNMCC)

2. Simultaneous ordering of any combination of direct probe, amplified probe, and/or quantification for the same organism in a single encounter is **not reimbursable**.

Coding

Code	Description
CPT	
87472	Infectious agent detection by nucleic acid (DNA or RNA); Bartonella henselae and Bartonella quintana, quantification
87487	Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia pneumoniae, quantification
87495	Infectious agent detection by nucleic acid (DNA or RNA); cytomegalovirus, direct probe technique
87496	Infectious agent detection by nucleic acid (DNA or RNA); cytomegalovirus, amplified probe technique
87525	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis G, direct probe technique
87526	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis G, amplified probe technique
87527	Infectious agent detection by nucleic acid (DNA or RNA); hepatitis G, quantification
87532	Infectious agent detection by nucleic acid (DNA or RNA); Herpes virus-6, amplified probe technique
87540	Infectious agent detection by nucleic acid (DNA or RNA); Legionella pneumophila, direct probe technique

Code	Description
87541	Infectious agent detection by nucleic acid (DNA or RNA); Legionella pneumophila, amplified probe technique
87542	Infectious agent detection by nucleic acid (DNA or RNA); Legionella pneumophila, quantification
87580	Infectious agent detection by nucleic acid (DNA or RNA); Mycoplasma pneumoniae, direct probe technique
87581	Infectious agent detection by nucleic acid (DNA or RNA); Mycoplasma pneumoniae, amplified probe technique
87582	Infectious agent detection by nucleic acid (DNA or RNA); Mycoplasma pneumoniae, quantification

Related Information

Table of Terminology

Term	Definition
CDC	Centers for Disease Control and Prevention
CDI	Clostridioides difficile infection
CIDT	Culture-independent diagnostic test
CMV	Cytomegalovirus
CPT	Current procedural terminology
DFA	Direct fluorescent antibody testing
DNA	Deoxyribonucleic acid
EVD	Ebola virus disease
FDA	Food and Drug Administration
FRET	Fluorescent resonance energy transfer
HHV-6	Human herpesvirus 6
IDSA	Infectious Diseases Society of America
ITS	Internal transcribed region
Mpox	Monkeypox
MRSA	Methicillin-Resistant Staphylococcus Aureus
NAATs	Nucleic acid amplification tests

Term	Definition
NGU	Nongonococcal urethritis
PCR	Polymerase chain reaction
PID	Pelvic inflammatory disease
qPCR	Quantitative polymerase chain reaction
rDNA	Recombinant deoxyribonucleic acid
RNA	Ribonucleic acid
rRT-PCR	Real-time reverse transcriptase-polymerase chain reaction
RSV	Respiratory syncytial virus infection
RT-PCR	Reverse transcriptase-polymerase chain reaction
SARS	Severe acute respiratory syndrome

Evidence Review

Scientific Background

Nucleic acid hybridization technologies, including polymerase chain reaction (PCR), ligase- or helicase-dependent amplification, and transcription-mediated amplification, are beneficial tools for pathogen detection in blood culture and other clinical specimens due to high specificity and sensitivity (Khan, 2014). The use of nucleic acid-based methods to detect bacterial pathogens in a clinical laboratory setting offers "increased sensitivity and specificity over traditional microbiological techniques" due to its specificity, sensitivity, reduction in time, and high-throughput capability; however, "contamination potential, lack of standardization or validation for some assays, complex interpretation of results, and increased cost are possible limitations of these tests" (Mothershed & Whitney, 2006).

Guidelines and Recommendations

World Health Organization (WHO)

For detection of mpox, the WHO recommends "detection of viral DNA by polymerase chain reaction (PCR)" as the preferred laboratory test and recommends that any individual with a suspected case should be offered testing. They note that the best specimens for diagnosis are taken directly from the rash. Antigen and antibody detection may not be able to distinguish between orthopoxviruses (WHO, 2022).

2018 Infectious Diseases Society of America (IDSA)

Specific guidelines for testing of many organisms listed within the policy coverage criteria is found in the updated 2018 Infectious Diseases Society of America (IDSA) guidelines and recommendations titled, "A Guide to Utilization of the Microbiology Laboratory for Diagnosis of Infectious Diseases: 2018 Update by the Infectious Diseases Society of America and the American Society for Microbiology" (Miller et al., 2018). "This document is organized by body system, although many organisms are capable of causing disease in >1 body system. There may be a redundant mention of some organisms because of their propensity to infect multiple sites. One of the unique features of this document is its ability to assist clinicians who have specific suspicions regarding possible etiologic agents causing a specific type of disease. When the term "clinician" is used throughout the document, it also includes other licensed, advanced practice providers. Another unique feature is that in most chapters, there are targeted recommendations and precautions regarding selecting and collecting specimens for analysis for a disease process. It is very easy to access critical information about a specific body site just by consulting the table of contents. Within each chapter, there is a table describing the specimen needs regarding a variety of etiologic agents that one may suspect as causing the illness. The test methods in the tables are listed in priority order according to the recommendations of the authors and reviewers" (Miller et al., 2018).

