BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Identification of Microorganisms Using Nucleic Acid Probes

Policy #: 548
Latest Review Date: July 2024
Category: Laboratory

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage, the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000, which meet the requirements of the Clinical Trials NCD, are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual, Chapter 32, Sections 69.0-69.11).*

POLICY:

Effective for dates of service on or after March 1, 2024

For nucleic acid probe panel testing, see LCD L38988/Article A58710.

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique** (without quantification of viral load) as a **covered benefit** for the following microorganisms (see Table 1 at the end of this section for details on coding):

- Bartonella henselae or quintana
- BK polyomavirus (BKPyV, Human polyomavirus 1)
- Candida species
- Chlamydia pneumoniae
- Chlamydia trachomatis
- Clostridium difficile
- Enterococcus, vancomycin-resistant (e.g., enterococcus vanA, vanB)
- Enterovirus
- Gardnerella vaginalis
- Herpes simplex virus
- Human papillomavirus
- Influenza virus
- Legionella pneumophila
- Mycobacterium species
- Mycobacterium tuberculosis
- Mycobacterium avium intracellulare
- Mycoplasma genitalium
- Mycoplasma pneumoniae
- Neisseria gonorrhoeae
- Orthopoxvirus (Monkeypox)
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- Staphylococcus aureus
- Staphylococcus aureus, methicillin-resistant
- Streptococcus, group A
- Streptococcus, group B
- Tick-borne bacteria
- Trichomonas vaginalis
- Zika virus

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique** (with or without quantification of viral load) as a **covered benefit** for the following microorganisms:

- Cytomegalovirus
- Hepatitis B virus
- Hepatitis C virus

- HIV-1
- HIV-2
- Human herpes virus-6

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique with or without quantification of viral load for microorganisms that are not included in the above list of microorganisms** as a **non-covered benefit and investigational,** including, but not limited to:

- Hepatitis G virus

Blue Advantage will treat the **use of nucleic acid testing expanded panels using a direct or amplified probe technique (with or without quantification of viral load)** as a **non-covered benefit** and **investigational** for the following microorganisms, including but not limited to:

- Infectious Disease (fungus and/or bacteria) Panel

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique (with or without quantification of viral load)** as a **covered benefit** to test for BK polyomavirus in renal transplant recipients receiving immunosuppressive therapy.

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique (with or without quantification of viral load)** as a **covered benefit** to test for BK polyomavirus in persons with renal failure in the setting of an immunosuppressed state (including but not limited to persons with a history of solid organ transplant on immunosuppressive therapy, history of hematopoietic cell transplantation, hematologic malignancy, HIV, or autoimmune disease on immunosuppressive therapy).

CURRENT CODING:

CPT Codes:

The table below provides a list of CPT codes for various nucleic acid probes.

Table 1. CPT Codes for Nucleic Acid Probes

Pathogen	Direct Probe	Amplified Probe	Quantification
Anaplasma phagocytophilum		87468 (Med Nec)	
Babesia microti		87469 (Med Nec)	
Bartonella henselae or quintana		87471 (Med Nec)	87472 (Inv) 0301U, 0302U (Inv)

BK polyomavirus	87797 (Med Nec)	87798 (Med Nec)	87799 (Med Nec)
Bloodstream pathogen identification		87154 (Med Nec)	
Borrelia borgdorferi a	87475 (Med Nec)	87476 (Med Nec)	
Borrelia miyamotoi		87478 (Med Nec)	
Candida species b	87480 (Med Nec)	87481 (Med Nec) 0068U (Med Nec)	87482 (Inv)
Central Nervous System Pathogen Panel		87483 (Med Nec)	0323U (Inv)
Chlamydia pneumoniae	87485 (Med Nec)	87486 (Med Nec)	87487 (Inv)
Chlamydia trachomatis	87490 (Med Nec)	87491 (Med Nec) 0353U (Med Nec- deleted 06/30/24) 0402U (Med Nec) (code effective 10/1/23) 0455U (Med Nec) (Code effective 07/01/24)	87492 (Inv)
Clostridium difficile	87493 (Med Nec)		
Cytomegalovirus	87495 (Med Nec)	87496 (Med Nec)	87497 (Med Nec)
Ehrlichia chaffeensis		87484 (Med Nec)	
Enterococcus, Vancomycin resistant (e.g., enterococcus van A, van B)		87500 (Med Nec)	
Enterovirus		87498 (Med Nec)	

