

## Medical Policy



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### **Title: Identification of Microorganisms Using Nucleic Acid Testing**

- See Also:*
- *Influenza Virus Diagnostic Testing and Treatment in the Outpatient Setting*
  - *Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease*

#### **Professional**

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#### **Institutional**

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Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected <i>Chlamydomphila pneumoniae</i> infection	Interventions of interest are: • Nucleic acid probe for <i>Chlamydomphila pneumoniae</i>	Comparators of interest are: • No <i>Chlamydomphila pneumoniae</i> -specific testing	Relevant outcomes include: • Test accuracy • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With hepatitis	Interventions of interest are: • Nucleic acid probe for hepatitis G	Comparators of interest are: • No hepatitis G-specific testing	Relevant outcomes include: • Test accuracy • Test validity • Other test performance measures • Symptoms • Change in disease status
Individuals: • With signs and/or symptoms of gastroenteritis	Interventions of interest are: • Nucleic acid-based gastrointestinal pathogen panel	Comparators of interest are: • No gastrointestinal pathogen-specific testing • Culture or nucleic acid-based testing for individual pathogens	Relevant outcomes include: • Test accuracy • Test validity • Other test performance measures • Symptoms • Change in disease status

## **DESCRIPTION**

Nucleic acid probes are available for the identification of a wide variety of microorganisms, offering more rapid identification than 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, when microbial identification using standard culture is difficult or impossible, and/or when treatment decisions are based on quantitative results.

## **BACKGROUND**

### **Standard Microorganism Detection Techniques**

Classically, identification of microorganisms relied 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.

### **Nucleic Acid Probe Techniques**

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 (RT)-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.

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. In addition, CPT codes have been added for additional microorganisms, such as *Staphylococcus aureus*.

### Comparison of Probe Techniques

The direct probe technique, amplified probe technique, and probe with quantification methods vary in terms of the degree to which the nucleic acid is amplified and the method for measurement of the signal.

The “direct probe” technique refers to detection methods in which nucleic acids are detected without an initial amplification step.

The “amplified probe” technique refers to detection methods in which either target, probe, or signal amplification is used to improve the sensitivity of the assay over direct probe techniques, without quantification of nucleic acid amounts.

- **Target amplification methods** include PCR (including PCR using specific probes, nested or multiplex PCR), nucleic acid–based sequence amplification (NASBA), transcription-mediated amplification (TMA), and strand displacement amplification (SDA). NASBA and TMA involve amplification of an RNA (rather than a DNA) target
- **Probe amplification methods** include ligase chain reaction (LCR).
- **Signal amplification methods** include branched DNA probes (bDNA) and hybrid capture methods using an anti-DNA/RNA hybrid antibody.

The “probe with quantification” techniques refer to quantitative PCR (qPCR) or real-time PCR (rt-PCR) methods that use a reporter at each stage of the PCR to generate absolute or relative amounts of a known nucleic acid sequence in the original sample. These methods may use DNA-specific dyes (ethidium bromide or SYBR green), hybridization probes (cleavage-based [TaqMan] or displaceable), or primer incorporated probes.

For reference, examples of some commercially available probe methods are outlined in Table 1.

Table 1: Example Probe Methods

Probe Method	Sample Commercially Available Products	Microorganism(s)
<b>Direct probe</b>	BD Affirm™ VPIII Microbial Identification System (Becton, Dickinson, Franklin Lakes, NJ)	<i>Candida</i> , <i>Gardnerella</i> , <i>Trichomonas</i> species
	GasDirect (Hologic, Bedford, MA)	Group A <i>Streptococcus</i>
<b>Amplified probe</b>	Amplified MTD test (Hologic, Bedford, MA)	<i>Mycobacterium tuberculosis</i>
<b>Probe with quantification</b>	Cobas® Amplicor HIV-1 Monitor Test (Roche Molecular Diagnostics, Pleasanton, CA)	<i>Human immunodeficiency virus-1</i>

Direct assays will generally have lower sensitivity than amplified probes. In practice, most commercially available probes are amplified, with a few exceptions. For the purposes of this evidence review, indications for direct and/or amplified probes without quantification are considered together, while indications for a probe with quantification are considered separately.

### Microorganisms and Clinical Disease

Various bacteria, viruses, and fungi that can cause clinical disease and can be detected with various nucleic acid probe techniques are briefly outlined below.

#### ***Bartonella henselae* or *quintana***

*Bartonella henselae* is thought to be responsible for cat scratch disease. In most patients (90%-95%), the infection is a localized skin and lymph node disorder that occurs close to the site of inoculation, and which is characterized by chronic regional lymphadenopathy that develops about 2 weeks after contact with a cat. Less commonly, *Bartonella henselae* infection may lead to disseminated infection, which can manifest as visceral organ involvement, often with fever and hepatosplenomegaly, a variety of ocular manifestations, and neurological manifestations (most commonly, encephalopathy).

*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.

*Bartonella quintana* has classically been associated with "trench fever," which is characterized by systemic symptoms (bone pain, malaise, headache), along with recurring fevers of varying durations. Among HIV-infected patients, *B. quintana* has been associated with bacillary angiomatosis.

*Bartonella* are fastidious organisms, making culture difficult. Histology of lesions affected by bacillary angiomatosis may be characteristic. Histology of affected lymph nodes or other tissue with *B. henselae* may demonstrate findings that are suggestive of cat-scratch disease, but which may be seen in other conditions. Two antigenic methods are available, one using indirect

fluorescence assay (IFA) and one using enzyme immunosorbent assay (EIA), for both *B. henselae* and *B. quintana* infections. A positive serologic test is generally considered supportive, but not definitive, for *Bartonella* infection. Serologic methods may have limited yield in immunosuppressed patients.

### ***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.

### ***Chlamydophila pneumoniae***

*Chlamydophila 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. 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, enteroviruses can cause "aseptic" or viral meningitis, encephalitis, acute paralysis, and/or myocarditis. Enteroviral infections can cause life-threatening systemic infections in neonates, which are often associated with myocarditis or fulminant hepatitis. 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 to monitor the response to direct-acting antiviral, interferon, and/or ribavirin therapy in patients with hepatitis C.

### **Herpes Simplex Virus**

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

### **Human Herpesvirus-6**

Human herpesvirus-6 (HHV-6) is the common collective name for HHV-6A and HHV-6B. These closely related viruses are 2 of the 9 herpesviruses known to have humans as their primary host. HHV-6 is widespread in the general population. In immunocompetent hosts, HHV-6 primary infection typically causes a mild, self-limited illness in childhood, often roseola. HHV-6 may also cause meningitis and encephalitis in children and adults. Diagnosis is typically based on rising serologic titers.

In immunosuppressed patients, HHV-6 reactivation may cause meningitis, encephalitis, pneumonitis, and/or bone marrow suppression.<sup>1</sup>

### **HIV-1 and 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.

### ***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 (ie, acid fast bacilli), these organisms may take 9 to 16 days to culture. DNA probes have also been used to identify specific mycobacterial groups (ie, mycobacterial tuberculosis, avian complex, intracellulare) after culture. In addition, amplification techniques for *Mycobacterium tuberculosis* may be used in patients who have a positive smear. The rapid identification of *M. 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 below 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 *M. pneumoniae* recover completely, although the course is sometimes prolonged for up to 4 weeks or more. Extrapulmonary complications of *M. pneumoniae* 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, but culture requires specific sampling and plating techniques. 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***

Also referred to as *Streptococcus agalactiae*, group B streptococcus (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, the American College of Obstetrics and Gynecology, and the American Academy of Pediatricians 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 of 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.

## REGULATORY STATUS

A list of current U.S. Food and Drug Administration (FDA)-approved or cleared nucleic acid-based microbial tests is available online:

<http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm330711.htm>

The Association of Molecular Pathology website also provides a list of current FDA approved tests for diagnosis of infectious diseases (available online at:

<http://www.amp.org/FDATable/FDATable.pdf> ). Table 2 lists tests that are FDA-approved/cleared but do **not** have specific CPT codes.

**Table 2. FDA-Approved/Cleared Tests Without CPT Codes**

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

FDA: U.S. Food and Drug Administration; FISH: fluorescence in situ hybridization; PCR: polymerase chain reaction; PNA: peptide nucleic acid; RT: reverse transcriptase.

