Medical Policy

BlueCross BlueShield of Kansas
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Title: Identification of Microorganisms Using Nucleic Acid Probes

See Also: *Influenza Virus Diagnostic Testing and Treatment in the Outpatient Setting*

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DESCRIPTION

Nucleic acid probes can identify microorganisms more rapidly than traditional culture. Direct probes identify organisms that are present using immunoassays or fluorescence in situ hybridization (FISH). Polymerase chain reaction (PCR) can be used to amplify probe signals to increase the sensitivity of detection. Quantitative probes are also available for some organisms, with which an estimate of the number of organisms present is made.

Background

Until recently, identification of microorganisms depended either on culture of body fluids or tissues or identification of antigens, using a variety of techniques including direct fluorescent antibody technique and qualitative or quantitative immunoassays. These techniques are problematic when the microorganism exists in very small numbers or is technically difficult to culture. Indirect identification of microorganisms by immunoassays for specific antibodies reactive with the microorganism is limited by difficulties in distinguishing between past exposure and current infection; although to some extent immunoglobulin M (IgM) versus IgG antibodies can be helpful. Response to treatment is typically assessed according to the patient's clinical response or by rising titers of specific antibodies and falling antigen titers.

The availability of nucleic acid probes has permitted the rapid direct identification of microorganisms' DNA or RNA. Amplification techniques result in exponential increases in copy numbers of a targeted strand of microorganism-specific DNA. The most commonly used amplification technique is the polymerase chain reaction (PCR) or reverse transcriptase PCR. In addition to PCR, other nucleic acid amplification techniques have been developed such as transcription-mediated amplification (TMA), loop-mediated isothermal DNA amplification (LAMP), strand displacement amplification, nucleic acid sequence-based amplification and branched chain DNA signal amplification. After amplification, target DNA can be readily detected using a variety of techniques. The amplified product can also be quantified to give an assessment of how many microorganisms are present. Quantification of the amount of nucleic acids permits serial assessments of response to treatment; the most common clinical application of quantification is the serial measurement of human immunodeficiency virus (HIV) RNA (called viral load), which serves as a prognostic factor. Until 1998, these nucleic acid probe techniques were coded using nonspecific CPT codes describing the multiple steps in the laboratory process. However, in 1998, the CPT codes were revised to include a series of new codes that describe the direct probe technique, amplified probe technique, and quantification for 22 different microorganisms. These series of CPT codes were introduced as a group; however, at present, probe technologies and clinical applications for some microorganisms are either not widely disseminated or are used primarily for research purposes. In addition, CPT codes have been added for additional microorganisms, such as *Staphylococcus aureus*. A number of different microorganisms are reviewed as follows:

Bartonella henselae or quintana: *Bartonella henselae or quintana* is thought to be responsible for cat scratch disease, which is characterized by chronic regional lymphadenopathy developing about 2 weeks after contact with a cat. A cat scratch skin antigen test is positive in the majority of patients with cat scratch disease, but this test cannot distinguish between active and remote infection.

Bartonella may also cause an opportunistic infection in HIV-infected patients, in whom it is characterized by an acute febrile bacteremic illness, evolving to an asymptomatic

bacteremia and finally indolent vascular skin lesions. The organism is typically detected using culture techniques, although an incubation period of 5 to more than 30 days is required. DNA probe technology has been investigated as a diagnostic technique.

Borrelia burgdorferi: *Borrelia burgdorferi* is responsible for Lyme disease. Antibody assays are typically the first diagnostic laboratory test performed; but these assays may be negative during early disease, and, in the later course of the disease, immunologic assays cannot distinguish between past and present infections, a severe limiting factor in areas of high prevalence. The spirochete is also difficult to culture, in part because the number of organisms in clinical specimens is extremely low. Therefore, in some instances, PCR amplification has been used to confirm the diagnosis of active Lyme disease. High sensitivities have been reported from synovial fluid samples; sensitivities of the PCR technique for cerebrospinal fluid, blood, and urine have been disappointing (low and/or variable).

Candida species: A commonly occurring yeast, *Candida species* normally can be found on diseased skin, throughout the entire gastrointestinal tract, expectorated sputum, the female genitalia, and in urine of patients with indwelling Foley catheters. Clinically significant Candida infections are typically diagnosed by clinical observation or by identification of the yeast forms on biopsy specimens. *Candida species* are a common cause of vaginitis.

Chlamydia pneumoniae: *Chlamydia pneumoniae* is an important cause of pneumonia, bronchitis, and sinusitis. Culture and isolation of the microorganism is difficult; a microimmunofluorescence serum test may be used. The use of PCR amplification now offers a rapid diagnosis.

Chlamydia trachomatis: *Chlamydia trachomatis* is a significant intracellular pathogen causing, most prominently, urogenital disease (including pelvic inflammatory disease) and perinatal infections. *C trachomatis* is also responsible for lymphogranuloma venereum (LGV). Due to its prevalence and association with pelvic inflammatory disease and perinatal disease, widespread testing of chlamydia is recommended; routine chlamydia testing has been adopted as a quality measure by Healthcare Effectiveness Data and Information Set (HEDIS). This microorganism can be diagnosed by: 1) identifying the typical intracytoplasmic inclusions in cytology specimens; 2) isolation in tissue culture; 3) demonstration of chlamydial antigen by enzyme-linked immunosorbent assay or by immunofluorescent staining; or 4) demonstration of DNA using a direct probe or amplification technique.

Cytomegalovirus: Cytomegalovirus (CMV) is a common virus that infects many, but rarely causes clinical disease in healthy individuals. However, this virus can cause protean disease syndromes, most prominently in immunosuppressed patients, including transplant recipients or those infected with the HIV virus. CMV can also remain latent in tissues after recovery of the host from an acute infection. Diagnosis depends on

demonstration of the virus or viral components or demonstration of a serologic rise. DNA probe techniques, including amplification, have also been used to identify patients at risk for developing CMV disease as a technique to triage antiviral therapy.

Clostridium difficile: *Clostridium difficile* is an anaerobic, toxin-producing bacteria present in the intestinal tract. It causes clinical colitis when the normal intestinal flora is altered and overgrowth of *C difficile* occurs. The common precipitant that disrupts the normal intestinal flora is previous treatment with antibiotics. The disorder has varying severity but can be severe and in extreme cases, life-threatening. *C difficile* is easily spread from person-to-person contact and is a common cause of hospital-acquired outbreaks. Hospital infection control measures, such as wearing gloves and handwashing with soap and water, are effective methods of reducing the spread of *C difficile*. The standard diagnosis is made by an assay for the *C difficile* cytotoxin or by routine culture methods.

Enterovirus: Enteroviruses are single-stranded ribonucleic acid (RNA) viruses. This group of viruses includes the polioviruses, coxsackieviruses, echoviruses, and other enteroviruses. In addition to 3 polioviruses, there are more than 60 types of non-polio enteroviruses that can cause disease in humans. Most people who are infected with a non-polio enterovirus have no disease symptoms at all. Infected persons who develop illness usually develop either mild upper respiratory symptoms, flu-like symptoms with fever and muscle aches, or an illness with rash. Less commonly, some persons have "aseptic" or viral meningitis. The use of amplified probe DNA test(s) can be used to detect enteroviruses.

Gardnerella vaginalis: A common microorganism, *Gardnerella vaginalis* is typically found in the human vagina and is usually asymptomatic. However, *G vaginalis* is found in virtually all women with bacterial vaginosis and is characterized by inflammation and perivaginal irritation. The microorganism is typically identified by culture. The role of *G vaginalis* in premature rupture of membranes and preterm labor is also under investigation.

Hepatitis B, C, and G: Hepatitis is typically diagnosed by a pattern of antigen and antibody positivity. However, the use of probe technology permits the direct identification of hepatitis DNA or RNA, which may also provide prognostic information. Quantification techniques are used as a technique for monitoring the response to interferon and/or ribavirin therapy in patients with hepatitis C.

Herpes simplex virus (HSV): Herpes simplex infection of the skin and mucous membranes is characterized by a thin-walled vesicle on an inflammatory base typically in the perioral, ocular, or genital area, although any skin site may be involved. The diagnosis may depend on pathologic examination of cells scraped from a vesicle base or by tissue culture techniques. Herpes simplex encephalitis is one of the most common and serious sporadic encephalitides in immunocompetent adults. The PCR technique to

detect HSV in the cerebrospinal fluid has been used to provide a rapid diagnosis of herpes virus encephalitis.

Herpes virus-6: Human herpes virus-6 (HHV-6) is widespread in the general population and is also responsible for roseola, a benign rash and fever occurring in young children. HHV-6 may also cause meningitis, encephalitis, pneumonitis, and hepatitis in children and adults. Diagnosis is typically based on rising serologic titers.

HIV-1, HIV-2: DNA probe technology for HIV-1 is widely disseminated, and HIV-1 quantification has become a standard laboratory test in HIV-1 infected patients. HIV-2 can result in severe immunosuppression and the development of serious opportunistic diseases. Although HIV-2 has been reported in the United States, it is most commonly found in Western Africa. Blood donations are routinely tested for HIV-2, but due to its rarity in this country, clinical testing for HIV-2 is typically limited to those in contact with persons in a country where HIV-2 is endemic or when the clinical picture suggests HIV infection, but testing for HIV-1 is negative.

Influenza virus*:* Influenza virus is a very common pathogen that accounts for a high burden of morbidity and mortality, especially in elderly and immunocompromised patients. The most common means of identifying influenza is by viral culture, which takes 48-72 hours to complete. Influenza is highly contagious and has been the etiology of numerous epidemics and pandemics. Identification of outbreaks is important so that isolation measures may be undertaken to control the spread of disease. Anti-viral treatment can be effective if instituted early in the course of disease. Therefore, rapid identification of influenza virus is important in making treatment decisions for high-risk patients and in instituting infection control practices.

Legionella pneumophila: *Legionella pneumophila* is among the most common microbial etiologies of community-acquired pneumonia. Laboratory diagnosis depends on culture, direct fluorescent antibody tests, urinary antigens, or DNA probe. DNA probe techniques have also been used in epidemiologic investigations to identify the source of a Legionella outbreak.

Mycobacteria species: Although mycobacterium can be directly identified in sputum samples (i.e., acid fast bacilli), these organisms may take 9 to 16 days to culture. DNA probes have also been used to identify specific mycobacterial groups (i.e., mycobacterial tuberculosis, avian complex, or intracellulare) after culture. In addition, amplification techniques for mycobacterium tuberculosis may be used in patients who have a positive smear. The rapid identification of *Mycobacteria tuberculosis* permits prompt isolation of the patient and identification of the patient's contacts for further testing.

Mycoplasma pneumoniae*: Mycoplasma pneumoniae* is an atypical bacterium that is a common cause of pneumonia. It is most prevalent in younger patients, younger than age 40 years and in individuals who live or work in crowded areas such as schools or

medical facilities. The infection is generally responsive to antibiotics of the macrolide or quinolone class. Most patients with mycoplasma pneumonia recover completely, although the course is sometimes prolonged for up to 4 weeks or more. Extra-pulmonary complications of mycoplasma pneumonia occur uncommonly, including hemolytic anemia and the rash of erythema multiforme.

Neisseria gonorrhoeae: Isolation by culture is the conventional form of diagnosis for this common pathogen. Direct DNA probes and amplification techniques have also been used. Neisseria is often tested for at the same time as Chlamydia.

Papillomavirus: *Papillomavirus species* are common pathogens that produce epithelial tumors of the skin and mucous membranes, most prominently the genital tract. Physical examination is the first diagnostic technique. Direct probe and amplification procedures have been actively investigated in the setting of cervical lesions. The ViraPap test is an example of a commercially available direct probe technique for identifying papillomavirus. There has also been interest in evaluating the use of viral load tests of papilloma virus to identify patients at highest risk of progressing to invasive cervical carcinoma.

Streptococcus, group A: Also referred to as *Streptococcus pyogenes,* this pathogen is the most frequent cause of acute bacterial pharyngitis. It can also give rise to a variety of cutaneous and systemic conditions, including rheumatic fever and post-streptococcal glomerulonephritis. Throat culture is the preferred method for diagnosing *Streptococcus pharyngitis.* In addition, a variety of commercial kits are now available that use antibodies for the rapid detection of group A carbohydrate antigen directly from throat swabs. While very specific, these kits are less sensitive than throat cultures, so a negative test may require confirmation from a subsequent throat culture. DNA probes have also been used for direct identification of streptococcus and can be used as an alternative to a throat culture as a back-up test to a rapid, office-based strep test.