Gardnerella vaginalis	87510 (Med Nec)	87511 (Med Nec)	87512 (Inv)
Gastrointestinal Pathogen Panel		87505-87507 (Med Nec) 0369U (Med Nec) (code effective 4/1/23) 0097U (Med Nec) (code deleted eff 4/1/22)	
Genitourinary Pathogen Panel		0321U (Inv) 0372U(Inv), 0374U (Inv) (codes effective 4/1/23) 0416U (Inv) (code deleted effective 03/31/24)	0371U (Inv) (code effective 4/1/23)
Hepatitis B		87516 (Med Nec)	87517 (Med Nec)
Hepatitis C	87520 (Med Nec)	87521 (Med Nec)	87522 (Med Nec)
Hepatitis G	87525 (Inv)	87526 (Inv)	87527 (Inv)
Herpes simplex virus	87528 (Med Nec)	87529 (Med Nec)	87530 (Inv)
Human Herpes virus-6	87531 (Med Nec)	87532 (Med Nec)	87533 (Med Nec)
Human Immunodeficiency Virus 1 (HIV-1)	87534 (Med Nec)	87535 (Med Nec)	87536 (Med Nec)
Human Immunodeficiency Virus 2 (HIV-2)	87537 (Med Nec)	87538 (Med Nec)	87539 (Med Nec)
Human Papillomavirus (HPV)		87623 (Med Nec) 87624-87625 (Med Nec) 0429U (Med Nec)	0354U (Med Nec) (code deleted effective 03/31/24) 0096U (Med Nec) 0463U (Med Nec) (code effective 07/01/24)

Infectious Agent detection and identification		0370U (Inv) (code effective 4/1/23)	0112U (Inv)
Infectious disease panel (fungus and/or bacteria)		0140U-0142U (Inv)	
Influenza virus		87501-87503 (Med Nec)	
Legionella pneumophila	87540 (Med Nec)	87541 (Med Nec)	87542 (Inv)
Mycobacterium species	87550 (Med Nec)	87551 (Med Nec)	87552 (Inv)
Mycobacterium tuberculosis	87555 (Med Nec)	87556 (Med Nec)	87557 (Inv)
Mycobacterium avium intracellulare	87560 (Med Nec)	87561 (Med Nec)	87562 (Inv)
Mycoplasma genitalium		87563 (Med Nec) 0402U (Med Nec) (code effective 10/1/23)	
Mycoplasma pneumoniae	87580 (Med Nec)	87581 (Med Nec)	87582 (Inv)
Neisseria gonorrhoeae	87590 (Med Nec)	87591 (Med Nec) 0353U (Med Nec- deleted 06/30/24) 0402U (Med Nec) (code effective 10/1/23) 0455U (Med Nec) (Code effective 07/01/24)	87592 (Inv)
Orthopoxvirus (Monkeypox)		87593 (Med Nec)	
Respiratory virus panel		87631-87634 (Med Nec) 0098U – 0100U (Med Nec) (code deleted eff 3/31/21) 0115U (Med Nec) 0202U (Med Nec)	0151U (Med Nec) (code deleted eff 4/1/22)