## **POLICY**

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

- A. The use of nucleic acid testing using a direct or amplified probe technique (*without* quantification of viral load) may be considered **medically necessary (med nec)** for the following microorganisms (see Policy Guidelines):

NOTE: (med nec) in the chart below applies only when the service is clinically indicated.

<b>Microorganism</b>	<b>Direct Probe</b>	<b>Amplified Probe</b>	<b>Quantification</b>
<i>Bartonella henselae</i> or <i>quintana</i>	87470 (med nec)	87471 (med nec)	87472 (E/I)
<i>Candida</i> species (See Policy Guidelines #3)	87480 (med nec)	87481 (med nec)	87482 (E/I)
<i>Chlamydia trachomatis</i>	87490 (med nec)	87491 (med nec)	87492 (E/I)
<i>Clostridium difficile</i>	87493 (med nec)	87798 (med nec)	87799 (E/I)
<i>Enterococcus</i> , vancomycin resistant (eg, <i>enterococcus vanA</i> , <i>vanB</i> )	87797 (med nec)	87500 (med nec)	87799 (E/I)
<i>Enterovirus</i>	87797 (med nec)	87498 (med nec)	87799 (E/I)
<i>Gardnerella vaginalis</i>	87510 (med nec)	87511 (med nec)	87512 (E/I)
Gastrointestinal Pathogen Panel	<i>See Item F on page 13 of this policy.</i>		
Herpes simplex virus	87528 (med nec)	87529 (med nec)	87530 (E/I)
Human papillomavirus	N/A	87623 (med nec) 87624 (med nec) 87625 (med nec)	N/A
<i>Legionella pneumophila</i>	87540 (med nec)	87541 (med nec)	87542 (E/I)
Meningitis / Encephalitis Panel	N/A	87483 (med nec)	N/A
<i>Mycobacterium</i> species	87550 (med nec)	87551 (med nec)	87552 (E/I)
<i>Mycobacterium tuberculosis</i>	87555 (med nec)	87556 (med nec)	87557 (E/I)
<i>Mycobacterium avium intracellulare</i>	87560 (med nec)	87561 (med nec)	87562 (E/I)
<i>Mycoplasma pneumoniae</i>	87580 (med nec)	87581 (med nec)	87582 (E/I)
<i>Neisseria gonorrhoeae</i>	87590 (med nec)	87591 (med nec)	87592 (E/I)
Respiratory Virus Panel	<i>See item E on page 13 of this policy.</i>		
<i>Staphylococcus aureus</i>	87797 (med nec)	87640 (med nec)	87799 (E/I)
<i>Staphylococcus aureus</i> , methicillin resistant	87797 (med nec)	87641 (med nec)	87799 (E/I)

Microorganism	Direct Probe	Amplified Probe	Quantification
<i>Streptococcus</i> , group A	87650 (med nec)	87651 (med nec)	87652 (E/I)
<i>Streptococcus</i> , group B	87797 (med nec)	87653 (med nec)	87799 (E/I)
<i>Trichomonas vaginalis</i>	87660 (med nec)	87661 (med nec)	87799 (E/I)

- B. The use of nucleic acid testing using a direct or amplified probe technique (*with or without* quantification of viral load) may be considered **medically necessary** "**(med nec)**" for the following microorganisms:

NOTE: (med nec) in the chart below applies only when the service is clinically indicated.

Microorganism	Direct Probe	Amplified Probe	Quantification
Cytomegalovirus	87495 (med nec)	87496 (med nec)	87497 (med nec)
Hepatitis B virus	87515 (med nec)	87516 (med nec)	87517 (med nec)
Hepatitis C virus	87520 (med nec)	87521 (med nec)	87522 (med nec)
HIV-1	87534 (med nec)	87535 (med nec)	87536 (med nec)
HIV-2	87537 (med nec)	87538 (med nec)	87539 (med nec)
Human herpesvirus-6	87531 (med nec)	87532 (med nec)	87533 (med nec)
Influenza virus	<i>See medical policy titled: Influenza Virus Diagnostic Testing and Treatment in the Outpatient Setting</i>		

- C. CPT codes 87797 and 87798 describe the use of direct probe and amplified probe respectively for infectious agents not otherwise specified. The following may be considered **medically necessary** (not an all-inclusive list):

1. *Adenovirus*
2. *Bacillus anthracis*
3. *Coxiella burnetii* (Q fever)
4. Dengue virus
5. *Enterococcus faecalis*
6. *Escherichia coli* and *Pseudomonas aeruginosa*
7. *Escherichia coli* and/or *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*
8. *Escherichia coli*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*
9. *Francisella tularensis*
10. Gram-positive/gram-negative bacteria panel
11. Human *metapneumonvirus*
12. *Leishmania*
13. *Yersinia pestis*
14. Actinomyces
15. Babesiosis (*Babesia*)

16. Beta-tyrosinase
17. BK polyomavirus
18. *Bordetella pertussis* and *B. parapertussis*
19. *Borrelia miyamotoi*
20. *Brucella* spp.
21. *Burkholderia* infections
22. Chancroid (*Haemophilus ducreyi*)
23. Chikungunya virus
24. Colorado tick fever virus
25. Ebola
26. Ehrlichiosis (*Ehrlichia*)
27. *Entamoeba histolytica*
28. Epidemic typhus (*Rickettsia prowazekii*)
29. Epstein Barr Virus (EBV)
30. *Haemophilus influenzae*
31. Hantavirus
32. Hemorrhagic fevers of the family *Bunyaviridae* (Rift Valley fever, Crimean-Congo hemorrhagic fever, hemorrhagic fever with renal syndromes) - clinical presentation suggestive of these conditions
33. Hepatitis D virus
34. Hepatitis E virus
35. Human granulocytic anaplasmosis (*Anaplasma phagocytophilum* [formerly *Ehrlichia phagocytophilum*])
36. Human T Lymphotropic Virus type 1 and type 2 (HTLV-I and HTLV-II)
37. JC polyomavirus
38. Malaria
39. Measles virus
40. Microsporidia
41. Mumps
42. *Mycoplasma hominis*
43. *Neisseria meningitides*
44. Parvovirus
45. Psittacosis (*Chlamydophila (Chlamydia) psittaci*)
46. Respiratory syncytial virus (RSV)
47. Rocky Mountain Spotted Fever (*Rickettsia rickettsii*)
48. Rubella
49. Severe acute respiratory syndrome (SARS) (coronavirus)
50. Shiga toxin (from *E. coli* and Shigella)
51. Syphilis (*Treponema pallidum*)
52. *Toxoplasma gondii*
53. Ureaplasma urealyticum
54. Varicella-Zoster
55. West Nile Virus
56. Whipple's disease (*T. whippelii*)

- D. CPT code 87799 describes the use of quantification for infectious agents not otherwise specified. The following may be considered **medically necessary**:
1. *Adenovirus* viral load
  2. BK polyomavirus viral load
  3. Epstein Barr viral load
- E. The Respiratory Virus Panel (CPT codes 87631, 87632, 87633) will be **reviewed for medical necessity** on a case-by-case basis.
- F. The Gastrointestinal Pathogen Panel (CPT codes 87505, 87506, 87507) may be considered **medically necessary** in patients with:
1. Severe diarrhea longer than 72 hours in duration, **OR**
  2. Severe diarrhea and ONE of the following:
    - a) bloody stools, OR
    - b) fever, OR
    - c) the patient is immunocompromised.
- G. The use of nucleic acid testing using a direct or amplified probe technique (*with or without* quantification of viral load) indications is considered **experimental / investigational** for the following microorganisms:

Microorganism	Direct Probe	Amplified Probe	Quantification
<i>Borrelia burgdorferi</i>	<i>See medical policy titled: Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease</i>		
<i>Chlamydia pneumoniae</i>	87485 (E/I)	87486 (E/I)	87487 (E/I)
Hepatitis G virus	87525 (E/I)	87526 (E/I)	87527 (E/I)

- H. The use of nucleic acid testing for indications not addressed in the above policy are considered **experimental / investigational**.

CPT codes 87797, 87798, and 87799 describe the use of direct probe, amplified probe, and quantification, respectively, for infectious agents not otherwise specified. A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy.

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.