Streptococcus, group B (GBS): Also referred to as *Streptococcus agalactiae*, GBS is the most common cause of sepsis, meningitis, or death among newborns. Early-onset disease, within 7 days of birth, is related to exposure to GBS colonizing the mother's anogenital tract during birth. The Centers for Disease Control and Prevention (CDC), the American College of Obstetrics and Gynecology (ACOG), and the American Academy of Pediatricians (AAP) recommend either maternal risk assessment or screening for GBS in the perinatal period. Screening consists of obtaining vaginal and anal specimens for culture at 35 to 37 weeks' gestation. The conventional culture and identification process requires 48 hours. Therefore there has been great interest in developing rapid assays using DNA probes to shorten the screening process, so that screening could be performed in the intrapartum period with institution of antibiotics during labor.

Trichomonas vaginalis: Trichomonas is a single-cell protozoan that is a common cause of vaginitis. The organism is sexually transmitted and can infect the urethra or

vagina. The most common way of diagnosing trichomonas is by clinical signs and by directly visualizing the organism by microscopy in a wet prep vaginal smear. Culture of trichomonas is limited by poor sensitivity. Treatment with metronidazole results in a high rate of eradication. The disease is usually self-limited without sequelae, although infection has been associated with premature birth and higher rates of HIV transmission, cervical cancer, and prostate cancer.

A list of current U.S. Food and Drug Administration (FDA)-approved or cleared nucleic acid-based microbial tests is available at:
http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm330711.htm

The Association of Molecular Pathology (AMP) website also provides a list of current U.S. FDA approved tests for diagnosis of infectious diseases (available online at: http://www.amp.org/FDATable/FDATable.pdf). The table below lists tests that are FDA-approved/cleared but do **not** have specific CPT codes.

FDA Approved/Cleared Diagnostic Test	Test Type
Bacillus anthracis	Real-time PCR
Coxiella burnetii (Q fever)	Real-time PCR
Enterococcus faecalis	PNA (Peptide nucleic acid) FISH
Escherichia coli and Pseudomonas aeruginosa	PNA FISH
Escherichia coli and/or Klebsiella pneumoniae and Pseudomonas aeruginosa	PNA FISH
Escherichia coli, Klebsiella pneumoniae and Pseudomonas aeruginosa	PNA FISH
Francisella tularensis	Real-time PCR
Leishmania	Real-time PCR
Yersinia pestis	Real-time PCR
Adenovirus	Multiplex Real-time RT-PCR
Avian Flu	Real-time RT-PCR
Human metapneumovirus	Multiplex Real-time RT-PCR
Influenza virus A/H5	Real-time RT-PCR
Influenza virus H1N1	Real-time RT-PCR
Dengue virus	Real-time RT-PCR

POLICY

Note: A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy.

I. The status of nucleic acid identification using direct probe, amplified probe, or quantification for the 30 microorganisms listed in the CPT book are summarized in the following table. NOTE: "(med nec)" in the chart below applies only when the service is clinically indicated:

Microorganism	Direct Probe	Amplified Probe	Quantification
Bartonella henselae or quintana	87470 (inv)	87471 (inv)	87472 (inv)
Borrelia burgdorferi	87475 (inv)	87476 (inv)	87477 (inv)
Candida species	87480 (med nec)	87481 (inv)	87482 (inv)
Chlamydia pneumoniae	87485 (inv)	87486 (inv)	87487 (inv)
Chlamydia trachomatis	87490 (med nec)	87491 (med nec)	87492 (inv)
Clostridium difficile	87493 (med nec)	87798 (inv)	87799 (inv)
Cytomegalovirus	87495 (med nec)	87496 (med nec)	87497 (med nec)
Enterovirus	87797 (inv)	87498 (inv)	87799 (inv)
Enterococcus, Vancomycin resistant (e.g., enterococcus vanA, vanB)	87797 (inv)	87500 (med nec)	87799 (inv)
Gardnerella vaginalis	87510 (med nec)	87511 (inv)	87512 (inv)
Hepatitis B	87515 (med nec)	87516 (med nec)	87517 (med nec)
Hepatitis C	87520 (med nec)	87521 (med nec)	87522 (med nec)
Hepatitis G	87525 (inv)	87526 (inv)	87527 (inv)
Herpes simplex virus	87528 (med nec)	87529 (med nec)	87530 (inv)
Herpes virus-6	87531 (inv)	87532 (inv)	87533 (inv)
HIV-1	87534 (med nec)	87535 (med nec)	87536 (med nec)
HIV-2	87537 (med nec)	87538 (med nec)	87539 (med nec)
Influenza virus	*See medical policy titled: Influenza Virus Diagnostic Testing and Treatment in the Outpatient Setting*		
Legionella pneumophila	87540 (inv)	87541 (inv)	87542 (inv)
Mycobacterium species	87550 (med nec)	87551 (inv)	87552 (inv)
Mycobacterium tuberculosis	87555 (med nec)	87556 (med nec)	87557 (inv)
Mycobacterium avium intracellulare	87560 (med nec)	87561 (inv)	87562 (inv)
Mycoplasma pneumoniae	87580 (inv)	87581 (inv)	87582 (inv)
Neisseria gonorrhoeae	87590 (med nec)	87591 (med nec)	87592 (inv)

Microorganism	Direct Probe	Amplified Probe	Quantification
Papillomavirus	87620 (med nec)	87621 (med nec)	87622 (inv)
Respiratory Virus Panel	*See item IV on page 11 of this policy.*		
Staphylococcus aureus	87797 (inv)	87640 (med nec)	87799 (inv)
Staphylococcus aureus, methicillin resistant	87797 (inv)	87641 (med nec)	87799 (inv)
Streptococcus group A*	87650 (med nec)	87651 (inv)	87652 (inv)
Streptococcus group B	87797 (inv)	87653 (med nec)	87799 (inv)
Trichomonas vaginalis	87660 (med nec)	87661 (med nec) (Eff 01-01-2014) 87798 (med nec) (Eff 01-01-2014 use 87661)	87799 (inv)

*The direct DNA probe test for streptococcus A is designed to be an alternative to a confirmatory culture. Therefore, the simultaneous use of confirmatory culture and DNA probe test is considered not medically necessary. Antibiotic sensitivity of streptococcus A cultures is frequently not performed for throat cultures. However, if an antibiotic sensitivity is considered, then the most efficient method of diagnosis would be a combined culture and antibiotic sensitivity.

Note: If NOC codes 87797, 87798, 87799 are billed for PCR for microorganisms when specific codes exist, the claim will be returned for correct coding.

II. Other polymerase chain reaction (PCR) testing (87797, 87798, and 87799 describing the use of direct probe, amplified probe, and quantification respectively) for infectious agents that do not have specific CPT codes may be considered **medically necessary** for the following indications (not an all-inclusive list):
   A. Adenovirus - to diagnose adenovirus myocarditis, and infection in immunocompromised hosts, including transplant recipients
   B. Avian influenza A virus (H5N1) - with both symptoms consistent with Avian influenza A virus and a history of travel to or contact with persons or birds from a country with documented H5N1 avian influenza infections within 10 days of symptom onset. (http://www.oie.int/eng/en_index.htm)
   C. Babesiosis *(Babesia*) - when the morphologic characteristics observed on microscopic examination of blood smears do not allow differentiation between Babesia and Plasmodium
   D. Bacillus anthracis
   E. BK polyomavirus - in transplant recipients and persons with immunosuppressive diseases (e.g., AIDS)
   F. Bordetella pertussis
   G. *Brucella spp*. - signs and symptoms of Brucellosis
   H. *Burkholderia* infections
   I. Chancroid *(Haemophilus ducreyi)* - for genital ulcer disease

J. Colorado tick fever virus
K. *Coxiella burnetii* - for acute Q fever
L. Ehrlichiosis *(Ehrlichia)*
M. Epidemic typhus *(Rickettsia prowazekii*)
N. *Epstein Barr Virus (EBV)* - for detection of EBV in post-transplant lymphoproliferative disorder or for tissue samples with lymphoma and other immunocompromised states
O. *Francisella tularensis*, for diagnosis of tularemia
P. Hemorrhagic fevers of the family *Bunyaviridae* (Rift Valley fever, Crimean-Congo hemorrhagic fever, hemorrhagic fever with renal syndromes) - clinical presentation suggestive of these conditions
Q. Human granulocytic anaplasmosis (formerly *Ehrlichia phagocytophilum*)
R. Human metapneumonvirus
S. JC polyomavirus - in transplant recipients, immunosuppressive diseases and for progressive multifocal leukoencephalopathy when receiving natalizumab (Tysabri)
T. Leishmaniasis
U. Lymphogranuloma venereum *(Chlamydia trachomatis*)
V. Malaria
W. Measles virus
X. Microsporidia
Y. Mumps
Z. *Neisseria meningitides*
AA. Parvovirus
BB. Psittacosis *(Chlamydophila (Chlamydia) psittaci)*
CC. Rocky Mountain Spotted Fever (*Rickettsia rickettsii*)
DD. Severe acute respiratory syndrome (SARS) (coronavirus)
EE. Syphilis *(Treponema pallidum)*
FF. *Toxoplasma gondii*
GG. Varicella-Zoster
HH. West Nile Virus - in tissue specimens
II. Whipple's disease *(T. whippeli*)
JJ. Yersinia pestis

III. The following other quantitative PCR tests (87799) are considered **medically necessary**:
A. Adenovirus viral load, to monitor response to antiviral therapy in infected immunocompromised hosts, including transplant recipients
B. BK polyomavirus viral load, for diagnosis and monitoring response to therapy in infected kidney transplant recipients
C. Cytomegalovirus (CMV) viral load, to monitor response to therapy
D. Epstein Barr viral load, to monitor for EBV viral replication in solid organ transplant recipients

IV. The Respiratory Virus Panel (87631, 87632, 87633) will be **reviewed for medical necessity** on a case-by-case basis.

V. PCR testing for the following indications is considered **experimental / investigational** because of insufficient evidence in the peer-reviewed literature:
   A. Actinomycosis
   B. Astrovirus
   C. Bacterial vaginosis *(Atopobium vaginae, Mobiluncus mulieris, M. curtisii, Megasphaera, Bacterial vaginosis Associated Bacteria panel [BVAB]*)
   D. Bacteroides spp. *(B. fragilis, B. ureolyticus*)
   E. Caliciviruses (noroviruses and sapoviruses)
   F. Campylobacteriosis *(Campylobacter* infection)
   G. Coccidiodomycosis *(Coccidioides* species)
   H. Cryptococcus *(Cryptococcus neoformans*)
   I. Cyclosporiasis (Cyclospora infection)
   J. Dengue fever
   K. Donovanosis, or granuloma inguinale *(Klebsiella granulomatis*)
   L. Eastern equine encephalitis
   M. *Entamoeba histolytica*
   N. Genital mycoplasma infections from *Ureaplasma urealyticum* and *Mycoplasma hominis* (unless culture is unavailable)
   O. Haemophilus influenzae
   P. Hantavirus
   Q. Hepatitis A virus
   R. Hepatitis D virus
   S. Human bocavirus
   T. Human herpesvirus type 7 (HHV-7)
   U. Human herpesvirus type 8 (HHV-8)
   V. Human metapneumovirus
   W. LaCrosse encephalitis
   X. Leptospirosis *(Leptospira* organisms)
   Y. Molluscum contagiosum
   Z. *Moraxella catarrhalis*
   AA. *Mycoplasma fermentans*
   BB. *Mycoplasma genitalium*
   CC. *Mycoplasma penetrans*
   DD. Nanobacteria
   EE. Non-albicans Candida
   FF. Onychomycosis
   GG. Parainfluenza virus
   HH. Peptic ulcer disease *(Helicobacter pylori*) (other than in persons with MALT lymphomas and marginal zone lymphomas)
   II. Pneumococcal infections *(S. pneumoniae*)
   JJ. Pneumocystis pneumonia *(Pneumocystis jiroveci* (formerly *P. carinii*))

KK. *Prevotella spp*.
LL. *Proteus mirabilis*
MM. Pseudomonas *(P. aeruginosa*)
NN. Respiratory syncytial virus (RSV)
OO. Rhinovirus
PP. Rotavirus
QQ. *Saccharomyces cerevisiae*
RR. Serratia spp. (including *S. marcescens*)
SS. Shiga toxin (from *E. coli* and Shigella)
TT. Sporotrichosis *(Sporothrix schenckii*)
UU. St. Louis encephalitis
VV. *Staphylococcus saprophyticus*
WW. Trichosporonosis *(Trichosporon* spp.)
XX. Western equine encephalitis

Policy Guidelines

1. It should be noted that the technique for quantification includes both amplification and direct probes; therefore, simultaneous coding for both quantification with either amplification or direct probes, is not warranted.

2. In the evaluation of Group B streptococcus, the primary advantage of a DNA probe technique compared to traditional culture techniques is the rapidity of results. This advantage suggests that the most appropriate use of the DNA probe technique is in the setting of impending labor, for which prompt results could permit the initiation of intrapartum antibiotic therapy.