		0373U (Med Nec) (code effective 4/1/23)	
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) c		87635 (Med Nec)	
Staphylococcus aureus		87640 (Med Nec)	
Staphylococcus aureus, methicillin resistant		87641 (Med Nec)	
Streptococcus group A d	87650 (Med Nec)	87651 (Med Nec)	87652 (Inv)
Streptococcus group B e		87653 (Med Nec)	
Trichomonas vaginalis	87660 (Med Nec)	87661 (Med Nec) 0353U (Med Nec- deleted 06/30/24) 0402U (Med Nec) (code effective 10/1/23) 0455U (Med Nec) (Code effective 07/01/24)	
Unlisted (infectious agent detection by nucleic acid, DNA or RNA, not otherwise specified) f	87797 (Inv) 87800 (Inv, eff 10/24/22)	87798 (Inv) 87801 Inv, eff 10/24/22)	87799 (Inv)
Vaginal pathogen panel		0330U (Inv)	
Zika Virus		87662 (Med Nec)	

a Refer to medical policy MP 359: Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease.

b For Candida species, culture for yeast remains the criterion standard for identifying and differentiating these organisms. Although sensitivity and specificity are higher for nucleic acid amplification tests (NAATs) than for standard testing methods, the CDC and other association guidelines do not recommend NAATs as first-line testing for Candida species. The CDC (2015) classifies uncomplicated vulvovaginal candidiasis as being sporadic or infrequent; or mild to

moderate; or, in non-immunocompromised women, as likely to be caused by C. albicans. A presumptive diagnosis can be made in the clinical care setting. However, for complicated infections, the CDC states that NAATs may be necessary to test for multiple Candida subspecies. Complicated vulvovaginal candidiasis is classified as being recurrent or severe; or, in women with uncontrolled diabetes, debilitation, or immunosuppression, as less likely to be caused by a C. albicans species.

c Use of NAAT for SARS-CoV-2 is for confirming Coronavirus Disease 2019 (COVID-19) diagnoses. This medical policy does not address antibody testing (serological IgG assays).

d 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.

e 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.
f Refer to BK polyomavirus in Table 1. CPT Codes for Nucleic Acid Probes

Table Key:
Med Nec—meets medical criteria for coverage
Inv—does not meet medical criteria for coverage
Eff—effective

Effective for dates of service April 17, 2022, to February 28, 2024

For nucleic acid probe panel testing, see LCD L38988/Article A58710.

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique** (without quantification of viral load) as a **covered benefit** for the following microorganisms (see Table 1 at the end of this section for details on coding):

- Bartonella henselae or quintana
- Candida species
- Chlamydia pneumoniae
- Chlamydia trachomatis
- Clostridium difficile
- Enterococcus, vancomycin-resistant (e.g., enterococcus vanA, vanB)
- Enterovirus
- Gardnerella vaginalis
- Herpes simplex virus
- Human papillomavirus
- Influenza virus
- Legionella pneumophila

- Mycobacterium species
- Mycobacterium tuberculosis
- Mycobacterium avium intracellulare
- Mycoplasma genitalium
- Mycoplasma pneumoniae
- Neisseria gonorrhoeae
- Orthopoxvirus (Monkeypox)
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- Staphylococcus aureus
- Staphylococcus aureus, methicillin-resistant
- Streptococcus, group A
- Streptococcus, group B
- Tick-borne bacteria
- Trichomonas vaginalis
- Zika virus

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique** (with or without quantification of viral load) as a **covered benefit** for the following microorganisms:

- Cytomegalovirus
- Hepatitis B virus
- Hepatitis C virus
- HIV-1
- HIV-2
- Human herpes virus-6

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique with or without quantification of viral load for microorganisms that are not included in the above list of microorganisms** as a **non-covered benefit and investigational,** including, but not limited to:

- Hepatitis G virus

Blue Advantage will treat the **use of nucleic acid testing expanded panels using a direct or amplified probe technique (with or without quantification of viral load)** as a **non-covered benefit** and **investigational** for the following microorganisms, including but not limited to:

- Infectious Disease (fungus and/or bacteria) Panel

CURRENT CODING:

CPT Codes CODES:

The table below provides a list of CPT Codes for various nucleic acid probes.