### 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. Antibiotic sensitivity of streptococcus A cultures is generally 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.
3. For uncomplicated infections, testing for only 1 candida species, *C. albicans*, may be considered medically necessary. For complicated infections, testing for multiple candida subspecies may be considered medically necessary. The Centers for Disease Control and Prevention classifies uncomplicated vulvovaginal candidiasis as being sporadic or infrequent; or mild to moderate; or likely to be *C. albicans*; or in nonimmunocompromised women. Complicated vulvovaginal candidiasis is classified as being recurrent or severe; or not a *C. albicans* species; or in women with uncontrolled diabetes, debilitation, or immunosuppression (Centers for Disease Control and Prevention, 2010).
4. 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.
5. Many probes have been combined into panels of tests. For the purposes of this policy, other than the gastrointestinal pathogen panel, the meningitis / encephalitis panel, and the respiratory virus panel, only individual probes are reviewed.

### RATIONALE

This evidence review was updated with literature reviews. The most recent literature review was conducted for the period of through November 16, 2015.

The clinical utility of the nucleic acid probes has been determined on the basis of direct published evidence and/or a chain of indirect evidence. Ideally, the determination that a specific nucleic acid probe has evidence to support its use would be based on the following:

- Is there evidence of analytic validity (test technical performance)?
- Is there evidence of clinical validity (sensitivity, specificity, positive predictive value [PPV] and negative predictive value [NPV])?
- Is there either direct evidence or a chain of indirect evidence that there is clinical utility? Potential reasons for a nucleic acid probe to be associated with improved clinical outcomes compared with standard detection techniques include the following (note: in all cases, for there to be clinical utility, making a diagnosis should be associated with

changes in clinical management, which could include initiation of effective treatment, discontinuation of other therapies, or avoidance of invasive testing):

- ✓ Significantly improved speed and/or efficiency in making a diagnosis.
- ✓ Improved likelihood of obtaining any diagnosis in cases where standard culture is difficult. Potential reasons for difficulty in obtaining standard culture include low numbers of the organisms (eg, HIV), fastidious or lengthy culture requirements (eg, *Mycobacteria*, *Chlamydia*, *Neisseria* species), or difficulty in collecting an appropriate sample (eg, herpes simplex encephalitis).
- ✓ There is no way to definitively make a diagnosis without nucleic acid testing.
- ✓ The use of nucleic acid probe testing provides qualitatively different information than that available from standard culture, such as information regarding disease prognosis or response to treatment. These include cases where quantification of viral load provides prognostic information or is used to measure response to therapy.

Although nucleic acid probe technologies offer the potential for rapid, sensitive detection for a variety of microorganisms, there are technical and clinical considerations that should be accounted for in evaluating the technologies. These include:

- Lack of standardization in primers. For some microorganisms, the specific short segments of complementary DNA (probes or primers) used to initiate DNA replication are not commercially available, and different reference laboratories may use different products.
- Risk of cross-specimen contamination.
- Risk of nonspecific amplification, particularly if probes lack specificity.
- Challenges in clinical interpretation of results. 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.

### ***Bartonella henselae* or *quintana***

Microbiologic detection of *Bartonella henselae* or *quintana* is difficult. A monoclonal antibody (mAb) to *B. henselae* has become commercially available, along with several types of PCR testing.

A single-step PCR-based assay which amplifies a fragment of the 16S-23S ribosomal RNA (rRNA) intergenic region conserved in *Bartonella* species had 80% and 100% sensitivity in feline samples with 10 to 30 CFU/mL bacteria and greater than 50 CFU/mL bacteria, respectively.<sup>2</sup> An earlier study demonstrated high sensitivity of a PCR-based assay for the *Bartonella* riboflavin synthase gene in bacterial samples and samples from feline samples and human lymph node samples.<sup>3</sup> Another study reported high sensitivity of a PCR-based enzyme immunoassay in human lymph node samples.<sup>4</sup>

In 2005, Hansmann et al reported on the diagnostic value of a PCR test for the *B. henselae* *htrA* gene in lymph node biopsy specimens or cytopunctures from 70 patients with suspected cat-scratch disease.<sup>5</sup> Twenty-nine patients were considered to have definite cat-scratch disease based on clinical criteria; 16 were considered to have possible cat-scratch disease; and 26 subjects had an alternative diagnosis and served as controls. PCR analysis had specificity of 100%. In patients with definite cat-scratch disease, PCR testing was positive for 76% (95% confidence interval [CI], 56.5% to 89.7%); in those with possible cat-scratch disease, PCR testing was positive in 20% (95% CI, 4.3% to 48.1%).

A 2009 study by Caponetti et al<sup>6</sup> compared immunohistochemical analysis (IHC) for diagnosing *B. henselae* on surgical specimens with PCR detection and serologic testing. The study included 24 formalin-fixed, paraffin-embedded (FFPE) cases of lymphadenitis with histologic and/or clinical suspicion of *B. henselae*. Control cases included 14 cases of lymphadenopathy. FFPE tissue sections were evaluated with a mAb to *B. henselae*, Steiner silver stain (SSS), and PCR that targeted *B. henselae* and *B. quintana*. 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 bartonellae. 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.

*B. henselae* infections can cause a wide range of symptoms, from self-limited regional lymphadenopathy to disseminated infection involving visceral organs, the central nervous system, or the heart. *B. henselae* may also present with fever of unknown origin. Antibiotic therapy is not always needed for uncomplicated infections, but it is required for severe or systemic infections. In cases where *B. henselae* is suspected and treatment will change as a result of a positive test, the use of *Bartonella* PCR testing has potential for clinical utility.

### ***Candida* Species**

*Candida* infections are most commonly caused by *Candida albicans* but other species may be responsible. In complicated or severe cases, eg, candidemia and invasive focal infections, or in compromised patients, it may be necessary to identify the infecting *Candida* species for appropriate treatment planning. 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%.<sup>7,8</sup> Some tests have been able to detect up to 6 *Candida* species.<sup>9</sup> A real-time qPCR 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.<sup>8</sup> 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.

Vulvovaginal candidiasis can typically be diagnosed by microscopy, and most cases are caused by *C. albicans*. Other species, such as *Candida glabrata*, may be responsible but are less common and may be difficult to detect by microscopy. Therefore, identification of *Candida* subspecies is not usually necessary and should be limited to use in complicated, recurrent or persistent cases that are resistant to azole/antifungal treatment. Additionally, symptomatic patients with negative microscopy may warrant subspecies testing.<sup>10</sup>

### ***Chlamydophila pneumoniae* or *Chlamydia trachomatis***

Probes are commercially available for the detection of *Chlamydophila pneumoniae* or *Chlamydia trachomatis*. A study by Stanek et al<sup>11</sup> 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 *C. trachomatis* or *C. pneumoniae*. Of 65 positive samples, 61 (93.8%) were found to be positive with the new PCR. Another study<sup>12</sup> demonstrated

the VERSANT® CT/GC DNA 1.0 Assay performed with 99.2% specificity for *C. trachomatis* detection and sensitivity of 100%.

For *C. trachomatis*, microbial culture is technically difficult, and nucleic acid amplification tests for *C. trachomatis* are generally preferred over other diagnostic methods, including direct fluorescent antibody tests, enzyme immunoassays, and nucleic acid hybridization tests.<sup>13</sup> Diagnosis of *C. trachomatis* has clinical utility in a variety of settings. 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. Antibiotic treatment is indicated in neonatal conjunctivitis caused by *C. trachomatis*.

PCR-based tests specific for *C. pneumoniae* have been described in the investigational setting.<sup>14,15</sup> Gaydos et al compared tissue culture, PCR/EIA, direct fluorescent antibody (DFA) stain, and serology for the diagnosis of *C. pneumoniae* in 56 patients with respiratory symptoms and 80 asymptomatic individuals.<sup>15</sup> Determining test characteristics is limited by the lack of a true gold standard, given the difficulty in culturing *C. pneumoniae*. However, when culture- and/or DFA-positive results were used as a reference, PCR had a sensitivity and specificity of 76.5% and 99.0%, respectively. However, the use of PCR-based tests for *C. pneumoniae* in clinical practice has not been well defined.

### ***Clostridium difficile***

DNA probes for *Clostridium difficile* using PCR have been commercially available since 2009.<sup>16-19</sup> Eastwood et al<sup>17</sup> 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*, the use of PCR-based testing for *C. difficile* has potential to improve health outcomes.