3. Many probes have been combined into panels of tests. For the purposes of this policy, other than the respiratory virus panel, only individual probes are reviewed.

RATIONALE

Although nucleic acid probe technologies offer the potential for rapid, sensitive detection for a variety of microorganisms, there are many technologic limitations, and the clinical application of these techniques is still developing. This technology requires the identification and manufacture of nucleic acid probes, i.e., short strands of either DNA or RNA, that are specific to the target microorganism. Amplification requires the use of specific short segments of complementary DNA, called primers, to initiate the repetitive rounds of DNA duplication. For many of the microorganisms, these probes or primers are not commercially available, and different reference laboratories may use different products. Early amplification techniques of polymerase chain reaction (PCR), raised considerable concerns regarding contamination from one specimen to another, creating the potential for false positive results. Nonspecific amplification is also a concern related in part to the specificity of the probes used. The clinical interpretation of results may also be challenging. Amplification of organisms representing latent infection or colonization cannot be distinguished from active, clinically significant infections. In addition, amplification techniques may amplify fragments of nucleic acids, representing dead microorganisms, thus further clouding the

clinical interpretation. Finally, specificities, sensitivities, and positive and negative predictive values have not been reported in large groups of patients for many of the microorganisms. Newer nucleic acid amplification techniques have been developed to reduce concerns regarding possible laboratory cross contamination and improve the clinical relevance of test results with higher sensitivity rates. In general, nucleic acid probe techniques are used when traditional culture is difficult due to the low numbers of the organisms (i.e., human immunodeficiency virus, [HIV]), fastidious or lengthy culture requirements (i.e., mycobacterium, chlamydia, or neisseriae), or difficulty in collecting an appropriate sample (herpes simplex encephalitis). (1-4) Quantification is a useful clinical tool when the viral load can be used as a prognostic indicator or to follow the patient's response to therapy; this is an established practice in patients with HIV or hepatitis C. The clinical utility, and medical necessity, of these probes will be determined in part by the accuracy of the test (sensitivity, specificity, and predictive value) compared to standard identification techniques. The rapidity of results will also be considered, with the clinical utility of early identification considered in the context of each clinical situation to determine medical necessity.

Bartonella henselae or quintana. Microbiologic detection of *Bartonella henselae* or *quintana* is difficult, and molecular testing is not readily available. However, a monoclonal antibody (mAB) to *B henselae* has become commercially available. A 2009 study (5) evaluated the usefulness of immunohistochemical analysis (IHC) for diagnosing *Bhenselae* on surgical specimens and compared these results with polymerase chain reaction (PCR) detection and serologic testing. The study included 24 formalin-fixed, paraffin-embedded (FFPE) cases of lymphadenitis with histologic and/or clinical suspicion of *Bhenselae*. Control cases included 14 cases of lymphadenopathy. FFPE tissue sections were evaluated with a mAB to *Bhenselae*, Steiner silver stain (SSS), and PCR that targeted *Bhenselae* and *Bquintana*. Positive cases were as follows: SSS, 11 (46%); PCR, 9 (38%); and IHC, 6 (25%). Only 2 cases (8%) were positive for all 3 techniques. All control cases were negative for IHC and PCR. The diagnostic sensitivity of these 3 tests is low for Bartonella. SSS seems to be the most sensitive test but is the least specific. PCR is more sensitive than IHC and may, therefore, serve as a helpful second-line test on all IHC negative cases.

Borrelia burgdorferi. DNA probes are available to aid in diagnosis of Lyme disease caused by Borrelia burgdorferi. A 2012 study (6) evaluated the sensitivity of 5 direct diagnostic methods (culture and nested PCR of a 2-mm skin biopsy specimen, nested PCR, and quantitative PCR [qPCR] performed on the same 1-mL aliquot of plasma and a novel qPCR-blood culture method) in 66 untreated adult patients with erythema migrans, the most common clinical manifestation. The results found one or more of these tests were positive in 93.9% of the patients. Culture was more sensitive than PCR for both skin and blood, but the difference was only statistically significant for blood samples ($p<0.005$). Blood culture was significantly more likely to be positive in patients with multiple erythema migrans skin lesions compared to those with a single lesion ($p=0.001$). Positive test results among the 48 patients for whom all 5 assays were performed invariably included either a positive blood or a skin culture. Results of this study demonstrated that direct detection methods such as PCR and culture are highly sensitive in untreated adult patients with erythema migrans. Erythema migrans eventually resolves even without antibiotic treatment. However, the infecting pathogen can spread to other tissues and organs, causing more severe manifestations that can involve a patient's skin, nervous system, joints, or heart. Diagnosed cases are usually treated with antibiotics for 2-4 weeks, and most patients make an uneventful recovery. (7) Therefore, laboratory evidence of infection is essential for diagnosis, except in the case of typical erythema migrans.

Candida species. DNA probes are available to aid in the diagnosis of possible Candida species infections. Amplified peptide nucleic acid tests have demonstrated high sensitivity and specificity levels of up to 100%. (8, 9) Some tests have been able to detect up to 6 Candida species. (10) A real-time quantitative PCR assay, developed for the detection of the most common pathogenic Candida species using a single-reaction PCR assay targets a selected region of the 28S subunit of the fungal *rDNA* gene. In a 2012 study, the sensitivity and specificity of an assay based on quantitative real-time assay using duplex mutation primers were 100 and 97.4%, respectively. (9) The data suggest that this assay may be appropriate for use in clinical laboratories as a simple, low-cost, and rapid screening test for the most frequently encountered Candida species.

Chlamydia pneumonia or trachomatis. Probes are commercially available for the detection of Chlamydia pneumonia or trachomatis. A 2011 study (7) demonstrated a Chlamydia-specific real-time PCR which targeted the conserved *16S rRNA* gene. The test can detect at least 5 DNA copies and shows very high specificity without cross-amplification from other bacterial DNA. The PCR was validated with 128 clinical samples positive or negative for Chlamydia trachomatis or *C pneumoniae*. Of 65 positive samples, 61 (93.8%) were found to be positive with the new PCR. Another study (11) demonstrated the VERSANT® CT/GC DNA 1.0 Assay performed with 99.2% specificity for *Chlamydia trachomatis* detection and sensitivity of 100%. As a clinical consideration, patients with suspected *Ctrachomatis* accept antibiotic treatment before their infection status had been confirmed. Treatment of individuals with *C trachomatis* genital infection prevents sexual transmission and complications, including pelvic inflammatory disease. Treatment of pregnant women will prevent the transmission of infection to infants during delivery. The benefits of treatment of respiratory infections due to *C pneumoniae* are more difficult to assess, primarily because of the lack of U.S. Food and Drug Administration (FDA)-approved, specific diagnostic tests for detection of the organism in clinical samples. (12)

Clostridium difficile. DNA probes for *Clostridium difficile* using PCR have been commercially available since 2009. (13-16) Eastwood et al. (14) compared the performance characteristics of numerous DNA probes with cytotoxic assays and cultures. The results demonstrated a mean sensitivity of 82.8% (range 66.7-91.7%) and a mean specificity of 95.4% (range 90.9-98.8%). Rapid identification of *C difficile* allows for early treatment of the disease and timely institution of isolation measures to reduce transmission. Because of the advantages of early identification of *C difficile*, these probes may be considered medically necessary.

Cytomegalovirus (CMV). There is interest in using viral load tests for cytomegalovirus (CMV), specifically to identify asymptomatic immunosuppressed patients (i.e., transplant recipients) who would be candidates for preemptive antiviral therapy. For example, among transplant recipients, CMV infections account for about two thirds of deaths in the immediate post-transplant period (i.e., up to 50 days post-transplant), and thus, a variety of preventive therapies have been investigated. One strategy proposes that all at-risk patients (i.e., seropositive patients, or seronegative patients receiving a seropositive organ) be treated prophylactically with antiviral therapy during the first 100 days after transplantation. While this strategy has been shown to be effective in reducing the risk of CMV disease, it results in a large number of patients being treated unnecessarily. Therefore, preemptive therapy has become an accepted option, in which antiviral therapy is initiated when a laboratory technique identifies an increasing viral load. Late CMV disease, defined as occurring after 100 days, is also a concern, and viral loads can also be monitored to prompt antiviral therapy. A variety of laboratory techniques are available to evaluate viral loads. For example, pp65 antigenemia refers to a fluorescent antigen detection technique

that identifies an antigen specific to CMV. However, this test is described as labor intensive and requiring specialized personnel for interpretation, and thus, a variety of tests to detect CMV DNA have been developed, including but not limited to Hybrid Capture (Digene Corporation), Amplicor CMV Monitor Tests (Roche Molecular System), and TaqMan. The specific techniques used may vary by local availability, but studies have suggested that all provide complementary information. (17-21)

Enterovirus. Amplified DNA probes are available for detecting this group of viruses including the polioviruses, coxsackieviruses, echoviruses, and other enteroviruses. In addition to 3 polioviruses, there are more than 60 types of non-polio enteroviruses that can cause disease in humans. Several FDA-approved test kits are available including the GeneXpert Enterovirus Assay (GXEA), with a sensitivity, specificity, positive predictive value and negative predictive value of 82.1%, 100%, 100% and 96.2%, respectively. In this study, molecular assays were superior to viral culture for detecting Enterovirus RNA in cerebrospinal fluid (CSF). GXEA showed a high specificity but a lower sensitivity for the detection of Enterovirus RNA compared to the RT-qPCR assay. (22) Management is supportive and addresses symptoms. No antiviral medications are currently approved for the treatment of Enterovirus infections. These amplified probes can be part of a panel that includes other respiratory viruses. (See “respiratory panels.”)

Vancomycin-resistant Enterococcus. Probes are available for detecting vancomycin resistance of organisms; e.g., for Enterococcus. These probes are able to detect vancomycin resistance in a rapid and accurate manner so that appropriate antibiotic selection can be made and infectious precautions, such as isolation, can be instituted. (23, 24)

Gardnerella vaginalis. A 2006 study (25) evaluated vaginal specimens, from 321 symptomatic women, that were analyzed for bacterial vaginosis by both Gram stain using Nugent criteria and a DNA hybridization test (Affirm VPIII hybridization test). Of the 321 patients, 115 (35.8%) were Gram-positive for bacterial vaginosis and 126 (39.2%) were negative. 80 patients (25.0%) demonstrated intermediate Gram staining that was also considered negative. The DNA hybridization test detected *Gardnerella vaginalis* in 107 (93.0%) of 115 vaginal specimens positive for bacterial vaginosis diagnosed by Gram stain. Compared to the Gram stain, the DNA hybridization test had a sensitivity of 87.7% and a specificity of 96.0%. Positive and negative predictive values of the DNA hybridization test were 93.0% and 92.7%, respectively. The study concluded the Affirm VPIII hybridization test correlated well with Gram stain and may be used as a rapid diagnostic tool to exclude bacterial vaginosis in women with genital complaints.

Hepatitis B. Viral load has also been investigated in patients with hepatitis B receiving the antiviral therapy lamivudine. Research interest has focused on assessing response to therapy and identifying the emergence of resistant strains of hepatitis B. (26-29) Although clearly, many aspects of viral load measurements in hepatitis B are primarily research tools, it does appear that measurements of viral load may be used to determine when to initiate therapy. For example, treatment may not be required in asymptomatic Hbe-Ag-negative patients with normal liver enzymes who have a viral load below 10-5 genomes per milliliter. In contrast, there are questions about how viral load measurements should be used to monitor the response to therapy. (30)

Hepatitis C. Diagnostic tests for hepatitis C can be divided into 2 general categories: 1) serological assays that detect antibody to hepatitis C virus (anti-HCV); and 2) molecular assays that detect, quantify, and/or characterize HCV RNA genomes within an infected patient. Detection of HCV RNA

in patient specimens by polymerase chain reaction (PCR) provides evidence of active HCV infection and is potentially useful for confirming the diagnosis and monitoring the antiviral response to therapy. Two main technologies exist for assessing HCV RNA levels or viral load. Quantitative PCR is the most sensitive test for determining hepatitis C viral load. Molecular tests have also been developed to classify HCV into distinct genotypes; the clinical importance of HCV genotype is related directly to treatment options. After the introduction of the HCV RNA PCR test, it became clear that interferon therapy can cure hepatitis C infections in a certain number of patients. Widespread therapy was introduced after a co-drug ribavirin was found to reduce relapse rates, and 2 pivotal trials with recombinant interferon showed sustained virological responses in about 50% of patients, with much higher positive outcomes in genotype 2 and 3. (31) Therapy-induced sustained virological remission has been shown to reduce liver-related death, liver failure, and to a lesser extent hepatocellular carcinoma.