Table. CPT Codes for Nucleic Acid Probes

Pathogen	Direct Probe	Amplified Probe	Quantification
Anaplasma phagocytophilum		87468 (Med Nec)	
Babesia microti		87469 (Med Nec)	
Bartonella henselae or quintan[a]		87471 (Med Nec)	87472 (Inv) 0301U, 0302U (Inv)
Bloodstream pathogen identification		87154 (Med Nec)	
Borrelia borgdorferi[a]	87475 (Med Nec)	87476 (Med Nec)	
Borrelia miyamotoi		87478 (Med Nec)	
Candida species	87480 (Med Nec)	87481 (Med Nec) 0068U (Med Nec)	87482 (Inv)
Central Nervous System Pathogen Panel		87483 (Med Nec)	
Chlamydia pneumoniae	87485 (Med Nec)	87486 (Med Nec)	87487 (Inv)
Chlamydia trachomatis	87490 (Med Nec)	87491 (Med Nec)	87492 (Inv)
Clostridium difficile	87493 (Med Nec)		
Cytomegalovirus	87495 (Med Nec)	87496 (Med Nec)	87497 (Med Nec)
Enterococcus, Vancomycin resistant (e.g., enterococcus van A, van B)		87500 (Med Nec)	
Enterovirus		87498 (Med Nec)	

Gardnerella vaginalis	87510 (Med Nec)	87511 (Med Nec)	87512 (Inv)
Hepatitis B		87516 (Med Nec)	87517 (Med Nec)
Hepatitis C	87520 (Med Nec)	87521 (Med Nec)	87522 (Med Nec)
Hepatitis G	87525 (Inv)	87526 (Inv)	87527 (Inv)
Herpes simplex virus	87528 (Med Nec)	87529 (Med Nec)	87530 (Inv)
Human Herpes virus-6	87531 (Med Nec)	87532 (Med Nec)	87533 (Med Nec)
Human Immunodeficiency Virus 1 (HIV-1)	87534 (Med Nec)	87535 (Med Nec)	87536 (Med Nec)
Human Immunodeficiency Virus 2 (HIV-2)	87537 (Med Nec)	87538 (Med Nec)	87539 (Med Nec)
Human Papillomavirus (HPV)		87623 (Med Nec) 87624-87625 (Med Nec) 0429U (Med Nec)	0096U (Med Ned) 0354U (Med Nec)
Infectious Agent detection and identification		0370U (Inv)	0112U (Inv)
Infectious disease		0140U-0142U (Inv)	
Influenza virus	87501 (Med Nec)	87502 (Med Nec)	87503 (Med Nec)
Legionella pneumophila	87540 (Med Nec)	87541 (Med Nec)	87542 (Inv)

Mycobacterium species	87550 (Med Nec)	87551(Med Nec)	87552 (Inv)
Mycobacterium tuberculosis	87555 (Med Nec)	87556 (Med Nec)	87557 (Inv)
Mycobacterium avium intracellulare	87560 (Med Nec)	87561 (Med Nec)	87562 (Inv)
Mycoplasma genitalium		8763 (Med Nec) 0402U (Med Nec)	
Mycoplasma pneumoniae	87580 (Med Nec)	87581 (Med Nec)	87582 (Inv)
Neisseria gonorrhoeae	87590 (Med Nec)	87591 (Med Nec)	87592 (Inv)
Orthopoxvirus (Monkeypox)		87593 (Med Nec)	
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[c]		87635 (Med Nec)	
Staphylococcus aureus		87640 (Med Nec)	
Staphylococcus aureus, methicillin-resistant		87641 (Med Nec)	
Streptococcus group A[d]	87650 (Med Nec)	87651 (Med Nec)	87652 (Inv)
Streptococcus group B[e]		87653 (Med Nec)	
Trichomonas vaginalis	87660 (Med Nec)	87661 (Med Nec)	
Unlisted (infectious agent detection by nucleic acid (DNA or RNA, not otherwise specified)[f]	87797 87800	87798 87801	87799
Zika Virus		87662 (Med Nec)	

[a] Refer to medical policy #359, Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease.

[b] For uncomplicated infections, testing for only one 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 non-immunocompromised 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.