Centers of Disease Control and Prevention (CDC)

Candida Auris (C. auris)

The CDC writes that "Molecular methods based on sequencing the D1-D2 region of the 28s rDNA or the Internal Transcribed Region (ITS) of rDNA can identify C. auris." The CDC further notes that various PCR methods have been developed for identifying C. auris (CDC, 2024d).

Chlamydia Pneumoniae (C. pneumoniae)

The CDC writes that RT-PCR is the "preferred" method of detecting an acute C. pneumoniae infection (CDC, 2024e).

Clostridioides difficile (C. diff)

The CDC states that there are four laboratory tests that can be used to diagnose Clostridioides difficile infection (CDI). "FDA-approved PCR assays are same-day tests that are highly sensitive and specific for the presence of a toxin-producing C. diff organism." The CDC does note that "molecular assays can be positive for C. diff in asymptomatic individuals and those who do not have an infection" and "when using multi-pathogen (multiplex) molecular methods, read the results with caution as the pre-test probability of C. diff infection might be less" (CDC, 2024b).

Cytomegalovirus (CMV)

The CDC states that "The enzyme-linked immunosorbent assay is the most common serologic test for measuring antibody to CMV." The CDC also notes that "congenital CMV infection cannot be diagnosed with antibody testing (IgG and IgM)" and recommends "the standard laboratory test for diagnosing congenital CMV infection is a PCR on saliva, with a confirmatory test on urine." (CDC, 2024f).

Mpox Virus

The CDC defines a suspect case of Mpox as a "new characteristic rash or meets one of the epidemiologic criteria and has a high clinical suspicion for mpox." A probable case is defined as "no suspicion of other recent Orthopoxvirus exposure (e.g., Vaccinia virus in ACAM2000 vaccination) AND demonstration of the presence of Orthopoxvirus DNA by polymerase chain reaction of a clinical specimen OR Orthopoxvirus using immunohistochemical or electron microscopy testing methods OR Demonstration of detectable levels of anti-orthopoxvirus IgM antibody during the period of 4 to 56 days after rash onset." A confirmed case of Mpox is defined as "demonstration of the presence of Mpox virus DNA by polymerase chain reaction testing or Next-Generation sequencing of a clinical specimen OR isolation of Mpox virus in culture from a clinical specimen" (CDC, 2024k).

The CDC states that "Mpox is diagnosed using real time PCR tests" and further notes "clinicians should collect two swabs from each lesion (generally from 2-3 lesions) in case additional testing, such as clade-specific testing, is needed for these patients" (CDC, 2024l).

MRSA

The CDC remarks that "Providers can test some patients to see if they carry MRSA in their nose or on their skin. This test involves rubbing a cotton-tipped swab in the patient's nostrils or on the skin. The only way to know if MRSA is the cause of an infection is to test for the bacteria in a laboratory." The CDC further states "There are many methods laboratorians can use to test for MRSA" and lists that "Phenotypic methods recommended for the detection of MRSA include: cefoxitin broth microdilution, oxacillin broth microdilution, and cefoxitin disk diffusion testing." The CDC includes additional methods including "Nucleic acid amplification tests, such as the polymerase chain reaction (PCR), to detect the mecA gene, which mediates oxacillin resistance in staphylococci" but notes "mecA PCR tests will not detect novel resistance mechanisms or uncommon phenotypes (e.g., mecC or borderline-resistant oxacillin resistance)" (CDC, 2024h).

Non-Polio Enterovirus

The CDC remarks that their laboratories "routinely" perform qualitative testing for enteroviruses, parechoviruses, and uncommon picornaviruses and states that "CDC and some health departments test with molecular sequencing methods, or a real-time reverse transcription polymerase chain reaction (rRT-PCR) lab test" (CDC, 2024j).

Respiratory Syncytial Virus (RSV)

The CDC writes that "PCR tests can be used to diagnose anyone for RSV. Antigen tests are only effective when testing infants and young children" (CDC, 2024c).

Miscellaneous

The CDC does not mention the need to quantify [through PCR] *Bartonella*, *Legionella pneumophila*, or *Mycoplasma pneumoniae*. However, PCR can be performed for both *Bartonella*, *Legionella pneumophila*, and *Mycoplasma pneumoniae* specimen (CDC, 2024a, 2024g, 2024i). "Nucleic Acid Amplification Tests (NAATs) are the preferred method of diagnostic testing for *M. pneumoniae* infections" (CDC, 2024i). No guidance was found on Hepatitis G.

Committee on Infectious Diseases, American Academy of Pediatrics, 31st Edition (2018-2021, Red Book)

The Committee on Infectious Diseases released joint guidelines with the American Academy of Pediatrics. In it, they note that "the presumptive diagnosis of mucocutaneous candidiasis or thrush usually can be made clinically." They also state that FISH probes may rapidly detect Candida species from positive blood culture samples, although PCR assays have also been developed for this purpose (AAP Committee on Infectious Diseases, 2018).