Hepatitis G. It is possible that hepatitis C is part of a group of GB viruses, rather than just a single virus. It is unclear if hepatitis G causes a type of acute or chronic illness. When diagnosed, acute hepatitis G infection has usually been mild and brief and there is no evidence of serious complications, but it is possible that, like other hepatitis viruses, it can cause severe liver damage resulting in liver failure. The only method of detecting hepatitis G is by reverse transcriptase-polymerase chain reaction (RT-PCR) and direct sequencing for 4 randomly selected samples followed by phylogenetic analysis.

Herpes simplex virus. Typing of herpes simplex virus (HSV) isolates is required to identify the virus isolated in culture. The methods available for this include antigen detection by immunofluorescence (IF) assays and polymerase chain reaction (PCR). A 2009 cross-sectional study (32) utilized 4 reference strains and 42 HSV isolates obtained from patients between September 1998 and September 2004. These were subjected to testing using a MAb-based IF test and a PCR that detects the polymerase (pol) gene of HSV isolates. The observed agreement of the MAb IF assay with the pol PCR was 95.7%. A total of 54.8% (23/42) of isolates tested by IF typing were found to be HSV-1, 40.5% (17/42) were HSV-2, and 2 (4.8%) were untypable using the MAb IF assay. The 2 untypable isolates were found to be HSV-2 using the pol PCR. According to the American Academy of Family Physicians, antiviral medications have expanded treatment options for the 2 most common cutaneous manifestations, HSV-1 and HSV-2. Acyclovir therapy remains an effective option; however, famciclovir and valacyclovir offer improved oral bioavailability and convenient oral dosing schedules but at a higher cost. Patients who have 6 or more recurrences of genital herpes per year can be treated with daily regimens which are effective in suppressing 70 to 80% of symptomatic recurrences.

Herpes virus-6. Herpes virus-6 is the common collective name for Human herpesvirus 6A (HHV-6A) and Human herpesvirus 6B (HHV-6B). These closely related viruses are 2 of the 9 herpesviruses known to have humans as their primary host. HHV-6A has been described as more neurovirulent (33) and as such, is more frequently found in patients with neuroinflammatory diseases, such as multiple sclerosis. (34) HHV-6B primary infection is the cause of the common childhood illness exanthem subitum. Additionally, HHV-6B reactivation is common in transplant recipients, which can cause several clinical manifestations such as encephalitis, bone marrow suppression and pneumonitis. (35)

Human immunodeficiency virus 1 (HIV-1). Validated DNA probes are widely available for diagnosis and HIV-1 quantification. Quantification is regularly done to determine viral load in infected patients to monitor response to anti-retroviral therapies.

Human immunodeficiency virus (HIV-2). DNA probes are available for diagnosis and quantification of HIV-2. HIV-2 is most commonly found in Western Africa, although it has been reported in the United States. Blood donations are routinely tested for HIV-2, but clinical testing for HIV-2 is typically limited to those in contact with persons in a country where HIV-2 is endemic or when clinical evaluation suggests HIV infection, but testing for HIV-1 is negative. HIV-2 quantification is regularly done to determine viral load in infected patients to monitor response to anti-retroviral therapies.

Human papillomavirus (HPV). There has also been research interest in exploring the relationship of human papilloma viral load and progression of low-grade cervical lesions to cervical cancer. While studies have reported that high-grade lesions are associated with higher viral loads, (36, 37) clinical utility is based on whether or not the presence of increasing viral loads associated with low-grade lesions is associated with disease progression. For example, current management of cervical smears with “atypical cells of uncertain significance” suggests testing with HPV, and then, if positive, followed by colposcopy. It is hypothesized that colposcopy might be deferred if a low viral load were associated with a minimal risk. However, how treatment decisions may be tied to measurements of viral load is unclear. (38-40)

Influenza virus. Numerous different strains of influenza virus can be identified by DNA probes. Published studies indicate improved sensitivity of PCR for identifying influenza and distinguishing influenza from related viruses. Lassauniere et al. (41) used a multiplex real-time PCR probe to identify 13 respiratory viruses, including influenza A and B. Screening of 270 samples that were negative on immunofluorescence assays revealed the presence of a respiratory virus in 44.1%. Probes have also been developed to identify specific strains of influenza associated with epidemics, such as the H1N1 influenza virus. (42) Because of the importance of early identification of outbreaks for infection control purposes, use of this test may be considered medically necessary.

Legionella pneumophila. DNA probes for *Legionella pneumophila* have been developed. A recent study (43) compared the usefulness of 2 quantitative real-time PCR assays (qrt-PCRmip targeting L pneumophila, and qrt-PCR16S targeting all Legionella species) performed on lower respiratory tract (LRT) samples for diagnostic and prognostic purposes in 311 patients hospitalized for community-acquired pneumonia (CAP). The Now Legionella urinary antigen test from Binax (Portland, ME, USA) was used as a reference test. One subset of 255 CAP patients admitted to Chambery hospital in 2005 and 2006 was evaluated and the sensitivities, specificities, positive predictive and negative predictive values for both qrt-PCR tests were 63.6, 98.7, 77.7 and 97.4%, respectively. High bacterial loads in LRT samples at hospital admission were significantly associated with the need for hospitalization in an intensive care unit and for prolonged hospitalization.

Mycobacterium species. DNA probes are available to distinguish between Mycobacterium species. In a recent study, (44) the extracted DNA specimens from Mycobacterium species and non-Mycobacterial species were tested using peptide nucleic acid (PNA) probe-based real-time PCR assay to evaluate potential cross-reactivity. A total of 531 respiratory specimens (482 sputum

specimens and 49 bronchoalveolar washing fluid specimens) were collected from 230 patients in July and August, 2011. All specimens were analyzed for the detection of Mycobacteria by direct smear examination, Mycobacterial culture, and PNA probe-based real-time PCR assay. In cross-reactivity tests, no false positive or false negative results were evident. When the culture method was used as the gold standard test for comparison, PNA probe-based real-time PCR assay for detection of *Mycobacterium tuberculosis* complex (MTBC) had a sensitivity and specificity of 96.7% (58/60) and 99.6% (469/471), respectively. Assuming the combination of culture and clinical diagnosis as the standard, the sensitivity and specificity of the real-time PCR assay for detection of MTBC were 90.6% (58/64) and 99.6% (465/467), respectively. The new real-time PCR for the detection of non-tuberculous mycobacteria had a sensitivity and specificity of 69.0% (29/42) and 100% (489/489), respectively.

Mycobacterium tuberculosis. DNA probes are available to diagnose *Mycobacterium tuberculosis* infection. In a recent study, (45) an in-house IS6110 real-time PCR (IH IS6110), MTB Q-PCR Alert (Q-PCR) and GenoType® MTBDRplus (MTBDR) were compared for the direct detection of *Mtuberculosis* complex (MTBC) in 87 specimens. This included 82 first smear-positive specimens and three smear-negative specimens. The sensitivities of IH IS6110, Q-PCR, MTBDR, and IH ITS for MTBC detection were 100%, 92%, 87%, and 87% respectively, compared to culture. Both IS6110-based real-time PCRs (in-house and Q-PCR) were similar in performance with 91.2% concordant results for MTBC detection. However, none of the real-time PCR assays tested provide drug resistance data. Detection and drug resistance profiling are necessary for successful treatment of infection.

Mycobacterium avium and Mycobacterium intracellulare. DNA probes are available to diagnose *Mycobacterium avium* and *Mycobacterium intracellulare* infection. A recent study (46) evaluated the performance of the GenoType Mycobacteria Direct (GTMD) test for rapid molecular detection and identification of the MTBC and 4 clinically important non-tuberculous mycobacteria (*M avium, M intracellulare, M kansasii*, and *M malmoense*) in smear-negative samples. A total of 1,570 samples (1,103 bronchial aspiration, 127 sputum, and 340 extrapulmonary samples) were analyzed. When evaluated, the performance criteria in combination with a positive culture result and/or the clinical outcome of the patients, the overall sensitivity, specificity, and positive and negative predictive values were found to be 62.4, 99.5, 95.9, and 93.9%, respectively, whereas they were 63.2, 99.4, 95.7, and 92.8%, respectively, for pulmonary samples and 52.9, 100, 100, and 97.6%, respectively, for extrapulmonary samples. Among the culture-positive samples which had Mycobacterium species detectable by the GTMD test, 3 samples were identified to be *Mintracellulare* and one sample was identified to be *M avium*. However, 5 *M intracellulare* samples and an *M kansasii* sample could not be identified by the molecular test and were found to be negative. The GTMD test is a reliable, practical, and easy tool for rapid diagnosis of smear-negative pulmonary and extrapulmonary tuberculosis so that effective precautions may be taken and appropriate treatment may be initiated.

Mycoplasma pneumonia. Probes for *Mycoplasma pneumonia* have been developed. (47, 48) Chalker et al. (47) tested 3,987 nose and throat swabs from patients presenting with symptoms of a respiratory tract infection. *Mycoplasma* DNA was present in 1.7% of patients overall and was more common in children aged 5-14 years, in whom 6.0% of samples were positive. Probes have also been developed to test for mycoplasma strains with macrolide resistance. Peuchant et al. (48) found that 9.8% (5/51) of mycoplasma strains were macrolide resistant. However, the clinical utility of this probe is uncertain given that the disease is usually self-limited. It is unclear

whether early identification of Mycoplasma, and/or identification of resistance, leads to improved outcomes.

Neisseria gonorrhoeae: Probes for *Neisseria gonorrhoeae* have been developed for commercial use. These probes are often a combination test with *Ctrachomatis*. A recent study (49) demonstrated the positive predictive value of the screening PCR (cobas 4800 CT/NG PCR screening assay) in urine specimens remained high (98.75%) even though the prevalence of *gonorrhoeae* was low. Another study (11) demonstrated the VERSANT® CT/GC DNA 1.0 assay performed with 99.4% and 99.2% of specificity for *Ngonorrhoeae* and *Ctrachomatis* detection, respectively, whereas sensitivity was 100% both for *Ctrachomatis* and *Ngonorrhoeae*. As a comparator, culture methods were 100% specific, but far less sensitive. As a clinical consideration, patients accept antibiotic treatment before their infection status has been confirmed.

Respiratory Viral Panel. A broad spectrum of pathogens is causative for respiratory tract infections, but symptoms are mostly similar. The identification of the causative viruses is only feasible using multiplex PCR or several monoplex PCR tests in parallel. Several studies of various respiratory viral panels, (50-52), demonstrate the multiplex assay detected clinically important viral infections in a single genomic test and thus, may be useful for detecting causative agents for respiratory tract disorders. A 2011 study by Brittain-Long (53) on a randomized population of 406 patients with access to a rapid- multiplex-PCR assay used to detect 13 viruses had lower antibiotic prescription rates (4.5% vs. 12.3%, respectively) versus delayed identification with no significant difference in outcome at follow-up (p=0.359). Access to a rapid method for etiologic diagnosis of respiratory tract infections may reduce antibiotic prescription rates at the initial visit in an outpatient setting. Rapid identification of influenza may also lead to more effective early treatment with antivirals and more effective infection control measures.

Staphylococcus aureus and methicillin-resistant Staphylococcus aureus. Probes are available for the detection of *Staphylococcus aureus.* (54, 55) These probes are able to not only distinguish between coagulase-negative Staphylococcus and *S aureus,* they can also detect methicillin-resistant species (MRSA) with high accuracy. (24, 25) Given the importance of establishing an early and accurate diagnosis in clinical situations in which an *S aureus* infection is likely and there is substantial likelihood of MRSA, testing may be considered medically necessary in these situations. Probes are also available for the detection of enterovirus, although the clinical applicability of these probes has not been demonstrated.

Streptococcus, Group A. Confirmation of the diagnosis of *streptococcus A* is typically based on culture. However a direct DNA probe test for *streptococcus A*, using a throat swab, has been used as an alternative to culture, with the advantage of a 45-minute turnaround, compared to several days for culture. The summary of clinical studies included in the product label indicates a 97.4% agreement with confirmatory culture. (56) Furthermore, a recent study (57) of a laboratory-developed internally-controlled rapid Group A streptococcus (GAS) PCR assay using flocked swab throat specimens compared the GAS PCR assay to GAS culture results using a collection of archived throat swab samples obtained during a study comparing the performance of conventional and flocked throat swabs. The sensitivity of the GAS PCR assay as compared to the reference standard was 96.0% (95% confidence interval [CI]: 90.1% to 98.4%), specificity 98.6% (95% CI: 95.8% to 99.5%), positive predictive value (PPV) 96.9% (95% CI: 91.4% to 99.0%) and negative predictive value (NPV) of 98.1% (95% CI: 95.2% to 99.2%). For

conventional swab cultures, sensitivity was 96.0% (95% CI: 90.1% to 98.4%), specificity 100% (95% CI: 98.2% to 100%), PPV 100%, (95% CI: 96.1% to 100%) and NPV 98.1% (95% CI: 95.2% to 99.3%). The GAS PCR assay appeared to perform as well as conventional throat swab culture, the current standard of practice. Since the GAS PCR assay, including DNA extraction, can be performed in approximately 1 hour, prospective studies of this assay are warranted to evaluate the clinical impact of the assay on management of patients with pharyngitis.