### **Cytomegalovirus**

Diagnosis of CMV can be made by culture and/or serologies. However, CMV culture for establishing a diagnosis is limited by the slow growth of CMV and low sensitivity. Serologies provide indirect evidence of current and/or historical infection. A variety of tests to detect CMV DNA have been developed, including but not limited to Hybrid Capture (Digene Corp.), Amplicor CMV Monitor Tests (Roche Molecular Diagnostics), and TaqMan. The specific techniques used may vary by local availability, but studies have suggested that all provide complementary information.<sup>20-24</sup>

Clinically, molecular assays for CMV are primarily used to quantify CMV viral load, particularly to identify asymptomatic immunosuppressed patients (ie, 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 posttransplant period (ie, up to 50 days posttransplant), and thus, a variety of preventive therapies have been investigated. One strategy proposes that all at-risk patients (ie, 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.

### **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, PPV, and NPV 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. GXEA showed a high specificity but a lower sensitivity for the detection of enterovirus RNA compared with the RT-qPCR assay.<sup>25</sup> In at least some clinical situations, the yield of virus identification with PCR has been shown to be higher than with viral culture (eg, suspected pediatric enteroviral encephalomyelitis).<sup>26</sup>

Enteroviruses are associated with a wide spectrum of clinical symptoms, including exanthematous/ enanthematous syndromes (eg, hand-foot-and-mouth disease, herpangina), viral meningitis and encephalitis, acute paralysis, and myocarditis. In neonates, enteroviruses can cause life-threatening systemic infections. In general, management is supportive and addresses symptoms. No antiviral medications are currently approved for the treatment of enterovirus infections. However, there are some situations in which PCR-based testing for enteroviruses allows for discontinuation of therapy for alternative diagnoses (eg, bacterial meningitis). For example, the use of enterovirus PCR testing has been associated with shorter hospital length of stay among febrile infants evaluated for serious bacterial infection with lumbar puncture.<sup>27</sup> Similarly, an observational study reported that the use of enterovirus PCR testing is associated with reduced hospital stay and reduced antibiotic duration in adults with aseptic meningitis.<sup>28</sup>

### **Vancomycin-Resistant *Enterococcus***

Probes are available for detecting vancomycin resistance of organisms (eg, 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.<sup>29,30</sup>

### ***Gardnerella vaginalis***

A 2006 study<sup>31</sup> 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. A total of 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 with the Gram stain, the DNA hybridization test had a sensitivity of 87.7% and a specificity of 96.0%. PPVs and NPVs 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.

### **Gastrointestinal Pathogen Panel**

Infectious gastroenteritis may be caused by a broad spectrum of pathogens resulting in the primary symptom of diarrhea. Panels for gastrointestinal pathogens uses multiplex amplified probe techniques and multiplex reverse transcription for the simultaneous detection of many gastrointestinal pathogens such as *C. difficile*, *Escherichia coli*, *Salmonella*, *Shigella*, norovirus, rotavirus, and *Giardia*. Several studies of gastrointestinal pathogen panels demonstrate overall high sensitivities and specificities and indicate the panels may be useful for detecting causative agents for gastrointestinal infections.<sup>32-34</sup> Studies suggest that panels limited to bacterial pathogens have similarly high sensitivities and specificities compared with bacterial culture.<sup>35</sup> Beckmann et al reported findings on the use of a commercially available gastrointestinal pathogen panel (Luminex Molecular Diagnostics, Toronto, ON) in a group of 120 pediatric patients with suspected viral gastroenteritis and in a group of 151 adult and 25 pediatric patients (n=176) returning from the tropics with gastrointestinal symptoms.<sup>36</sup> Positive results were detected in 21 samples from adults (11% of 185 samples) and in 66 pediatric samples (52% of samples).

Other studies have evaluated panels for bacteria associated with hemorrhagic diarrhea (*Salmonella* species, *Shigella* species, enterohemorrhagic *E. coli*, and *Campylobacter* species) and have reported high sensitivities and specificities.<sup>37</sup> Other panels are comprised of only viral infectious gastroenteritis pathogens.<sup>38</sup> The yield of testing is likely to vary based on panel composition.<sup>39</sup>

Access to a rapid method for etiologic diagnosis of gastrointestinal infections may lead to more effective early treatment and infection-control measures. However, in most instances, when there is suspicion for a specific pathogen, individual tests could be ordered. There may be a subset of patients with an unusual presentation who would warrant testing for a panel of pathogens at once, but that subset has not been well defined.

### **Hepatitis B**

Hepatitis B genotyping has been used to predict response to various antiviral agents. In addition, viral load is used to determine which patients with hepatitis B are candidates for antiviral therapy. Guidelines from the National Institutes of Health (2009)<sup>40</sup> and the American Association for the Study of Liver Diseases<sup>41</sup> include quantitative hepatitis B DNA levels in the diagnostic criteria for chronic and resolved hepatitis B and inactive hepatitis B carrier states.

### **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 PCR provides evidence of active HCV infection and is used to confirm the diagnosis and monitor the response to antiviral therapy. The use of direct-acting antiviral agents (with or without interferon) has the potential to treat and cure chronic hepatitis C. Therapy-induced sustained virologic 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 real-time PCR and direct sequencing for 4 randomly selected samples followed by phylogenetic analysis.

## Herpes Simplex Virus

Typing of HSV isolates is required to identify the virus isolated in culture. The methods available for this include antigen detection by immunofluorescence (IF) assays and PCR. A 2009 cross-sectional study<sup>42</sup> 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.

## Human Herpesvirus 6

Human herpesvirus 6 (HHV-6) can be detected with a number of immunoassays. The high rate of seropositivity in the general population makes interpreting positive results difficult. Historically, paired samples with a rise in antibody titer have been needed to diagnose an active infection.

Qualitative and quantitative PCR tests are available for HHV-6 in blood and other samples. At least 1 evaluation of rt-PCR detecting viral mRNA transcripts in hematopoietic stem cell transplant (HSCT) subjects showed good analytic validity.<sup>43</sup>

Most often, in healthy patients, HHV-6 causes no symptoms or a mild-self-limited illness. In these cases, a definitive diagnosis of HHV-6 has little utility. However, primary HHV-6 infection can cause severe disease including thrombocytopenia, hepatitis, myocarditis, and meningoencephalitis. In immunosuppressed patients, particularly HSCT recipients, HHV-6 reactivation may cause a range of severe symptoms. A number of antiviral agents are active against HHV-6 (eg, ganciclovir, foscarnet). A variety of treatment strategies are used for immunosuppressed patients, which can be classified as prophylactic (all at-risk patients treated), preemptive (patients treated when viral replication is detected), and curative (patients treated when disease is confirmed).<sup>44</sup> The use of a quantitative HHV-6 assay may be used in treatment-related decisions.

## Human Immunodeficiency Virus 1

Validated DNA probes are widely available for diagnosis and HIV-1 quantification. Quantification is standard of care to determine viral load in infected patients to monitor response to antiretroviral therapies.

### **Human Immunodeficiency Virus 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 antiretroviral therapies.

### **Human Papillomavirus**

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,<sup>45,46</sup> 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.<sup>47-49</sup> Persistent infection with various HPV genotypes has also been linked with cervical lesions and may influence treatment decisions. HPV genotypes 16 and 18 have been most associated with carcinogenesis. Patients with high-risk HPV genotypes may warrant direct referral to colposcopy.<sup>50,51</sup>

### **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<sup>52</sup> used a multiplex RT-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.<sup>53</sup> Because of the importance of early identification of outbreaks for infection-control purposes and of initiating antiviral therapy early in the course of illness (if indicated), there is clinical utility for the use of these tests.

### ***Legionella pneumophila***

Typically, methods to detect *Legionella pneumophila*, which is associated with 90% of culture-confirmed *Legionella* species infections, have included culture, serology, and/or urine antigen testing, which are limited by relatively low sensitivities and long turnaround times.