[c] Use of NAAT for SARS-CoV-2 is for confirming Coronavirus Disease 2019 (COVID-19) diagnoses. This medical policy does not address antibody testing (serological IgG assays).

[d] Antibiotic sensitivity of streptococcus A cultures is frequently not performed for throat cultures. However, if antibiotic sensitivity is considered, then the most efficient method of diagnosis would be a combined culture and antibiotic sensitivity.

[e] 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.

Testing submitted with these codes will be handled on a case-by-case basis. A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy.

Table Key:
Med Nec—meets medical criteria for coverage

Inv—does not meet medical criteria for coverage

Eff—effective

<u>Effective for dates of service April 1, 2020, to April 16, 2022</u>
For respiratory viral panels, see LCD L37713/ Article A56851.

For gastrointestinal viral panels, see LCD L37709/Article 56593.

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique** (without quantification of viral load) as a **covered benefit** for the following microorganisms (see Table 1 at the end of this section for details on coding):

- Bartonella henselae or quintana
- Candida species
- Chlamydia pneumoniae
- Chlamydia trachomatis
- Clostridium difficile
- Enterococcus, vancomycin-resistant (e.g., enterococcus vanA, vanB)

- Enterovirus
- Gardnerella vaginalis
- Herpes simplex virus
- Human papillomavirus
- Influenza virus
- Legionella pneumophila
- Mycobacterium species
- Mycobacterium tuberculosis
- Mycobacterium avium intracellulare
- Mycoplasma pneumoniae
- Neisseria gonorrhoeae
- Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)
- Staphylococcus aureus
- Staphylococcus aureus, methicillin-resistant
- Streptococcus, group A
- Streptococcus, group B
- Trichomonas vaginalis
- Zika virus

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique** (with or without quantification of viral load) as a **covered benefit** for the following microorganisms:

- Cytomegalovirus
- Hepatitis B virus
- Hepatitis C virus
- HIV-1
- HIV-2
- Human herpes virus-6

Blue Advantage will treat the **use of nucleic acid testing using a direct or amplified probe technique with or without quantification of viral load for microorganisms that are not included in the above list of microorganisms** as a **non-covered benefit and investigational,** including, but not limited to:

- Hepatitis G virus

Blue Advantage will treat the **use of nucleic acid testing expanded panels using a direct or amplified probe technique (with or without quantification of viral load)** as a **non-covered benefit** and **investigational** for the following microorganisms, including but not limited to:

- Infectious Disease (fungus and/or bacteria) Panel

CURRENT CODING:

CPT Codes

The table below provides a list of CPT Codes for various nucleic acid probes.

Table. CPT Codes for Nucleic Acid Probes

Pathogen	Direct Probe	Amplified Probe	Quantification
Bartonella henselae or quintan[a]		87471 (Med Nec)	87472 (Inv) 0301U, 0302U (Inv)
Bloodstream pathogen identification		87154 (Med Nec)	
Borrelia borgdorferi[a]	87475 (Med Nec)	87476 (Med Nec)	
Candida species[b]	87480 (Med Nec)	87481 (Med Nec) 0068U (Med Nec)	87482 (Inv)
Central Nervous System Pathogen Panel		87483 (Med Nec)	
Chlamydia pneumoniae	87485 (Med Nec)	87486 (Med Nec)	87487 (Inv)
Chlamydia trachomatis	87490 (Med Nec)	87491 (Med Nec)	87492 (Inv)
Clostridium difficile	87493 (Med Nec)		
Cytomegalovirus	87495 (Med Nec)	87496 (Med Nec)	87497 (Med Nec)
Enterococcus, Vancomycin resistant (e.g., enterococcus van A, van B)		87500 (Med Nec)	
Enterovirus		87498 (Med Nec)	
Gardnerella vaginalis	87510 (Med Nec)	87511 (Med Nec)	87512 (Inv)