Streptococcus, Group B. Several different rapid polymerase chain reaction (PCR)-based tests for Group B streptococcus (GBS) have been developed, with reported sensitivities and specificities similar to that of conventional culture. DNA probes have also been developed to identify GBS from cultured specimens. (58, 59)

Trichomonas vaginalis. Nye et al. (60) compared the performance characteristics of PCR testing for trichomonas with wet prep microscopy and culture in 296 female and 298 male subjects. In both women and men, DNA probe testing of vaginal swabs was more sensitive than culture. However, in men, wet prep testing was more sensitive than DNA probe testing. Munson et al. (61) compared DNA probe testing and culture in 255 vaginal saline preparations. The DNA probe identified trichomonas in 9.4% (24/255) of specimens that were negative on culture. This probe offers the ability to better distinguish between causes of vaginitis, which can be difficult clinically and using standard culture methods. Nucleic acid amplification tests have demonstrated higher clinical sensitivity than culture and wet mount microscopy (60), as well as single-probe nonamplified testing in general. A 2011 prospective multicenter study of 1,025 asymptomatic and symptomatic women found nucleic acid amplification testing had clinical sensitivity of 100% for both vaginal and endocervical swabs while urine specimen sensitivity was 95.2%. (62) Specificity levels ranged from 98.9% to 99.6%. Other studies have also reported similar results. (63) PCR amplification tests have higher clinical sensitivity and are considered the standard of care for diagnosing Trichomonas vaginalis when culturing is not an option.

Summary

Nucleic acid probes are available for the identification of a wide variety of microorganisms, offering more rapid identification compared to standard cultures. Nucleic acid probes can also be used to quantitate the number of microorganisms present. This technology offers advantages over standard techniques when rapid identification is clinically important and/or when treatment decisions are based on quantitative results. Using these criteria, nucleic acid probes for numerous microorganisms can be considered medically necessary, as delineated in the policy statement.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

87470 Infectious agent detection by nucleic acid (DNA or RNA); Bartonella henselae and Bartonella quintana, direct probe technique

87471 Infectious agent detection by nucleic acid (DNA or RNA); Bartonella henselae and Bartonella quintana, amplified probe technique

87472 Infectious agent detection by nucleic acid (DNA or RNA); Bartonella henselae and Bartonella quintana, quantification
87475 Infectious agent detection by nucleic acid (DNA or RNA); Borrelia burgdorferi, direct probe technique
87476 Infectious agent detection by nucleic acid (DNA or RNA); Borrelia burgdorferi, amplified probe technique
87477 Infectious agent detection by nucleic acid (DNA or RNA); Borrelia burgdorferi, quantification
87480 Infectious agent detection by nucleic acid (DNA or RNA); Candida species, direct probe technique
87481 Infectious agent detection by nucleic acid (DNA or RNA); Candida species, amplified probe technique
87482 Infectious agent detection by nucleic acid (DNA or RNA); Candida species, quantification
87485 Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia pneumoniae, direct probe technique
87486 Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia pneumoniae, amplified probe technique
87487 Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia pneumoniae, quantification
87490 Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, direct probe technique
87491 Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, amplified probe technique
87492 Infectious agent detection by nucleic acid (DNA or RNA); Chlamydia trachomatis, quantification
87511 Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, amplified probe technique
87512 Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, quantification
87515 Infectious agent detection by nucleic acid (DNA or RNA); hepatitis B virus, direct probe technique
87516 Infectious agent detection by nucleic acid (DNA or RNA); hepatitis B virus, amplified probe technique
87517 Infectious agent detection by nucleic acid (DNA or RNA); hepatitis B virus, quantification
87520 Infectious agent detection by nucleic acid (DNA or RNA); hepatitis C, direct probe technique
87521 Infectious agent detection by nucleic acid (DNA or RNA); hepatitis C, amplified probe technique, includes reverse transcription when performed
87522 Infectious agent detection by nucleic acid (DNA or RNA); hepatitis C, quantification, includes reverse transcription when performed
87493 Infectious agent detection by nucleic acid (DNA or RNA); Clostridium difficile, toxin gene(s), amplified probe technique
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

87497 Infectious agent detection by nucleic acid (DNA or RNA); cytomegalovirus, quantification
87498 Infectious agent detection by nucleic acid (DNA or RNA); enterovirus, amplified probe technique, includes reverse transcription when performed
87500 Infectious agent detection by nucleic acid (DNA or RNA); vancomycin resistance (eg, enterococcus species van A, van B), amplified probe technique
87510 Infectious agent detection by nucleic acid (DNA or RNA); Gardnerella vaginalis, direct 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
87528 Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, direct probe technique
87529 Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, amplified probe technique
87530 Infectious agent detection by nucleic acid (DNA or RNA); Herpes simplex virus, quantification
87531 Infectious agent detection by nucleic acid (DNA or RNA); Herpes virus-6, direct probe technique
87532 Infectious agent detection by nucleic acid (DNA or RNA); Herpes virus-6, amplified probe technique
87533 Infectious agent detection by nucleic acid (DNA or RNA); Herpes virus-6, quantification
87534 Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, direct probe technique
87535 Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, amplified probe technique, includes reverse transcription when performed
87536 Infectious agent detection by nucleic acid (DNA or RNA); HIV-1, quantification, includes reverse transcription when performed
87537 Infectious agent detection by nucleic acid (DNA or RNA); HIV-2, direct probe technique
87538 Infectious agent detection by nucleic acid (DNA or RNA); HIV-2, amplified probe technique, includes reverse transcription when performed
87539 Infectious agent detection by nucleic acid (DNA or RNA); HIV-2, quantification, includes reverse transcription when performed
87540 Infectious agent detection by nucleic acid (DNA or RNA); Legionella pneumophila, direct probe technique
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
87550 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria species, direct probe technique
87551 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria species, amplified probe technique
87552 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria species, quantification
87555 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria tuberculosis, direct probe technique

87556 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria tuberculosis, amplified probe technique
87557 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria tuberculosis, quantification
87560 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria avium-intracellulare, direct probe technique
87561 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria avium-intracellulare, amplified probe technique
87562 Infectious agent detection by nucleic acid (DNA or RNA); Mycobacteria avium-intracellulare, 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
87590 Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, direct probe technique
87591 Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, amplified probe technique
87592 Infectious agent detection by nucleic acid (DNA or RNA); Neisseria gonorrhoeae, quantification
87620 Infectious agent detection by nucleic acid (DNA or RNA); papillomavirus, human, direct probe technique
87621 Infectious agent detection by nucleic acid (DNA or RNA); papillomavirus, human, amplified probe technique
87622 Infectious agent detection by nucleic acid (DNA or RNA); papillomavirus, human, quantification
87631 Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), multiplex reverse transcription and amplified probe technique, multiple types or subtypes, 3-5 targets
87632 Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), multiplex reverse transcription and amplified probe technique, multiple types or subtypes, 6-11 targets
87633 Infectious agent detection by nucleic acid (DNA or RNA); respiratory virus (eg, adenovirus, influenza virus, coronavirus, metapneumovirus, parainfluenza virus, respiratory syncytial virus, rhinovirus), multiplex reverse transcription and amplified probe technique, multiple types or subtypes, 12-25 targets
87640 Infectious agent detection by nucleic acid (DNA or RNA); Staphylococcus aureus, amplified probe technique
87641 Infectious agent detection by nucleic acid (DNA or RNA); Staphylococcus aureus, methicillin resistant, amplified probe technique
87650 Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, direct probe technique
87651 Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, amplified probe technique

87652 Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group A, quantification
87653 Infectious agent detection by nucleic acid (DNA or RNA); Streptococcus, group B, amplified probe technique
87660 Infectious agent detection by nucleic acid (DNA or RNA); Trichomonas vaginalis, direct probe technique
87661 User Defined (description not available)
87797 Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; direct probe technique, each organism
87798 Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; amplified probe technique, each organism
87799 Infectious agent detection by nucleic acid (DNA or RNA), not otherwise specified; quantification, each organism

ICD-9 Diagnoses

008.45	Other specified bacteria; Clostridium difficile
010.0-018.9	Tuberculosis (code range)
021.0-021.9	Tularemia (code range)
023.0-023.9	Brucellosis (code range)
025	Melioidosis
030.0-030.9	Other bacterial diseases; Leprosy (code range)
031.0-031.9	Other bacterial diseases; Diseases due to other mycobacteria (code range)
033.0-033.9	Whooping cough (code range)
036.0	Meningococcal meningitis
038.12	Methicillin resistant Staphylococcus aureus septicemia
040.2	Whipple's disease
041.02	Streptococcus; Group B
041.12	Staphylococcus; Methicillin resistant Staphylococcus aureus
041.81	Mycoplasma
041.84	Other specified bacterial infections; Other anaerobes
041.86	Helicobacter pylori [H. pylori]
042	Human immunodeficiency virus [HIV] disease
045.0-045.93	Acute poliomyelitis (code range)
047.0-047.9	Meningitis due to enterovirus (code range)
048	Other enterovirus diseases of central nervous sys
052.0-052.9	Chickenpox (code range)
053.0-053.9	Herpes zoster (code range)
054.0-054.9	Viral diseases accompanied by Exanthem; Herpes simplex (code range)
055.0-055.9	Measles (code range)
057.0	Erythema infectiosum [fifth disease]
058.11	Roseola infantum due to human herpesvirus 6
058.21	Human herpesvirus 6 encephalitis
058.81	Human herpesvirus 6 infection
065.0	Crimean hemorrhagic fever [CHF Congo virus
066.1	Tick-borne fever
066.3	Other mosquito-borne fever
066.40-066.49	West Nile fever (code range)
070.20-070.33	Other diseases due to viruses and chlamydiae; Viral hepatitis B (code range)

070.41	Acute or unspecified hepatitis C with hepatic coma
070.44	Chronic hepatitis C with hepatic coma
070.51	Acute or unspecified hepatitis C without mention of hepatic coma
070.54	Chronic hepatitis C without mention of hepatic coma
070.70	Unspecified viral hepatitis C without hepatic coma
070.71	Unspecified viral hepatitis C with hepatic coma
072.0-072.9	Mumps (code range)
073.0-073.9	Ornithosis (code range)
076.0-076.9	Trachoma (code range)
077.0	Other diseases of conjunctiva due to viruses and Chlamydiae; inclusion conjunctivitis
077.98	Unspecified diseases of conjunctiva due to viruses and Chlamydiae; due to Chlamydiae
078.3	Cat-scratch disease
078.5	Cytomegaloviral disease
078.88	Other specified diseases due to Chlamydiae
079.0	Adenovirus
079.1	ECHO virus
079.2	Coxsackie virus
079.50-079.59	Retrovirus (code range)
079.82	SARS-associated coronavirus
079.83	Parvovirus B19
079.88	Other specified chlamydial infection
079.89	Other specified viral infections (includes papillomavirus)
079.98	Unspecified chlamydial infection
080	Louse-borne [epidemic] typhus
081.0	Murine [endemic] typhus
082.0	Louse-borne [epidemic] typhus
082.40-082.49	Ehrlichiosis (code range)
083.0	Q fever
084.0-084.9	Malaria (code range)
085.0-085.9	Leishmaniasis (code range)
088.0	Bartonellosis
088.82	Babesiosis
090.0-097.9	Congenital syphilis (code range)
098.0-098.89	Gonococcal infections (code range)
099.0	Chancroid
099.1	Lymphogranuloma venereum
099.3	Reiter's disease
130.0-130.9	Toxoplasmosis (code range)
131.00-131.09	Urogenital trichomoniasis (code range)
131.8	Urogenital trichomoniasis; other specified site
131.9	Trichomoniasis, unspecified
238.4	Polycythemia vera
238.77	Post-transplant lymphoproliferative disorder [PTLD]
465.9	Acute upper respiratory infections of multiple or unspecified sites; Unspecified site
482.42	Methicillin resistant pneumonia due to Staphylococcus aureus

482.84	Legionnaires' disease
483.1	Chlamydia
487.0-488.19	Influenza (code range)
771.1	Congenital cytomegalovirus infection
771.2	Other congenital infections (includes herpes simplex, tuberculosis)
786.2	Cough
795.00-795.05	Abnormal Papanicolaou smear of cervix and cervical HPV (code range)
795.71	Nonspecific serologic evidence of human immunodeficiency virus [HIV]
V01.82	Exposure to SARS-associated coronavirus
V02.61	Hepatitis B carrier
V02.62	Hepatitis C carrier
V02.7	Gonorrhea
V02.8	Other venereal diseases
V08	Human immunodeficiency virus (HIV) asymptomatic
V28.6	Antenatal screening for Streptococcus B
V42.0	Organ or tissue replaced by transplant; kidney
V42.82	Other specified organ or tissue; peripheral stem cells
V69.2	Problems related to lifestyle; high-risk sexual behavior
V72.32	Encounter for Papanicolaou cervical smear to confirm findings of recent normal smear following initial abnormal smear
V73.0	Special screening examination for viral and chlamydial diseases; poliomyelitis
V73.88	Other specified chlamydial diseases
V73.98	Unspecified chlamydial disease
V74.1	Special screening examination for bacterial and spirochetal diseases; pulmonary tuberculosis
V74.5	Special screening examination for bacterial and spirochetal diseases; venereal disease