DNA probes for *Legionella pneumophila* have been developed. A 2010 study<sup>54</sup> compared the usefulness of 2 quantitative RT-PCR assays (qrt-PCR<sub>mip</sub> targeting *L. pneumophila*, and qrt-PCR<sub>16S</sub> 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) 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, PPVs and NPVs for both qrt-PCR tests were 63.6%, 98.7%, 77.7%, and 97.4%, respectively. Diederer et al evaluated the use of an rt-PCR assay for *Legionella* species in 151 subjects with respiratory infections, 37 (25%) of whom fulfilled the European Working Group for *Legionella* Infections criteria for *Legionella* pneumonia

and were considered to have *Legionella pneumoniae*.<sup>55</sup> For a 16S rRNA-based PCR, the estimated sensitivity and specificity were 86% (95% CI, 72% to 95%) and 95% (95% CI, 90% to 98%), respectively. For a *mip* gene-based PCR, the estimated sensitivity and specificity were 92% (95% CI, 78% to 98%) and 98% (95% CI, 93% to 100%), respectively. Another study reported a significantly higher sensitivity for PCR versus culture in detecting *L. pneumophila* in samples taken within 2 days or less of hospitalization (94.7% vs 79.6%, respectively) or 3 to 14 days of hospitalization (79.3% and 47.8%, respectively).<sup>56</sup>

Delay in initiating appropriate antimicrobial therapy for Legionnaire's disease is associated with increased mortality, which makes a strong indirect argument for improved early detection with nucleic acid probes.

### **Meningitis / Encephalitis Panel**

The FilmArray ME Panel is designed to simultaneously test for 14 bacterial, viral and yeast pathogens using a small sample of cerebrospinal fluid (CSF) and can provide results in about an hour, which may enable clinicians to make informed treatment decisions earlier. Testing CSF for multiple organisms was not always possible because it can be difficult to obtain enough fluid from each patient to run multiple tests.

Bacteria and yeast pathogens identified by the FilmArray ME Panel are *Escherichia coli* K1, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, and *Cryptococcus neoformans/gattii*. Viruses identified by the FilmArray ME Panel are Cytomegalovirus, Enterovirus, Herpes simplex virus 1, Herpes simplex virus 2, Human herpesvirus 6, Human parechovirus, and Varicella zoster virus.

The FilmArray ME Panel does not detect all causes of central nervous system infections or provide information about which antimicrobial drugs may be most effective for treating bacterial infections. Standard CSF bacterial and fungal cultures should continue to be performed in conjunction with the FilmArray ME Panel as false negative and false positive results are possible with the FilmArray ME Panel, and bacterial growth is needed for drug susceptibility testing when results are positive. False negative results could potentially occur when the concentration of organisms in the CSF specimen is below the limit of detection for the FilmArray ME Panel.

The clinical performance of the FilmArray ME Panel was evaluated by a prospective study of CSF samples taken from 1,560 patients with suspected meningitis/encephalitis where results for the FilmArray ME Panel were compared to results from other tests methods, including culture. Another study included 150 clinical CSF samples that were previously determined to contain microorganisms, while a third study including 425 CSF samples that were artificially prepared with specific concentrations of bacteria or viruses. Study results demonstrated high agreement between the FilmArray ME Panel, comparator methods, and expected results.<sup>91-93</sup>

### ***Mycobacteria* Species**

DNA probes are available to distinguish between *Mycobacterium* species. In a recent study,<sup>57</sup> the extracted DNA specimens from *Mycobacterium* species and non-mycobacterial species were tested using peptide nucleic acid (PNA) probe-based RT-PCR assay to evaluate potential cross-reactivity. A total of 531 respiratory specimens (482 sputum specimens, 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 RT-PCR assay. In cross-reactivity tests, no false-positive or false-negative results were evident. When the culture method was used as the criterion standard test for comparison, PNA probe-based RT-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 RT-PCR assay for detection of MTBC were 90.6% (58/64) and 99.6% (465/467), respectively. The new RT-PCR for the detection of nontuberculous mycobacteria had a sensitivity and specificity of 69.0% (29/42) and 100% (489/489), respectively.

### ***Mycobacterium tuberculosis***

DNA probes are available to diagnose *M. tuberculosis* infection. In a recent study,<sup>58</sup> an in-house IS6110 RT-PCR (IH IS6110), MTB Q-PCR Alert (Q-PCR) and GenoType® MTBDRplus (MTBDR) were compared for the direct detection of (MTBC in 87 specimens. This included 82 first smear-positive specimens and 3 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 with culture. Both IS6110-based RT-PCRs (in-house and Q-PCR) were similar in performance with 91.2% concordant results for MTBC detection. However, none of the RT-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. One study<sup>59</sup> evaluated the performance of the GenoType Mycobacteria Direct (GTMD) test for rapid molecular detection and identification of the MTBC and 4 clinically important nontuberculous mycobacteria (*M. avium*, *M. intracellulare*, *M. kansasii*, *M. malmoense*) in smear-negative samples. A total of 1570 samples (1103 bronchial aspiration, 127 sputum, 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 PPVs and NPVs 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 *M. intracellulare* and 1 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 pneumoniae***

Probes for *Mycoplasma pneumoniae* have been developed.<sup>60,61</sup> In 1 study using probes, a very high sensitivity and specificity for *M. pneumoniae* infection was reported (99.1% and 100%, respectively).<sup>62</sup> Chalker et al<sup>60</sup> tested 3987 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 to 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<sup>61</sup> found that 9.8% (5/51) of mycoplasma strains were macrolide resistant.

In many cases, management of *M. pneumoniae* infection does not require definitive diagnosis (eg, community-acquired pneumonia). However, there are some cases where *M. pneumoniae* is associated with severe illnesses that can have a variety of causes, in which definitive diagnosis may make a difference in treatment. *M. pneumoniae* PCR can be used to detect *M. pneumoniae* in patients with Stevens-Johnson syndrome<sup>63</sup> and refractory/severe pneumonia.<sup>64</sup> At least 1 study suggests that inappropriate antibiotic use may worsen fulminant mycoplasma infection, and patients benefit from early administration of appropriate antimycoplasmal drugs with steroids.<sup>65</sup>

### ***Neisseria gonorrhoeae***

Probes for *Neisseria gonorrhoeae* have been developed for commercial use. These probes are often a combination test with *C. trachomatis*. A 2012 study<sup>66</sup> demonstrated the PPV 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<sup>12</sup> demonstrated the VERSANT® CT/GC DNA 1.0 assay performed with 99.4% and 99.2% of specificity for *N. gonorrhoeae* and *C. trachomatis* detection, respectively, whereas sensitivity was 100% both for *C. trachomatis* and *N. gonorrhoeae*. 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,<sup>67-69</sup> 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<sup>70</sup> 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.

### ***Staphylococcus aureus* and Methicillin-Resistant *Staphylococcus aureus***

Probes are available for the detection of *Staphylococcus aureus*.<sup>71,72</sup> 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.<sup>30,31</sup> 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, there is clinical utility for testing in these situations.

### ***Streptococcus, Group A***

While group A *Streptococcus pyogenes* (group A *Streptococcus* [GAS]) can cause a variety of clinical symptoms including impetigo, pharyngitis, and more invasive infections (eg, necrotizing fasciitis, pneumonia), most of the focus of rapid detection methods is on the diagnosis of GAS pharyngitis. Patients with confirmed acute GAS pharyngitis are typically treated with antibiotics, which shorten the duration of symptoms modestly and help prevent acute rheumatic fever. The diagnosis of GAS pharyngitis can be made by culture, which has a sensitivity of 90% to 95%, but is limited by a slow turnaround time (1-2 days), which may hamper decisions about initiating antibiotic therapy. Point-of-care rapid antigen detection tests (RADTs) are widely used to

diagnose GAS pharyngitis. RADTs are characterized by high specificity (~95%) but poor sensitivity (70%-90%) compared with culture.<sup>73</sup>

Several nucleic acid probes that detect either unamplified or amplified nucleotides have been developed. Typically, these tests have a shorter turnaround time than culture, and some are intended to be used as point-of-care tests. Table 3 (though not meant to be all-inclusive) offers some examples of tests, with data provided on turnaround times, sensitivities and specificities, and other characteristics appearing on relevant package inserts.