Hepatitis B		87516 (Med Nec)	87517 (Med Nec)
Hepatitis C	87520 (Med Nec)	87521 (Med Nec)	87522 (Med Nec)
Hepatitis G	87525 (Inv)	87526 (Inv)	87527 (Inv)
Herpes simplex virus	87528 (Med Nec)	87529 (Med Nec)	87530 (Inv)
Human Herpes virus-6	87531 (Med Nec)	87532 (Med Nec)	87533 (Med Nec)
Human Immunodeficiency Virus 1 (HIV-1)	87534 (Med Nec)	87535 (Med Nec)	87536 (Med Nec)
Human Immunodeficiency Virus 2 (HIV-2)	87537 (Med Nec)	87538 (Med Nec)	87539 (Med Nec)
Human Papillomavirus (HPV)		87623(Med Nec) 87624-87625 (Med Nec)	0096U (Med Nec) 0354U (Med Nec)
Infectious Agent detection and identification			0112U (Inv)
Infectious disease		0140U-0142U (Inv)	
Influenza virus	87501 (Med Nec)	87502 (Med Nec)	87503 (Med Nec)
Legionella pneumophila	87540 (Med Nec)	87541 (Med Nec)	87542 (Inv)
Mycobacterium species	87550 (Med Nec)	87551(Med Nec)	87552 (Inv)
Mycobacterium tuberculosis	87555 (Med Nec)	87556 (Med Nec)	87557 (Inv)

Mycobacterium avium intracellulare	87560 (Med Nec)	87561 (Med Nec)	87562 (Inv)
Mycoplasma pneumoniae	87580 (Med Nec)	87581 (Med Nec)	87582 (Inv)
Neisseria gonorrhoeae	87590 (Med Nec)	87591 (Med Nec)	87592 (Inv)
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[c]		87635 (Med Nec)	
Staphylococcus aureus		87640 (Med Nec)	
Staphylococcus aureus, methicillin-resistant		87641 (Med Nec)	
Streptococcus group A[d]	87650 (Med Nec)	87651 (Med Nec)	87652 (Inv)
Streptococcus group B[e]		87653 (Med Nec)	
Trichomonas vaginalis	87660 (Med Nec)	87661 (Med Nec)	
Unlisted (infectious agent detection by nucleic acid (DNA or RNA, not otherwise specified)[f]	87797 87800	87798 87801	87799
Zika Virus		87662 (Med Nec)	

[a] Refer to medical policy #359, Intravenous Antibiotic Therapy and Associated Diagnostic Testing for Lyme Disease.

[b] For uncomplicated infections, testing for only one 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 non-immunocompromised 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.

[c] Use of NAAT for SARS-CoV-2 is for confirming Coronavirus Disease 2019 (COVID-19) diagnoses. This medical policy does not address antibody testing (serological IgG assays).

[d] Antibiotic sensitivity of streptococcus A cultures is frequently not performed for throat cultures. However, if antibiotic sensitivity is considered, then the most efficient method of diagnosis would be a combined culture and antibiotic sensitivity.

[e] 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.

Testing submitted with these codes will be handled on a case-by-case basis. A discussion of every infectious agent that might be detected with a probe technique is beyond the scope of this policy.

Table Key:
Med Nec—meets medical criteria for coverage

Inv—does not meet medical criteria for coverage

Eff—effective

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment, or procedure is one made between the physician and their patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Nucleic Acid Probes

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

A nucleic acid probe is used to detect and identify species or subspecies of organisms by identifying nucleic acid sequences in a sample. Nucleic acid probes detect genetic materials, such as RNA or DNA, unlike other tests, which use antigens or antibodies to diagnose organisms.

The availability of nucleic acid probes has permitted the rapid direct identification of microorganism DNA or RNA. Amplification techniques result in exponential increases in copy

numbers of a targeted strand of microorganism-specific DNA. The most used amplification technique is polymerase chain reaction (PCR) or reverse transcriptase PCR. In addition to PCR, other nucleic acid amplification techniques have been developed, such as transcription-mediated amplification, loop-mediated isothermal DNA amplification, 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 assess how many microorganisms are present. Quantification of the number of nucleic acids permits serial assessments of response to treatment; the most common clinical application of quantification is the serial measurement of HIV RNA (called viral load).