ICD-10 Diagnoses (Effective October 1, 2014)

A04.7	Enterocolitis due to Clostridium difficile
A15.0	Tuberculosis of lung
A15.4	Tuberculosis of intrathoracic lymph nodes
A15.5	Tuberculosis of larynx, trachea and bronchus
A15.6	Tuberculous pleurisy
A15.7	Primary respiratory tuberculosis
A15.8	Other respiratory tuberculosis
A15.9	Respiratory tuberculosis unspecified
A17.0	Tuberculous meningitis
A17.1	Meningeal tuberculoma
A17.81	Tuberculoma of brain and spinal cord
A17.82	Tuberculous meningoencephalitis
A17.83	Tuberculous neuritis
A17.89	Other tuberculosis of nervous system
A17.9	Tuberculosis of nervous system, unspecified
A18.01	Tuberculosis of spine
A18.02	Tuberculous arthritis of other joints
A18.03	Tuberculosis of other bones
A18.09	Other musculoskeletal tuberculosis

A18.10 Tuberculosis of genitourinary system, unspecified
A18.11 Tuberculosis of kidney and ureter
A18.12 Tuberculosis of bladder
A18.13 Tuberculosis of other urinary organs
A18.14 Tuberculosis of prostate
A18.15 Tuberculosis of other male genital organs
A18.16 Tuberculosis of cervix
A18.17 Tuberculous female pelvic inflammatory disease
A18.18 Tuberculosis of other female genital organs
A18.2 Tuberculous peripheral lymphadenopathy
A18.31 Tuberculous peritonitis
A18.32 Tuberculous enteritis
A18.39 Retroperitoneal tuberculosis
A18.4 Tuberculosis of skin and subcutaneous tissue
A18.50 Tuberculosis of eye, unspecified
A18.51 Tuberculous episcleritis
A18.52 Tuberculous keratitis
A18.53 Tuberculous chorioretinitis
A18.54 Tuberculous iridocyclitis
A18.59 Other tuberculosis of eye
A18.6 Tuberculosis of (inner) (middle) ear
A18.7 Tuberculosis of adrenal glands
A18.81 Tuberculosis of thyroid gland
A18.82 Tuberculosis of other endocrine glands
A18.83 Tuberculosis of digestive tract organs, not elsewhere classified
A18.84 Tuberculosis of heart
A18.85 Tuberculosis of spleen
A18.89 Tuberculosis of other sites
A19.0 Acute miliary tuberculosis of a single specified site
A19.1 Acute miliary tuberculosis of multiple sites
A19.2 Acute miliary tuberculosis, unspecified
A19.8 Other miliary tuberculosis
A19.9 Miliary tuberculosis, unspecified
A21.0 Ulceroglandular tularemia
A21.1 Oculoglandular tularemia
A21.2 Pulmonary tularemia
A21.3 Gastrointestinal tularemia
A21.7 Generalized tularemia
A21.8 Other forms of tularemia
A21.9 Tularemia, unspecified
A23.0 Brucellosis due to Brucella melitensis
A23.1 Brucellosis due to Brucella abortus
A23.2 Brucellosis due to Brucella suis
A23.3 Brucellosis due to Brucella canis
A23.8 Other brucellosis
A23.9 Brucellosis, unspecified
A24.1 Acute and fulminating melioidosis

A24.2 Subacute and chronic melioidosis
A24.3 Other melioidosis
A24.9 Melioidosis, unspecified
A28.1 Cat-scratch disease
A30.0 Indeterminate leprosy
A30.1 Tuberculoid leprosy
A30.2 Borderline tuberculoid leprosy
A30.3 Borderline leprosy
A30.4 Borderline lepromatous leprosy
A30.5 Lepromatous leprosy
A30.8 Other forms of leprosy
A30.9 Leprosy, unspecified
A31.0 Pulmonary mycobacterial infection
A31.1 Cutaneous mycobacterial infection
A31.2 Disseminated mycobacterium avium-intracellulare complex (DMAC)
A31.8 Other mycobacterial infections
A31.9 Mycobacterial infection, unspecified
A37.00 Whooping cough due to Bordetella pertussis without pneumonia
A37.01 Whooping cough due to Bordetella pertussis with pneumonia
A37.10 Whooping cough due to Bordetella parapertussis without pneumonia
A37.11 Whooping cough due to Bordetella parapertussis with pneumonia
A37.80 Whooping cough due to other Bordetella species without pneumonia
A37.81 Whooping cough due to other Bordetella species with pneumonia
A37.90 Whooping cough, unspecified species without pneumonia
A37.91 Whooping cough, unspecified species with pneumonia
A39.0 Meningococcal meningitis
A41.02 Sepsis due to Methicillin resistant Staphylococcus aureus
A44.0 Systemic bartonellosis
A44.1 Cutaneous and mucocutaneous bartonellosis
A44.8 Other forms of bartonellosis
A44.9 Bartonellosis, unspecified
A48.1 Legionnaires' disease
A49.02 Methicillin resistant Staphylococcus aureus infection, unspecified site
A49.3 Mycoplasma infection, unspecified site
A50.01 Early congenital syphilitic oculopathy
A50.02 Early congenital syphilitic osteochondropathy
A50.03 Early congenital syphilitic pharyngitis
A50.04 Early congenital syphilitic pneumonia
A50.05 Early congenital syphilitic rhinitis
A50.06 Early cutaneous congenital syphilis
A50.07 Early mucocutaneous congenital syphilis
A50.08 Early visceral congenital syphilis
A50.09 Other early congenital syphilis, symptomatic
A50.1 Early congenital syphilis, latent
A50.2 Early congenital syphilis, unspecified
A50.30 Late congenital syphilitic oculopathy, unspecified
A50.31 Late congenital syphilitic interstitial keratitis

A50.32 Late congenital syphilitic chorioretinitis
A50.39 Other late congenital syphilitic oculopathy
A50.40 Late congenital neurosyphilis, unspecified
A50.41 Late congenital syphilitic meningitis
A50.42 Late congenital syphilitic encephalitis
A50.43 Late congenital syphilitic polyneuropathy
A50.44 Late congenital syphilitic optic nerve atrophy
A50.45 Juvenile general paresis
A50.49 Other late congenital neurosyphilis
A50.51 Clutton's joints
A50.52 Hutchinson's teeth
A50.53 Hutchinson's triad
A50.54 Late congenital cardiovascular syphilis
A50.55 Late congenital syphilitic arthropathy
A50.56 Late congenital syphilitic osteochondropathy
A50.57 Syphilitic saddle nose
A50.59 Other late congenital syphilis, symptomatic
A50.6 Late congenital syphilis, latent
A50.7 Late congenital syphilis, unspecified
A50.9 Congenital syphilis, unspecified
A51.0 Primary genital syphilis
A51.1 Primary anal syphilis
A51.2 Primary syphilis of other sites
A51.31 Condyloma latum
A51.32 Syphilitic alopecia
A51.39 Other secondary syphilis of skin
A51.41 Secondary syphilitic meningitis
A51.42 Secondary syphilitic female pelvic disease
A51.43 Secondary syphilitic oculopathy
A51.44 Secondary syphilitic nephritis
A51.45 Secondary syphilitic hepatitis
A51.46 Secondary syphilitic osteopathy
A51.49 Other secondary syphilitic conditions
A51.5 Early syphilis, latent
A51.9 Early syphilis, unspecified
A52.00 Cardiovascular syphilis, unspecified
A52.01 Syphilitic aneurysm of aorta
A52.02 Syphilitic aortitis
A52.03 Syphilitic endocarditis
A52.04 Syphilitic cerebral arteritis
A52.05 Other cerebrovascular syphilis
A52.06 Other syphilitic heart involvement
A52.09 Other cardiovascular syphilis
A52.10 Symptomatic neurosyphilis, unspecified
A52.11 Tabes dorsalis
A52.12 Other cerebrospinal syphilis
A52.13 Late syphilitic meningitis

A52.14 Late syphilitic encephalitis
A52.15 Late syphilitic neuropathy
A52.16 Charc ├┤ t's arthropathy (tabetic)
A52.17 General paresis
A52.19 Other symptomatic neurosyphilis
A52.2 Asymptomatic neurosyphilis
A52.3 Neurosyphilis, unspecified
A52.71 Late syphilitic oculopathy
A52.72 Syphilis of lung and bronchus
A52.73 Symptomatic late syphilis of other respiratory organs
A52.74 Syphilis of liver and other viscera
A52.75 Syphilis of kidney and ureter
A52.76 Other genitourinary symptomatic late syphilis
A52.77 Syphilis of bone and joint
A52.78 Syphilis of other musculoskeletal tissue
A52.79 Other symptomatic late syphilis
A52.8 Late syphilis, latent
A52.9 Late syphilis, unspecified
A53.0 Latent syphilis, unspecified as early or late
A53.9 Syphilis, unspecified
A54.00 Gonococcal infection of lower genitourinary tract, unspecified
A54.01 Gonococcal cystitis and urethritis, unspecified
A54.02 Gonococcal vulvovaginitis, unspecified
A54.03 Gonococcal cervicitis, unspecified
A54.09 Other gonococcal infection of lower genitourinary tract
A54.1 Gonococcal infection of lower genitourinary tract with periurethral and accessory gland abscess
A54.21 Gonococcal infection of kidney and ureter
A54.22 Gonococcal prostatitis
A54.23 Gonococcal infection of other male genital organs
A54.24 Gonococcal female pelvic inflammatory disease
A54.29 Other gonococcal genitourinary infections
A54.30 Gonococcal infection of eye, unspecified
A54.31 Gonococcal conjunctivitis
A54.32 Gonococcal iridocyclitis
A54.33 Gonococcal keratitis
A54.39 Other gonococcal eye infection
A54.40 Gonococcal infection of musculoskeletal system, unspecified
A54.41 Gonococcal spondylopathy
A54.42 Gonococcal arthritis
A54.43 Gonococcal osteomyelitis
A54.49 Gonococcal infection of other musculoskeletal tissue
A54.5 Gonococcal pharyngitis
A54.6 Gonococcal infection of anus and rectum
A54.81 Gonococcal meningitis
A54.82 Gonococcal brain abscess
A54.83 Gonococcal heart infection

A54.84 Gonococcal pneumonia
A54.85 Gonococcal peritonitis
A54.86 Gonococcal sepsis
A54.89 Other gonococcal infections
A54.9 Gonococcal infection, unspecified
A55 Chlamydial lymphogranuloma (venereum)
A57 Chancroid
A59.00 Urogenital trichomoniasis, unspecified
A59.01 Trichomonal vulvovaginitis
A59.02 Trichomonal prostatitis
A59.03 Trichomonal cystitis and urethritis
A59.09 Other urogenital trichomoniasis
A59.8 Trichomoniasis of other sites
A59.9 Trichomoniasis, unspecified
A60.00 Herpesviral infection of urogenital system, unspecified
A60.01 Herpesviral infection of penis
A60.02 Herpesviral infection of other male genital organs
A60.03 Herpesviral cervicitis
A60.04 Herpesviral vulvovaginitis
A60.09 Herpesviral infection of other urogenital tract
A60.1 Herpesviral infection of perianal skin and rectum
A60.9 Anogenital herpesviral infection, unspecified
A70 Chlamydia psittaci infections
A71.0 Initial stage of trachoma
A71.1 Active stage of trachoma
A71.9 Trachoma, unspecified
A74.0 Chlamydial conjunctivitis
A74.81 Chlamydial peritonitis
A74.89 Other chlamydial diseases
A74.9 Chlamydial infection, unspecified
A75.0 Epidemic louse-borne typhus fever due to Rickettsia prowazekii
A75.2 Typhus fever due to Rickettsia typhi
A77.0 Spotted fever due to Rickettsia rickettsii
A77.40 Ehrlichiosis, unspecified
A77.41 Ehrlichiosis chafeensis [E. chafeensis]
A77.49 Other ehrlichiosis
A77.9 Spotted fever, unspecified
A78 Q fever
A80.0 Acute paralytic poliomyelitis, vaccine-associated
A80.1 Acute paralytic poliomyelitis, wild virus, imported
A80.2 Acute paralytic poliomyelitis, wild virus, indigenous
A80.30 Acute paralytic poliomyelitis, unspecified
A80.39 Other acute paralytic poliomyelitis
A80.4 Acute nonparalytic poliomyelitis
A80.9 Acute poliomyelitis, unspecified
A87.0 Enteroviral meningitis
A87.8 Other viral meningitis