**Table 3: Examples of Commercially Available GAS Probes**

Test	Manufacturer	Characteristics
Gen-Probe Group A <i>Streptococcus</i> Direct Test <sup>74,75</sup>	Gen-Probe Inc., San Diego, CA	<ul style="list-style-type: none"> <li>• Nonamplified</li> <li>• Sensitivity of 91.7%, specificity of 99.3%, and overall agreement of 97.4% compared with culture</li> <li>• Turnaround time of 60 min</li> </ul>
Lyra Direct Strep Assay <sup>76</sup>	Quidel Corp., San Diego, CA	<ul style="list-style-type: none"> <li>• Amplified</li> <li>• Sensitivity of 96.5%, specificity of 98.0%</li> <li>• All negative test results should be confirmed by bacterial culture</li> <li>• Turnaround time of &lt;70 min</li> </ul>
Illumigene Group A <i>Streptococcus</i> DNA Amplification Assay <sup>77</sup>	Meridian Bioscience, Cincinnati, OH	<ul style="list-style-type: none"> <li>• Amplified</li> <li>• Sensitivity of 98.0%, specificity of 97.7%</li> <li>• Turnaround time of &lt;60 min</li> </ul>

A number of studies have reported test characteristics for various nucleic acid amplification tests for GAS. The test characteristics of some of the amplified nucleic acid molecular diagnostics for GAS, with sensitivities and specificities compared with standard culture, are summarized in Table 4.

**Table 4: Summary of Amplified Nucleic Acid Detection Tests for Group A *Streptococcus***

Study	Assay	Population	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Slinger et al (2011) <sup>78</sup>	Laboratory-developed internally controlled GAS PCR assay	306 archived throat swab samples	96.0% (90.1% to 98.4%)	98.6% (95.8% to 99.5%)	96.9% (91.4% to 99.0%)	98.1% (95.2% to 99.2%)
Anderson et al (2013) <sup>79</sup>	Illumigene GAS assay	796 pharyngeal swabs (12.8% GAS culture positive)	100% (95% to 100%) (99% after discrepant analysis)	94.2% (92% to 95%) (99.6% after discrepant analysis)	63.8% (54% to 72%)	100% (99% to 100%)
Henson et al (2013) <sup>80</sup>	Illumigene GAS assay	437 pharyngeal swabs (21.1% GAS culture positive)	100%	95.9%	NR	NR

Study	Assay	Population	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Upton et al (2016) <sup>81</sup>	Illumigene GAS assay	757 pharyngeal swabs from school-based setting (12.2% GAS culture positive)	82% (87% after discrepant analysis)	93% (98% after discrepant analysis)	61% (88% after discrepant analysis)	97% (97% after discrepant analysis)
Cohen et al (2015) <sup>82</sup>	Alere i Strep A assay	481 pharyngeal swabs (30.4% GAS culture positive)	95.9% (92.7% to 99.1%) (98.7% after discrepant analysis)	94.6% (92.2% to 97.0%) (98.5% after discrepant analysis)	88.7% (83.8% to 93.6%) (96.9% after discrepant analysis)	98.1% (96.7% to 99.6%) (99.4% after discrepant analysis)
Faron et al (2015) <sup>83</sup>	AmpliVue GAS assay	1192 pharyngeal swabs (14.5% GAS culture positive)	98.3% (95 to 100%)	93.2 (91% to 95%)	71.2%	99.7%
Boyanton et al (2016) <sup>84</sup>	Lyra Direct Strep assay	161 pharyngeal swabs from patients with negative RADTs	100%	100%	100%	100%

CI: confidence interval; GAS: group A *Streptococcus*; NPV: negative predictive value; NR: not reported; PCR: polymerase chain reaction; PPV: positive predictive value; RADT: rapid antigen detection test.

In most studies of the amplified PCR assays, the sensitivity and specificity of the probes are very high. Upton et al reported lower sensitivity and lower PPV for the Illumigene assay than previous studies using this assay.<sup>81</sup> The authors hypothesize that the lower PPV may be related to the fact that the study was conducted in a population of children attending school, lowering the pretest probability of actual GAS infection. Alternatively, the PCR assay may be detecting isolates of other *Streptococcus* species that carry the GAS pyrogenic exotoxin B gene, which is detected by the assay.

The high NPV of nucleic acid–based assays for GAS suggests that as point-of-care tests, they offer improved accuracy over the current standard, RADTs. The high sensitivity, approaching that of standard culture, suggests that it may be reasonable to use them as an alternative to culture.

### ***Streptococcus*, Group B**

Several different rapid 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.<sup>85,86</sup> The use of intrapartum antibiotic therapy for GBS is recommended in patients who are known to be carriers for GBS. The postpartum management of newborn infants to prevent early-onset GBS infection is affected by whether the maternal GBS status is positive, negative, or unknown, and whether antibiotic prophylaxis is administered. The availability of rapid testing in peripartum women allows initiation or discontinuation of peripartum antibiotic prophylaxis to prevent vertical transmission of GBS.

### ***Trichomonas vaginalis***

Nye et al compared the performance characteristics of PCR testing for *Trichomonas* with wet prep microscopy and culture in 296 female and 298 male subjects.<sup>87</sup> 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 compared DNA probe testing and culture in 255 vaginal saline preparations.<sup>88</sup> 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,<sup>87</sup> as well as single-probe nonamplified testing in general. A 2011 prospective multicenter study of 1025 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%.<sup>89</sup> Specificity levels ranged from 98.9% to 99.6%. Other studies have also reported similar results.<sup>90</sup> PCR amplification tests have higher clinical sensitivity and are considered the standard of care for diagnosing *Trichomonas vaginalis* when culturing is not an option.

### **Ongoing and Unpublished Clinical Trials**

A search of ClinicalTrials.gov in November 2015 did not identify any ongoing or unpublished trials that would likely influence this review.

### **Summary of Evidence**

The evidence for the use of nucleic acid probes for *Chlamydomphila pneumoniae* or hepatitis G virus in individuals with suspected *C. pneumoniae* or with hepatitis, respectively, includes prospective and retrospective evaluations of the tests' sensitivity and specificity. Relevant outcomes are test accuracy and validity, other test performance measures, symptoms, and change in disease status. The body of evidence is limited for both types of organisms. For *C. pneumoniae*, one study was identified that reported relatively high sensitivity and specificity for a polymerase chain reaction–based test. However, the total number of patients in this study was small (N=56), and most other studies were conducted in the investigational setting. In addition to the limitations in the evidence base on test characteristics, the clinical implications of these tests are unclear. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for the use of a nucleic acid–based gastrointestinal pathogen panel in individuals who have signs and/or symptoms of gastroenteritis includes prospective and retrospective evaluations of the tests' sensitivity and specificity. Relevant outcomes include test accuracy and validity, other test performance measures, symptoms, and change in disease status. The evidence suggests that gastrointestinal pathogen panels are likely to identify both bacterial and viral pathogens with high sensitivity, compared with standard methods. Access to a rapid method for etiologic diagnosis of gastrointestinal infections may lead to more effective early treatment and infection-control measures. However, in most instances, when a specific pathogen is suspected, individual tests could be ordered. There may be a subset of patients with an unusual presentation who would warrant testing for a panel of pathogens at once, but that subset has not been well defined.

### **Clinical Input Received From Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 2 academic medical centers and 4 specialty societies while this policy was under review in 2015. The input was characterized by a number of nonresponses, making it difficult to assess for consensus across reviewers for some infectious agents. However, there was clear agreement (support from all reviewers who responded to that question) in support of nucleic acid probes for *Bartonella* species, *Candida* species, *Chlamydia trachomatis*, *Clostridium difficile*, cytomegalovirus, *Enterococcus faecalis*, vancomycin-resistant *Enterococcus*, enterovirus, *Gardnerella vaginalis*, hepatitis B and C viruses, herpes simplex virus, human herpesvirus 6, HIV-1 and -2, human papillomavirus, influenza virus, *Mycobacteria* species, *Mycobacterium tuberculosis*, *Mycobacterium avium-intracellulare*, *Neisseria gonorrhoeae*, respiratory viruses, *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus*, group B Streptococcus, and *Trichomonas vaginalis*.

### **Practice Guidelines and Position Statements**

No guidelines or statements were identified.

### **U.S. Preventive Services Task Force Recommendations**

Not applicable.