The direct probe technique, amplified probe technique, and probe with quantification methods vary based on 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, transcription-mediated amplification, and strand displacement amplification. Nucleic acid-based sequence amplification and transcription-mediated amplification involve amplification of an RNA (rather than a DNA) target.
- Probe amplification methods include ligase chain reaction.
- Signal amplification methods include branched DNA (bDNA) probes and hybrid capture methods using an anti-DNA/RNA hybrid antibody.

The probe with quantification techniques refers to quantitative PCR or real-time 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.

Direct assays will generally have lower sensitivity than amplified probes. In practice, most commercially available probes are amplified, with a few exceptions. For 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.

Classically, identification of microorganisms relies either on the 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.

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 (e.g., HIV), fastidious or lengthy culture requirements (e.g., Mycobacteria, Chlamydia, Neisseria species), or difficulty in collecting an appropriate sample (e.g., 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 cultures, 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.

The risks of nucleic acid testing include false-positive and false-negative results; inaccurate identification of pathogens by the device, inaccurate interpretation of test results, or incorrect operation of the instrument.

- False-positive results can lead to unnecessary treatment, with its associated toxicities and side effects, including allergic reaction. In addition, true diagnosis and treatment could be delayed or missed altogether.
- False-negative results could delay diagnosis and initiation of proper treatment.
- It is possible that these risks can be mitigated by the use of a panel of selected pathogens indicated by the clinical differential diagnosis while definitive culture results are pending.

KEY POINTS:

The most recent literature update for this evidence review was performed through May 2, 2024.

Summary of Evidence

For individuals who have signs and/or symptoms of meningitis and/or encephalitis who receive a nucleic acid-based central nervous system pathogen panel, the evidence includes a systematic review and a pivotal prospective study. Access to a rapid method that can simultaneously test for multiple pathogens may lead to the faster initiation of more effective treatment and conservation of cerebrospinal fluid. The available central nervous system panel is highly specific for the included organisms. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who receive a nucleic acid-based gastrointestinal pathogen panel testing (GIPP), the evidence includes prospective and retrospective evaluations of the tests' sensitivity and specificity. The available 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. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have signs and/or symptoms of respiratory infection who receive a nucleic acid-based respiratory pathogen panel, the evidence includes a systematic review and two randomized controlled trials (RCTs). The systematic review reported that all three reviewed multiplex polymerase chain reaction systems were highly accurate. One RCT and one quasi-RCT evaluated utility of a respiratory panel and found benefits in time-to-treat and length of hospital stay. In addition, one sub analysis found fewer antibiotics being prescribed for patients diagnosed with the panel. The panel did not significantly affect duration of antibiotic use, readmission, or mortality rates. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For other nucleic acid probes addressed in this review, the tests' clinical utility was evaluated based on whether there is demonstrated clinical validity, along with either direct evidence of improved outcomes or a chain of evidence indicating that changes in management leading to improved outcomes are likely to occur with testing.

Practice Guidelines and Position Statements
Numerous guidelines have been identified concerning the use of NAATs for the diagnosis of the pathogens discussed in this review. Inclusion of information below does not imply coverage/non-coverage.

Table 2 provides an index of NAAT recommendation by virus/infection.

Table 2. Index of NAAT Recommendations by Virus/Infection

Microorganism	Guidelines Recommending the Use of NAATs (Location)	Guidelines Not Recommending the Use of NAATsa (Location)
Bartonella hensalae	NIH (2.1.1), IDSA (3.1), AAP (5.1)	NA
Candida species	AAP (5.1), CDC (1.5.1)b	IDSA (3.1, 3. 6)
CNS pathogen panel	IDSA (3.2, 3.3)	NA
Chlamydia pneumoniae	AAP (5.1), CDC (1.5.3), IDSA (3.1c)	NA
Chlamydia trachomatis	AAP (5.1), CDC (1.5.2c, 1.6c), IDSA (3.1),	NA