A87.9 Viral meningitis, unspecified
A88.0 Enteroviral exanthematous fever [Boston exanthem]
A92.0 Chikungunya virus disease
A92.1 O'nyong-nyong fever
A92.30 West Nile virus infection, unspecified
A92.31 West Nile virus infection with encephalitis
A92.32 West Nile virus infection with other neurologic manifestation
A92.39 West Nile virus infection with other complications
A92.4 Rift Valley fever
A92.8 Other specified mosquito-borne viral fevers
A93.0 Oropouche virus disease
A93.2 Colorado tick fever
A98.0 Crimean-Congo hemorrhagic fever
B00.0 Eczema herpeticum
B00.1 Herpesviral vesicular dermatitis
B00.2 Herpesviral gingivostomatitis and pharyngotonsillitis
B00.3 Herpesviral meningitis
B00.4 Herpesviral encephalitis
B00.50 Herpesviral ocular disease, unspecified
B00.51 Herpesviral iridocyclitis
B00.52 Herpesviral keratitis
B00.53 Herpesviral conjunctivitis
B00.59 Other herpesviral disease of eye
B00.7 Disseminated herpesviral disease
B00.81 Herpesviral hepatitis
B00.82 Herpes simplex myelitis
B00.89 Other herpesviral infection
B00.9 Herpesviral infection, unspecified
B01.0 Varicella meningitis
B01.11 Varicella encephalitis and encephalomyelitis
B01.12 Varicella myelitis
B01.2 Varicella pneumonia
B01.81 Varicella keratitis
B01.89 Other varicella complications
B01.9 Varicella without complication
B02.0 Zoster encephalitis
B02.1 Zoster meningitis
B02.21 Postherpetic geniculate ganglionitis
B02.22 Postherpetic trigeminal neuralgia
B02.23 Postherpetic polyneuropathy
B02.24 Postherpetic myelitis
B02.29 Other postherpetic nervous system involvement
B02.30 Zoster ocular disease, unspecified
B02.31 Zoster conjunctivitis
B02.32 Zoster iridocyclitis
B02.33 Zoster keratitis
B02.34 Zoster scleritis

B02.39 Other herpes zoster eye disease
B02.7 Disseminated zoster
B02.8 Zoster with other complications
B02.9 Zoster without complications
B05.0 Measles complicated by encephalitis
B05.1 Measles complicated by meningitis
B05.2 Measles complicated by pneumonia
B05.3 Measles complicated by otitis media
B05.4 Measles with intestinal complications
B05.81 Measles keratitis and keratoconjunctivitis
B05.89 Other measles complications
B05.9 Measles without complication
B08.21 Exanthema subitum [sixth disease] due to human herpesvirus 6
B08.3 Erythema infectiosum [fifth disease]
B10.01 Human herpesvirus 6 encephalitis
B10.81 Human herpesvirus 6 infection
B16.0 Acute hepatitis B with delta-agent with hepatic coma
B16.1 Acute hepatitis B with delta-agent without hepatic coma
B16.2 Acute hepatitis B without delta-agent with hepatic coma
B16.9 Acute hepatitis B without delta-agent and without hepatic coma
B17.10 Acute hepatitis C without hepatic coma
B17.11 Acute hepatitis C with hepatic coma
B18.0 Chronic viral hepatitis B with delta-agent
B18.1 Chronic viral hepatitis B without delta-agent
B18.2 Chronic viral hepatitis C
B19.10 Unspecified viral hepatitis B without hepatic coma
B19.11 Unspecified viral hepatitis B with hepatic coma
B19.20 Unspecified viral hepatitis C without hepatic coma
B19.21 Unspecified viral hepatitis C with hepatic coma
B20 Human immunodeficiency virus [HIV] disease
B25.0 Cytomegaloviral pneumonitis
B25.1 Cytomegaloviral hepatitis
B25.2 Cytomegaloviral pancreatitis
B25.8 Other cytomegaloviral diseases
B25.9 Cytomegaloviral disease, unspecified
B26.0 Mumps orchitis
B26.1 Mumps meningitis
B26.2 Mumps encephalitis
B26.3 Mumps pancreatitis
B26.81 Mumps hepatitis
B26.82 Mumps myocarditis
B26.83 Mumps nephritis
B26.84 Mumps polyneuropathy
B26.85 Mumps arthritis
B26.89 Other mumps complications
B26.9 Mumps without complication
B33.1 Ross River disease

B33.3 Retrovirus infections, not elsewhere classified
B33.8 Other specified viral diseases
B34.0 Adenovirus infection, unspecified
B34.1 Enterovirus infection, unspecified
B34.2 Coronavirus infection, unspecified
B34.3 Parvovirus infection, unspecified
B34.4 Papovavirus infection, unspecified
B34.8 Other viral infections of unspecified site
B50.0 Plasmodium falciparum malaria with cerebral complications
B50.8 Other severe and complicated Plasmodium falciparum malaria
B50.9 Plasmodium falciparum malaria, unspecified
B51.0 Plasmodium vivax malaria with rupture of spleen
B51.8 Plasmodium vivax malaria with other complications
B51.9 Plasmodium vivax malaria without complication
B52.0 Plasmodium malariae malaria with nephropathy
B52.8 Plasmodium malariae malaria with other complications
B52.9 Plasmodium malariae malaria without complication
B53.0 Plasmodium ovale malaria
B53.1 Malaria due to simian plasmodia
B53.8 Other malaria, not elsewhere classified
B54 Unspecified malaria
B55.0 Visceral leishmaniasis
B55.1 Cutaneous leishmaniasis
B55.2 Mucocutaneous leishmaniasis
B55.9 Leishmaniasis, unspecified
B58.00 Toxoplasma oculopathy, unspecified
B58.01 Toxoplasma chorioretinitis
B58.09 Other toxoplasma oculopathy
B58.1 Toxoplasma hepatitis
B58.2 Toxoplasma meningoencephalitis
B58.3 Pulmonary toxoplasmosis
B58.81 Toxoplasma myocarditis
B58.82 Toxoplasma myositis
B58.83 Toxoplasma tubulo-interstitial nephropathy
B58.89 Toxoplasmosis with other organ involvement
B58.9 Toxoplasmosis, unspecified
B60.0 Babesiosis
B95.1 Streptococcus, group B, as the cause of diseases classified elsewhere
B95.62 Methicillin resistant Staphylococcus aureus infection as the cause of diseases classified elsewhere
B96.0 Mycoplasma pneumoniae [M. pneumoniae] as the cause of diseases classified elsewhere
B96.81 Helicobacter pylori [H. pylori] as the cause of diseases classified elsewhere
B96.82 Vibrio vulnificus as the cause of diseases classified elsewhere
B96.89 Other specified bacterial agents as the cause of diseases classified elsewhere
B97.0 Adenovirus as the cause of diseases classified elsewhere
B97.11 Coxsackievirus as the cause of diseases classified elsewhere

B97.12 Echovirus as the cause of diseases classified elsewhere
B97.19 Other enterovirus as the cause of diseases classified elsewhere
B97.21 SARS-associated coronavirus as the cause of diseases classified elsewhere
B97.29 Other coronavirus as the cause of diseases classified elsewhere
B97.30 Unspecified retrovirus as the cause of diseases classified elsewhere
B97.31 Lentivirus as the cause of diseases classified elsewhere
B97.32 Oncovirus as the cause of diseases classified elsewhere
B97.33 Human T-cell lymphotrophic virus, type I [HTLV-I] as the cause of diseases classified elsewhere
B97.34 Human T-cell lymphotrophic virus, type II [HTLV-II] as the cause of diseases classified elsewhere
B97.35 Human immunodeficiency virus, type 2 [HIV 2] as the cause of diseases classified elsewhere
B97.39 Other retrovirus as the cause of diseases classified elsewhere
B97.5 Reovirus as the cause of diseases classified elsewhere
B97.6 Parvovirus as the cause of diseases classified elsewhere
B97.81 Human metapneumovirus as the cause of diseases classified elsewhere
B97.89 Other viral agents as the cause of diseases classified elsewhere
D45 Polycythemia vera
D47.Z1 Post-transplant lymphoproliferative disorder (PTLD)
G03.2 Benign recurrent meningitis [Mollaret]
J06.9 Acute upper respiratory infection, unspecified
J09.x1 Influenza due to identified novel influenza A virus with pneumonia
J09.x2 Influenza due to identified novel influenza A virus with other respiratory manifestations
J09.x3 Influenza due to identified novel influenza A virus with gastrointestinal manifestations
J09.x9 Influenza due to identified novel influenza A virus with other manifestations
J10.00 Influenza due to other identified influenza virus with unspecified type of pneumonia
J10.01 Influenza due to other identified influenza virus with the same other identified influenza virus pneumonia
J10.08 Influenza due to other identified influenza virus with other specified pneumonia
J10.1 Influenza due to other identified influenza virus with other respiratory manifestations
J10.2 Influenza due to other identified influenza virus with gastrointestinal manifestations
J10.81 Influenza due to other identified influenza virus with encephalopathy
J10.82 Influenza due to other identified influenza virus with myocarditis
J10.83 Influenza due to other identified influenza virus with otitis media
J10.89 Influenza due to other identified influenza virus with other manifestations
J11.00 Influenza due to unidentified influenza virus with unspecified type of pneumonia
J11.08 Influenza due to unidentified influenza virus with specified pneumonia
J11.1 Influenza due to unidentified influenza virus with other respiratory manifestations
J11.2 Influenza due to unidentified influenza virus with gastrointestinal manifestations
J11.81 Influenza due to unidentified influenza virus with encephalopathy
J11.82 Influenza due to unidentified influenza virus with myocarditis
J11.83 Influenza due to unidentified influenza virus with otitis media
J11.89 Influenza due to unidentified influenza virus with other manifestations
J12.9 Viral pneumonia, unspecified
J15.212 Pneumonia due to Methicillin resistant Staphylococcus aureus

J16.0	Chlamydial pneumonia
J17	Pneumonia in diseases classified elsewhere
J20.0	Acute bronchitis due to Mycoplasma pneumoniae
J20.3	Acute bronchitis due to coxsackievirus
J20.4	Acute bronchitis due to parainfluenza virus
J20.7	Acute bronchitis due to echovirus
K90.81	Whipple's disease
M02.311	Reiter's disease, right shoulder
M02.312	Reiter's disease, left shoulder
M02.321	Reiter's disease, right elbow
M02.322	Reiter's disease, left elbow
M02.331	Reiter's disease, right wrist
M02.332	Reiter's disease, left wrist
M02.341	Reiter's disease, right hand
M02.342	Reiter's disease, left hand
M02.351	Reiter's disease, right hip
M02.352	Reiter's disease, left hip
M02.361	Reiter's disease, right knee
M02.362	Reiter's disease, left knee
M02.371	Reiter's disease, right ankle and foot
M02.372	Reiter's disease, left ankle and foot
M02.38	Reiter's disease, vertebrae
M02.39	Reiter's disease, multiple sites
P35.1	Congenital cytomegalovirus infection
P35.2	Congenital herpesviral [herpes simplex] infection
P35.3	Congenital viral hepatitis
P35.8	Other congenital viral diseases
P35.9	Congenital viral disease, unspecified
P37.0	Congenital tuberculosis
P37.1	Congenital toxoplasmosis
P37.2	Neonatal (disseminated) listeriosis
P37.3	Congenital falciparum malaria
P37.4	Other congenital malaria
P37.8	Other specified congenital infectious and parasitic diseases
P37.9	Congenital infectious or parasitic disease, unspecified
R05	Cough
R75	Inconclusive laboratory evidence of human immunodeficiency virus [HIV]
R87.610	Atypical squamous cells of undetermined significance on cytologic smear of cervix (ASC-US)
R87.611	Atypical squamous cells cannot exclude high grade squamous intraepithelial lesion on cytologic smear of cervix (ASC-H)
R87.612	Low grade squamous intraepithelial lesion on cytologic smear of cervix (LGSIL)
R87.613	High grade squamous intraepithelial lesion on cytologic smear of cervix (HGSIL)
R87.619	Unspecified abnormal cytological findings in specimens from cervix uteri
R87.810	Cervical high risk human papillomavirus (HPV) DNA test positive
Z01.42	Encounter for cervical smear to confirm findings of recent normal smear following initial abnormal smear