### **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
- 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

- 87483 Infectious agent detection by nucleic acid (DNA or RNA); central nervous system pathogen (eg, *Neisseria meningitidis*, *Streptococcus pneumoniae*, *Listeria*, *Haemophilus influenzae*, *E. coli*, *Streptococcus agalactiae*, enterovirus, human parechovirus, herpes simplex virus type 1 and 2, human herpesvirus 6, cytomegalovirus, varicella zoster virus, *Cryptococcus*), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 12-25 targets
- 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
- 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
- 87505 Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, *Clostridium difficile*, *E. coli*, *Salmonella*, *Shigella*, norovirus, *Giardia*), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 3-5 targets
- 87506 Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, *Clostridium difficile*, *E. coli*, *Salmonella*, *Shigella*, norovirus, *Giardia*), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 6-11 targets
- 87507 Infectious agent detection by nucleic acid (DNA or RNA); gastrointestinal pathogen (eg, *Clostridium difficile*, *E. coli*, *Salmonella*, *Shigella*, norovirus, *Giardia*), includes multiplex reverse transcription, when performed, and multiplex amplified probe technique, multiple types or subtypes, 12-25 targets
- 87510 Infectious agent detection by nucleic acid (DNA or RNA); *Gardnerella vaginalis*, direct probe technique
- 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
- 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
- 87623 Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), low-risk types (eg, 6, 11, 42, 43, 44)
- 87624 Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), high-risk types (eg, 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68)
- 87625 Infectious agent detection by nucleic acid (DNA or RNA); Human Papillomavirus (HPV), types 16 and 18 only, includes type 45, if performed
- 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

- CPT codes 87797, 87798, and 87799 describe the use of direct probe, amplified probe, and quantification, respectively, for infectious agents not otherwise specified. A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy.

### 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 <i>Staphylococcus aureus</i>
482.84	Legionnaires' disease
483.1	Chlamydia

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, 2015)

A04.71	Enterocolitis due to Clostridium difficile, recurrent
A04.72	Enterocolitis due to Clostridium difficile, not specified as recurrent
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
- A48.2 Nonpneumonic Legionnaires' disease [Pontiac fever]
- A49.02 Methicillin resistant *Staphylococcus aureus* infection, unspecified site
- A49.3 *Mycoplasma* infection, unspecified site
- A50.01 Early congenital syphilitic ophthalmopathy
- 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 ophthalmopathy, unspecified
- A50.31 Late congenital syphilitic interstitial keratitis
- A50.32 Late congenital syphilitic chorioretinitis
- A50.39 Other late congenital syphilitic ophthalmopathy
- 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 ophthalmopathy
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	Charcot's arthropathy (tabetic)
A52.17	General paresis
A52.19	Other symptomatic neurosyphilis
A52.2	Asymptomatic neurosyphilis
A52.3	Neurosyphilis, unspecified
A52.71	Late syphilitic ophthalmopathy
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 <i>Rickettsia typhi</i>
A77.0	Spotted fever due to <i>Rickettsia rickettsii</i>
A77.40	Ehrlichiosis, unspecified
A77.41	Ehrlichiosis chafeensis [ <i>E. chafeensis</i> ]
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 lymphotropic virus, type I [HTLV-I] as the cause of diseases classified elsewhere
- B97.34 Human T-cell lymphotropic 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]
- H53.10 Unspecified subjective visual disturbances
- H53.11 Day blindness
- H53.19 Other subjective visual disturbances
- H53.2 Diplopia
- J06.9 Acute upper respiratory infection, unspecified
- 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
R11.0	Nausea
R11.10	Vomiting, unspecified
R11.11	Vomiting without nausea
R11.2	Nausea and vomiting, unspecified
R19.7	Diarrhea, unspecified
R21	Rash and other nonspecific skin eruption
R40.0	Somnolence
R40.1	Stupor
R41.0	Disorientation, unspecified
R41.82	Altered mental status, unspecified
R41.89	Other symptoms and signs involving cognitive functions and awareness
R50.9	Fever, unspecified
R51	Headache
R56.00	Simple febrile convulsions
R56.01	Complex febrile convulsions
R56.9	Unspecified convulsions
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
Z36.85	Encounter for antenatal screening for Streptococcus B
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

<b>REVISIONS</b>	
01-15-2013	<p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ Added to the Microorganism chart in item I: "Respiratory Virus Panel - See item IV on page 9 of this policy."</li> <li>▪ Added to the medically necessary indication list in item II F. <i>Bordetella pertussis</i></li> </ul> <p>Code Updates in Policy section:</p> <ul style="list-style-type: none"> <li>▪ Added CPT codes 87631, 87632, 87633 to item IV (effective 01-01-2013)</li> <li>▪ 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: <i>Clostridium difficile</i>; Enterovirus; <i>Staphylococcus aureus</i>; <i>Staphylococcus aureus</i>, methicillin resistant; <i>Streptococcus group B</i>; and <i>Trichomonas vaginalis</i></li> <li>▪ 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."</li> </ul>
11-12-2013	<p>Description section updated</p> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ On Item I <i>Trichomonas vaginalis</i>, updated Amplified Probe code from 87798 to 87661 to be used effective 01-01-2014.</li> <li>▪ Changed <i>Trichomonas vaginalis</i> from investigational to medically necessary on the effective date of the policy update.</li> </ul> <p>In Policy Guidelines:</p> <ul style="list-style-type: none"> <li>▪ 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."</li> <li>▪ 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."</li> <li>▪ Removed reference to the Association of Molecular Pathology (AMP) website as this is addressed in the Description section.</li> </ul> <p>Rationale section updated</p> <p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Added CPT codes and nomenclatures for CPT codes reflected in the Policy section.</li> <li>▪ ICD-10 codes added.</li> </ul> <p>References updated.</p>
01-01-2015	<p>Policy posted 01-16-2015</p> <p>In Coding section:</p> <ul style="list-style-type: none"> <li>▪ Added CPT Codes: 87505, 87506, 87507, 87623, 87624, 87625 (Effective January 1, 2015)</li> <li>▪ Deleted CPT Codes: 87620, 87621, 87622 (Effective January 1, 2015)</li> </ul>
03-20-2017	<p>Policy published 03-20-2017. Policy effective 03-20-2017.</p> <p>In Title section: Revised title to "Identification of Microorganisms Using Nucleic Acid Testing" from "Identification of Microorganisms Using Nucleic Acid Probes" added "See Also: Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease"</p> <p>Description section updated</p> <p>In Policy section:</p> <ul style="list-style-type: none"> <li>▪ <b>Revised to the current policy from the following prior policy:</b> "Note: A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy."</li> </ul>



<b>REVISIONS</b>			
03-20-2017 (continued)	Trichomonas vaginalis	87660 (med nec)	87661 (med nec)      87799 (inv)
	<p>*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.</p> <p>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.</p> <p>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):</p> <ul style="list-style-type: none"> <li>A. Adenovirus - to diagnose adenovirus myocarditis, and infection in immunocompromised hosts, including transplant recipients</li> <li>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. (<a href="http://www.oie.int/eng/en_index.htm">http://www.oie.int/eng/en_index.htm</a>)</li> <li>C. Babesiosis (<i>Babesia</i>) - when the morphologic characteristics observed on microscopic examination of blood smears do not allow differentiation between Babesia and Plasmodium</li> <li>D. Bacillus anthracis</li> <li>E. BK polyomavirus - in transplant recipients and persons with immunosuppressive diseases (e.g., AIDS)</li> <li>F. Bordetella pertussis</li> <li>G. <i>Brucella spp.</i> - signs and symptoms of Brucellosis</li> <li>H. <i>Burkholderia</i> infections</li> <li>I. Chancroid (<i>Haemophilus ducreyi</i>) - for genital ulcer disease</li> <li>J. Colorado tick fever virus</li> <li>K. <i>Coxiella burnetii</i> - for acute Q fever</li> <li>L. Ehrlichiosis (<i>Ehrlichia</i>)</li> <li>M. Epidemic typhus (<i>Rickettsia prowazekii</i>)</li> <li>N. <i>Epstein Barr Virus (EBV)</i> - for detection of EBV in post-transplant lymphoproliferative disorder or for tissue samples with lymphoma and other immunocompromised states</li> <li>O. <i>Francisella tularensis</i>, for diagnosis of tularemia</li> <li>P. Hemorrhagic fevers of the family <i>Bunyaviridae</i> (Rift Valley fever, Crimean-Congo hemorrhagic fever, hemorrhagic fever with renal syndromes) - clinical presentation suggestive of these conditions</li> <li>Q. Human granulocytic anaplasmosis (formerly <i>Ehrlichia phagocytophilum</i>)</li> <li>R. Human metapneumonovirus</li> <li>S. JC polyomavirus - in transplant recipients, immunosuppressive diseases and for progressive multifocal leukoencephalopathy when receiving natalizumab (Tysabri)</li> <li>T. Leishmaniasis</li> <li>U. Lymphogranuloma venereum (<i>Chlamydia trachomatis</i>)</li> <li>V. Malaria</li> <li>W. Measles virus</li> <li>X. Microsporidia</li> <li>Y. Mumps</li> <li>Z. <i>Neisseria meningitides</i></li> <li>AA. Parvovirus</li> <li>BB. Psittacosis (<i>Chlamydophila (Chlamydia) psittaci</i>)</li> <li>CC. Rocky Mountain Spotted Fever (<i>Rickettsia rickettsii</i>)</li> <li>DD. Severe acute respiratory syndrome (SARS) (coronavirus)</li> <li>EE. Syphilis (<i>Treponema pallidum</i>)</li> <li>FF. <i>Toxoplasma gondii</i></li> <li>GG. Varicella-Zoster</li> <li>HH. West Nile Virus - in tissue specimens</li> </ul>		