European Centre for Disease Prevention and Control (ECDC)

On May 23, 2022, the ECDC released a rapid risk assessment of the Mpoxmulti-country outbreak. They recommend that patients with probable cases should be tested with a "Mpox virus specific PCR or an orthopoxvirus specific PCR assay which is then confirmed through sequencing" (ECDC, 2022b).

On June 2, 2022, ECDC released interim advice on risk communication and community engagement during the 2022 Mpox outbreak in Europe. This is a joint report with the WHO regional office for Europe. They recommend speaking to your doctor about getting tested for Mpox if you develop a rash with a fever or feeling of discomfort or illness (ECDC, 2022a).

United Kingdom Heath Security Agency (UKHSA)

The UKHSA states that "Mpox is diagnosed by PCR test for the Mpox virus (MPXV) on a viral swab taken from one or more vesicles or ulcers." Specifically, it is recommended that healthcare workers "Take a viral swab in viral culture medium or viral transport medium (for example Virocult) from an open sore or from the surface of a vesicle. If other wounds are present, ensure that the sample is definitely taken from a vesicle, an ulcer or a crusted vesicle. Rub the swab over the lesion and place the swab in the collection tube. If there are pharyngeal lesions, a throat swab should also be taken" (UKHSA, 2024). UKHSA also suggests that "A viral throat swab can be taken for high-risk contacts of a confirmed or highly probable case who have developed systemic symptoms but do not have a rash or lesions that can be sampled. Please note that even if the throat swab is negative, the individual must continue with monitoring and isolation as instructed by their local health protection team, and should be reassessed and sampled if further symptoms develop." Lastly, "If follow-up testing is required from a confirmed or highly probable case, either because of clinical deterioration or to inform discharge from isolation to an inpatient setting, additional samples should be taken and should include the following:

- a lesion swab and throat swab in viral transport medium
- a blood sample in an EDTA tube
- a urine sample in a universal sterile container" (UKHSA, 2024).

The UKHSA states that "Following the identification of a cluster of sexually transmitted HCID Clade I mpox in 2023, there is an increased risk of mpox HCID infection circulating unrecognized on the background of Clade II infections." They therefore recommend "All diagnostic samples from all individuals testing positive for mpox should now be subject to clade confirmation. Positive mpox samples should be sent to RIPL for clade specific testing if clade differentiation is not available through local mpox testing services" (UKHSA, 2024).

The UKHSA states that mpox DNA viruses can be detected in semen up to 11 days after acute infection, and recommends that: "Following the initial 12 weeks and up to 6 months after recovery from infection, UKHSA recommends performing MPXV PCR on semen samples (and where necessary, oropharyngeal and/or rectal swabs) if the patient:

- is undergoing fertility treatment or planning pregnancy
- is undergoing planned semen storage (for example prior to chemotherapy)
- has an immunocompromised sexual partner (including a pregnant partner)
- is concerned about transmission to sexual partner or partners for any other reason and requests a test from their clinician" (UKHSA, 2024).

HHV-6 Foundation

The human herpesvirus 6 (HHV-6) foundation also states that "a negative finding in the plasma does not rule out a localized active infection in an organ (e.g. uterus, brain, thyroid, liver). Persistent HHV-6 infections have been found in the liver, brain, lungs, heart tissue and uterus, with no trace of HHV-6 DNA in the plasma. Quantitative testing on blood and tissues is preferred because it can differentiate between the very low levels occasionally found in healthy controls and high levels found in diseased tissues" (HHV-6 Foundation, 2024).

The HHV-6 foundation states that qualitative PCR DNA tests on whole blood are "useless for differentiating active from latent infection" but notes that the test may be useful for differentiating between herpes virus-6A and herpes virus-6B. The HHV-6 foundation states that quantitative PCR DNA tests on whole blood can differentiate active from latent infection "If the viral load is >200 copies per ml or 20 copies per microgram of DNA then this is an active infection."

US Food and Drug Administration (FDA)

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the US Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

A list of current US Food and Drug Administration (FDA, 2022) approved or cleared nucleic acid-based microbial tests is available at: **https://www.fda.gov/medical-devices/vitro-diagnostics/nucleic-acid-based-tests**.

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History

Date	Comments
11/01/25	New policy, approved October 14, 2025, effective for dates of service on or after February 6, 2026, following 90-day provider notification. Add to Routine Test Management Policy section. Coverage for nucleic acid identification by direct probe, amplified probe, or quantification may be considered reimbursable when the criteria listed in this policy is met; ordering multiple methods for the same organism in one encounter is not reimbursable.

Disclaimer: This policy for routine test management is a guide in evaluating the clinical appropriateness and reimbursement methodology for lab tests. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA).

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