Z11.1	Encounter for screening for respiratory tuberculosis
Z11.3	Encounter for screening for infections with a predominantly sexual mode of transmission
Z11.59	Encounter for screening for other viral diseases
Z11.8	Encounter for screening for other infectious and parasitic diseases
Z20.89	Contact with and (suspected) exposure to other communicable diseases
Z21	Asymptomatic human immunodeficiency virus [HIV] infection status
Z22.4	Carrier of infections with a predominantly sexual mode of transmission
Z22.51	Carrier of viral hepatitis B
Z22.52	Carrier of viral hepatitis C
Z36	Encounter for antenatal screening of mother
Z48.22	Encounter for aftercare following kidney transplant
Z72.51	High risk heterosexual behavior
Z72.52	High risk homosexual behavior
Z72.53	High risk bisexual behavior
Z94.0	Kidney transplant status
Z94.84	Stem cells transplant status

REVISIONS

03-01-2012	Description section updated
	In Policy section: ▪ Revised the policy section to create four parts, I nucleic acid identification for microorganisms with a specific CPT code (part I contains all the criteria from the original policy), II nucleic acid identification for microorganisms that do not have a specific CPT code (87797, 87798, and 87799), III quantitative PCR tests (87799), IV E/I testing. ▪ Added to part I: Clostridium difficile 87493 (med nec); Influenza virus 87501 (med nec)[4], 87502 (med nec)[4], 87503 (inv); Mycoplasma pneumonia 87580 (inv), 87581 (inv), 87582 (inv); Trichomonas vaginalis 87660 (med nec). ▪ Added parts II, III, and IV as follows: II. Other polymerase chain reaction (PCR) testing (87797, 87798, and 87799 describing the use of direct probe, amplified probe, and quantification respectively) for infectious agents that do not have specific CPT codes may be considered medically necessary for the following indications (not an all-inclusive list): A. Adenovirus - to diagnose adenovirus myocarditis, and infection in immunocompromised hosts, including transplant recipients B. Avian influenza A virus (H5N1) - with both symptoms consistent with Avian influenza A virus and a history of travel to or contact with persons or birds from a country with documented H5N1 avian influenza infections within 10 days of symptom onset. (http://www.oie.int/eng/en_index.htm) C. Babesiosis (Babesia) - when the morphologic characteristics observed on microscopic examination of blood smears do not allow differentiation between Babesia and Plasmodium D. BK polyomavirus - in transplant recipients and persons with immunosuppressive diseases (e.g., AIDS) E. Brucella spp. - signs and symptoms of Brucellosis F. Burkholderia infections G. Chancroid (Haemophilus ducreyi) - for genital ulcer disease

	H. Colorado tick fever virus I. Coxiella burnetii - for acute Q fever J. Ehrlichiosis (Ehrlichia) K. Epidemic typhus (Rickettsia prowazekii) L. Epstein Barr Virus (EBV) - for detection of EBV in post-transplant lymphoproliferative disorder or for tissue samples with lymphoma and other immunocompromised states M. Francisella tularensis, for diagnosis of tularemia N. Hemorrhagic fevers of the family Bunyaviridae (Rift Valley fever, Crimean-Congo hemorrhagic fever, hemorrhagic fever with renal syndromes) - clinical presentation suggestive of these conditions O. Human granulocytic anaplasmosis (formerly Ehrlichia phagocytophilum) P. JC polyomavirus - in transplant recipients, immunosuppressive diseases and for progressive multifocal leukoencephalopathy when receiving natalizumab (Tysabri) Q. Leishmaniasis R. Lymphogranuloma venereum (Chlamydia trachomatis) S. Malaria T. Measles virus U. Microsporidia V. Mumps W. Neisseria meningitides X. Parvovirus Y. Psittacosis (Chlamydophila (Chlamydia) psittaci) Z. Rocky Mountain Spotted Fever (Rickettsia rickettsii) AA. Severe acute respiratory syndrome (SARS) (coronavirus) BB. Syphilis (Treponema pallidum) CC. Toxoplasma gondii DD. Varicella-Zoster EE. West Nile Virus - in tissue specimens FF. Whipple's disease (T. whippeli) III. The following other quantitative PCR tests (87799) are considered medically necessary: A. Adenovirus viral load, to monitor response to antiviral therapy in infected immunocompromised hosts, including transplant recipients B. BK polyomavirus viral load, for diagnosis and monitoring response to therapy in infected kidney transplant recipients C. Cytomegalovirus (CMV) viral load, to monitor response to therapy D. Epstein Barr viral load, to monitor for EBV viral replication in solid organ transplant recipients IV. PCR testing for the following indications is considered experimental / investigational because of insufficient evidence in the peer-reviewed literature: A. Actinomycosis B. Astrovirus C. Bacterial vaginosis (Atopobium vaginae, Mobiluncus mulieris, M. curtisii) D. Bacteroides spp. (B. fragilis, B. ureolyticus) E. Caliciviruses (noroviruses and sapoviruses) F. Campylobacterosis (Campylobacter infection) G. Coccidiodomycosis (Coccidioides species) H. Cryptococcus (Cryptococcus neoformans) I. Cyclosporiasis (Cyclospora infection) J. Dengue fever K. Donovanosis, or granuloma inguinale (Klebsiella granulomatis) L. Eastern equine encephalitis M. Entamoeba histolytica N. Escherichia coli

	O. Genital mycoplasma infections from Ureaplasma urealyticum and Mycoplasma hominis (unless culture is unavailable) P. Haemophilus influenzae Q. Hantavirus R. Hepatitis A virus S. Hepatitis D virus T. Human bocavirus U. Human herpesvirus type 7 (HHV-7) V. Human herpesvirus type 8 (HHV-8) W. Human metapneumovirus X. LaCrosse encephalitis Y. Leptospirosis (Leptospira organisms) Z. Molluscum contagiosum AA. Moraxella catarrhalis BB. Mycoplasma fermentans CC. Mycoplasma genitalium DD. Mycoplasma penetrans EE. Nanobacteria FF. Non-albicans Candida GG. Onychomycosis HH. Parainfluenza virus II. Peptic ulcer disease (Helicobacter pylori) (other than in persons with MALT lymphomas and marginal zone lymphomas) JJ. Pneumococcal infections (S. pneumoniae) KK. Pneumocystis pneumonia (Pneumocystis jiroveci (formerly P. carinii)) LL. Prevotella spp. MM. Proteus mirabilis NN. Pseudomonas (P. aeruginosa) OO. Respiratory syncytial virus (RSV) PP. Rhinovirus QQ. Rotavirus RR. Saccharomyces cerevisiae SS. Serratia spp. (including S. marcescens) TT. Shiga toxin (from E. coli and Shigella) UU. Sporotrichosis (Sporothrix schenckii) VV. St. Louis encephalitis WW. Staphylococcus saprophyticus XX. Trichosporonosis (Trichosporon spp.) YY. Western equine encephalitis
	Added Rationale section
	In Coding section: ▪ Added CPT codes (found in policy section): 87493, 87501, 87502, 87503, 87580, 87581, 87582, 87660, 87797, 87798, 87799 ▪ Added Diagnosis codes: 008.45, 021.0-021.9, 023.0-023.9, 025, 033.0-033.9, 036.0, 038.12, 040.2, 041.02, 041.12, 041.81, 041.84, 041.86, 042, 045.0-045.93, 047.0-047.9, 048, 052.0-052.9, 053.0-053.9, 055.0-055.9, 057.0, 058.11, 058.21, 058.81, 065.0, 066.1, 066.3, 066.40-066.49, 070.70, 070.71, 072.0-072.9, 073.0-073.9, 076.0-076.9, 077.0, 077.98, 078.3, 078.88, 079.0, 079.1, 079.2, 079.50-079.59, 079.82, 079.83, 080-081.0, 082.0, 082.40-082.49, 083.0, 084.0-084.9, 085.0-085.9, 088.0, 088.82, 090.0-097.9, 099.0, 099.1, 099.3, 130.0-130.9, 131.00-131.09, 131.8, 131.9, 238.4, 238.77, 465.9, 482.42, 483.1, 487.0-488.19, 786.2, 795.00-795.05, 795.71, V01.82, V02.61, V02.62, V02.7, V02.8, V42.0, V42.82,

	V69.2, V72.32, V73.0, V73.88, V73.98, V74.1, V74.5
	Updated References
06-05-2012	In Policy section: ▪ Correction made by removing "~~(med nec)~~" from Quantification column (code 87503) from prior update. ▪ Add to IV. C. "*Megasphaera, Bacterial vaginosis Associated Bacteria panel [BVAB])*" to read: "Bacterial vaginosis (*Atopobium vaginae, Mobiluncus mulieris, M. curtisii, Megasphaera, Bacterial vaginosis Associated Bacteria panel [BVAB]*)"
11-19-2012	In Title section: ▪ Added reference to another medical policy to read, "*See Also: Influenza Virus Diagnostic Testing and Treatment in the Outpatient Setting"*
	Description section updated
	In Policy section: ▪ Revised Item I from: "The status of nucleic acid identification using direct probe, amplified probe , or quantification for microorganisms, with specific codes listed in the CPT book, is summarized as follows:" to "The status of nucleic acid identification using direct probe, amplified probe , or quantification for the 30 microorganisms listed in the CPT book are summarized in the following table (Note: "(med nec)" in the chart below applies only when the service is clinically indicated):" ▪ Updated Item I chart as follows: ▪ Removed superscript references 1, 2, 3, and 4. ▪ Added NOC code "87497 (inv)" to Enterovirus, Staphylococcus aureus, Staphylococcus aureus, methicillin resistant, and Streptococcus group B ▪ Added NOC code "87498 (inv)" to Clostridium difficile and Trichomonas vaginalis ▪ Added NOC code "87499 (inv)" Clostridium difficile, Enterovirus, Staphylococcus aureus, Staphylococcus aureus, methicillin resistant, Streptococcus group B, and Trichomonas vaginalis ▪ Added Microorganism Enterococcus, Vancomycin resistant (e.g., enterococcus vanA, vanB) with code 87497 (inv), 87500 (med nec), and 87499 (inv). ▪ On Microorganism Influenza virus removed codes 87501 (med nec), 87502 (med nec), and 87503 (inv) and replaced with a reference to "See the Influenza Virus Diagnostic Testing and Treatment in the Outpatient Setting medical policy" located on the web site. ▪ Added to Item I, "If NOC codes 87497, 87498, 87499 are billed for PCR for microorganisms when specific codes exist the claim will be returned for correct coding." ▪ Added to Item II the following medically necessary indications, "D. Bacillus anthracis", "U. Human metapneumonvirus", and "NN. Yersinia pestis" ▪ Added Item IV, "IV. The Respiratory Virus Panel will be reviewed for medical necessity on a case-by-case basis." ▪ Removed under Item V "N. Escherichia coli" as it is not a PCR test and was incorrectly included in the policy under a prior revision." ▪ Under Policy Guidelines added, "3.The Association of Molecular Pathology (AMP) web site provides a list of current FDA-approved tests for diagnosis of infectious diseases. (http://www.amp.org/FDATable/FDATable.pdf)
	Rationale section updated
	References updated

01-15-2013	In Policy section: ▪ Added to the Microorganism chart in item I: "Respiratory Virus Panel - See item IV on page 9 of this policy." ▪ Added to the medically necessary indication list in item II F. Bordetella pertussis
	Code Updates in Policy section: ▪ Added CPT codes 87631, 87632, 87633 to item IV (effective 01-01-2013) ▪ Corrected coding errors in the Microorganism chart in item I by replacing 87497 with 87797, 87498 with 87798, and 87499 with 87799 as appropriate for the following Microorganisms: Clostridium difficile; Enterovirus; Staphylococcus aureus; Staphylococcus aureus, methicillin resistant; Streptococcus group B; and Trichomonas vaginalis ▪ Corrected coding errors in the Note below the Microorganisms chart from, "Note: If NOC codes 87497, 87498, 87499 are billed for PCR for microorganisms when specific codes exist, the claim will be returned for correct coding." To, " Note: If NOC codes 87797, 87798, 87799 are billed for PCR for microorganisms when specific codes exist, the claim will be returned for correct coding."
11-12-2013	Description section updated
	In Policy section: ▪ On Item I Trichomonas vaginalis, updated Amplified Probe code from 87798 to 87661 to be used effective 01-01-2014. ▪ Changed Trichomonas vaginalis from investigational to medically necessary on the effective date of the policy update. In Policy Guidelines: ▪ Added to item 2, "This advantage suggests that the most appropriate use of the DNA probe technique is in the setting of impending labor, for which prompt results could permit the initiation of intrapartum antibiotic therapy." ▪ Added item 3, "Many probes have been combined into panels of tests. For the purposes of this policy, other than the respiratory virus panel, only individual probes are reviewed." ▪ Removed reference to the Association of Molecular Pathology (AMP) website as this is addressed in the Description section.
	Rationale section updated
	In Coding section: ▪ Added CPT codes and nomenclatures for CPT codes reflected in the Policy section. ▪ ICD-10 codes added.
	References updated.

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