<b>REVISIONS</b>	
03-20-2017 (continued)	<ul style="list-style-type: none"> <li>II. Whipple's disease (<i>T. whippelli</i>)</li> <li>JJ. Yersinia pestis</li> <li>III. The following other quantitative PCR tests (87799) are considered medically necessary:               <ul style="list-style-type: none"> <li>A. Adenovirus viral load, to monitor response to antiviral therapy in infected immunocompromised hosts, including transplant recipients</li> <li>B. BK polyomavirus viral load, for diagnosis and monitoring response to therapy in infected kidney transplant recipients</li> <li>C. Cytomegalovirus (CMV) viral load, to monitor response to therapy</li> <li>D. Epstein Barr viral load, to monitor for EBV viral replication in solid organ transplant recipients</li> </ul> </li> <li>IV. The Respiratory Virus Panel (87631, 87632, 87633) will be reviewed for medical necessity on a case-by-case basis.</li> <li>V. PCR testing for the following indications is considered experimental / investigational because of insufficient evidence in the peer-reviewed literature:               <ul style="list-style-type: none"> <li>A. Actinomycosis</li> <li>B. Astrovirus</li> <li>C. Bacterial vaginosis (<i>Atopobium vaginae</i>, <i>Mobiluncus mulieris</i>, <i>M. curtisii</i>, <i>Megasphaera</i>, <i>Bacterial vaginosis Associated Bacteria panel [BVAB]</i>)</li> <li>D. Bacteroides spp. (<i>B. fragilis</i>, <i>B. ureolyticus</i>)</li> <li>E. Caliciviruses (noroviruses and sapoviruses)</li> <li>F. Campylobacteriosis (<i>Campylobacter</i> infection)</li> <li>G. Coccidioidomycosis (<i>Coccidioides</i> species)</li> <li>H. Cryptococcus (<i>Cryptococcus neoformans</i>)</li> <li>I. Cyclosporiasis (<i>Cyclospora</i> infection)</li> <li>J. Dengue fever</li> <li>K. Donovanosis, or granuloma inguinale (<i>Klebsiella granulomatis</i>)</li> <li>L. Eastern equine encephalitis</li> <li>M. <i>Entamoeba histolytica</i></li> <li>N. Genital mycoplasma infections from <i>Ureaplasma urealyticum</i> and <i>Mycoplasma hominis</i> (unless culture is unavailable)</li> <li>O. Haemophilus influenzae</li> <li>P. Hantavirus</li> <li>Q. Hepatitis A virus</li> <li>R. Hepatitis D virus</li> <li>S. Human bocavirus</li> <li>T. Human herpesvirus type 7 (HHV-7)</li> <li>U. Human herpesvirus type 8 (HHV-8)</li> <li>V. Human metapneumovirus</li> <li>W. LaCrosse encephalitis</li> <li>X. Leptospirosis (<i>Leptospira</i> organisms)</li> <li>Y. Molluscum contagiosum</li> <li>Z. <i>Moraxella catarrhalis</i></li> <li>AA. <i>Mycoplasma fermentans</i></li> <li>BB. <i>Mycoplasma genitalium</i></li> <li>CC. <i>Mycoplasma penetrans</i></li> <li>DD. Nanobacteria</li> <li>EE. Non-albicans Candida</li> <li>FF. Onychomycosis</li> <li>GG. Parainfluenza virus</li> <li>HH. Peptic ulcer disease (<i>Helicobacter pylori</i>) (other than in persons with MALT lymphomas and marginal zone lymphomas)</li> <li>II. Pneumococcal infections (<i>S. pneumoniae</i>)</li> <li>JJ. Pneumocystis pneumonia (<i>Pneumocystis jiroveci</i> (formerly <i>P. carinii</i>))</li> <li>KK. <i>Prevotella</i> spp.</li> <li>LL. <i>Proteus mirabilis</i></li> <li>MM. Pseudomonas (<i>P. aeruginosa</i>)</li> <li>NN. Respiratory syncytial virus (RSV)</li> <li>OO. Rhinovirus</li> <li>PP. Rotavirus</li> </ul> </li> </ul>

<b>REVISIONS</b>	
03-20-2017 (continued)	<p>QQ. <i>Saccharomyces cerevisiae</i>                      RR. Serratia spp. (including <i>S. marcescens</i>)                      SS. Shiga toxin (from <i>E. coli</i> and Shigella)                      TT. Sporotrichosis (<i>Sporothrix schenckii</i>)                      UU. St. Louis encephalitis                      VV. <i>Staphylococcus saprophyticus</i>                      WW. Trichosporonosis (<i>Trichosporon</i> spp.)                      XX. Western equine encephalitis</p> <p><u>Policy Guidelines</u></p> <ol style="list-style-type: none"> <li>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.</li> <li>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.</li> <li>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."</li> </ol>
	Rationale section updated
	In Revisions section <ul style="list-style-type: none"> <li>▪ Removed revision details for the following dates: 03-01-2012, 06-05-2012, 11-19-2012</li> </ul>
	In Coding section: <ul style="list-style-type: none"> <li>▪ Removed CPT codes: 87475, 87476, 87477</li> <li>▪ Removed ICD-9 codes: 487.0-488.19</li> <li>▪ Removed ICD-10 codes: J09.x1, J09.x2, J09.x3, J09.x9, J10.00, J10.01, J10.08, J10.1, J10.2, J10.81, J10.82, J10.83, J10.89, J11.00, J11.08, J11.1, J11.2, J11.81, J11.82, J11.83, J11.89</li> <li>▪ Added CPT code: 87483</li> <li>▪ Added ICD-10 code: A48.2, H53.10, H53.11, H53.19, H53.2, R11.0, R11.10, R11.11, R11.2, R19.7, R21, R40.0, R40.1, R41.0, R41.82, R41.89, R50.9, R51, R56.00, R56.01, R56.9</li> </ul>
	References updated
04-01-2017	<p>Policy published 04-01-2017. Policy effective 03-20-2017</p> <p>In the Revisions section:                      The following clarifications were made to the Revisions chart:                     <ul style="list-style-type: none"> <li>▪ The "REVISIONS" header was repeated at the top of each page revisions were reflected.</li> <li>▪ The effective date was repeated on subsequent pages as applicable</li> </ul>                     The following clarifications were made to the 03-20-2017 Revision notations:                     <ul style="list-style-type: none"> <li>▪ The Policy published and Policy effective dates were corrected from " Policy published 03-xx-2017. Policy effective 03-xx-2017" to "Policy published 03-20-2017. Policy effective 03-20-2017."</li> <li>▪ The phrase "<b><u>Revised to the current policy from the following prior policy:</u></b>" was bolded and underlined.</li> </ul> </p>
10-01-2017	In Coding section: <ul style="list-style-type: none"> <li>▪ Added ICD Code: Z36.85</li> <li>▪ Removed ICD Code: Z36</li> </ul>

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