Clostridioides (Clostridium) difficile	NIH (2.1.2), AAP (5.1)	IDSA (3.1, 3.4)
Cytomegalovirus	CDC (1.1), NIH (2.1.3), IDSA (3.1c , 3.3)	AAP (5.1)
Enterovirus	IDSA (3.1), AAP (5.1)	NA
Gardnerella vaginalis	AAP (5.1), CDC (1.5.4)	IDSA (3.1)
GI pathogen panel	CDC (1.4c), IDSA (3.5), ACG (6.1)	NA
Hepatitis B	NIH (2.1.4), IDSA (3.1), AAP (5.1)	NA
Hepatitis C	CDC (1.5.5c), NIH (2.1.5), IDSA (3.1), AAP (5.1)	NA
Herpes simplex virus	CDC (1.5.6c), NIH (2.1.6), IDSA (3.1c, 3.3), AAP (5.1)	NA
Human herpesvirus 6	IDSA (3.1c, 3.3)	AAP (5.1)
Human papillomavirus	CDC (1.5.8c), AAP (5.1)	NA
HIV 1	CDC (1.5.7c), IDSA (3.1), AAP (5.1)	NA
Influenza virus	IDSA (3.1c), AAP (5.1)	NA
Legionella pneumophila	IDSA (3.1), AAP (5.1)	NA
Meningitis	NA	IDSA (3.2)
Mycobacteria species	CDC (1. 7), NIH (2.1.7), IDSA (3.1, 3.3)	AAP (5.1)
Mycoplasma pneumoniae	CDC (1.2c), IDSA (3.3), AAP (5.1)	NA

Neisseria gonorrhoeae	CDC (1.6c), IDSA (3.1), AAP (5.1)	NA
Respiratory panel	None Identified	NA
SARS-CoV-2	IDSA (3. 7)	NA
Staphylococcus aureus	IDSA (3.1), AAP (5.1)	NA
Streptococcus, group A	IDSA (3.1)	AAP (5.1)
Streptococcus, group B	AAP (5.2), ASM (7.1)	IDSA (3.1), AAP (5.1)
Trichomonas vaginalis	CDC (1.5.9), IDSA (3.1)c, AAP (5.1)	NA
Vancomycin-resistant Enterococcus	AST (4.1)	IDSA (3.1), AAP (5.1)
Zika virus	CDC (1.3), IDSA (3.1), AAP (5.1)	NA

AAP: American Academy of Pediatrics; ACG: American College of Gastroenterology; ASM: American Society for Microbiology; AST: American Society of Transplantation; CDC: Centers for Disease Control and Prevention; CNS: central nervous system; GI: gastrointestinal; HIV: human immunodeficiency virus; IDSA: Infectious Disease Society of America; NA: not applicable (none found); NAAT: nucleic acid amplification test; NIH: National Institutes of Health; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2.

a Guidelines Not Recommending includes not only guidelines that recommend against NAATs but also those that were neutral on the use of NAATs.

b CDC recommends culture for first-line identification of Candida species; it recommends NAAT for complicated infections and for second-line diagnosis.

c Indicates guidelines in which the issuing body specifically recommends that U.S. Food and Drug Administration (FDA)-cleared NAATs be used.

Centers for Disease Control and Prevention

The Centers for Disease Control and Prevention (CDC) have published multiple recommendations and statements regarding the use of NAATs to diagnose the viruses and infections discussed in this evidence review since 2009.

1.1 The CDC published guidance for laboratory testing for cytomegalovirus (CMV); the guideline stated that the standard laboratory test for congenital CMV is polymerase chain reaction (PCR) on saliva, with confirmation via urine test to avoid false-positive results from ingesting breast milk from CMV seropositive mothers. Serologic tests were recommended for persons >12 months of age.

1.2 The CDC published diagnostic methods for mycoplasma pneumoniae. They cited NAAT as a method of diagnosis, along with culture or serology.

1.3 The CDC published updated guidelines on Zika virus testing. Routine testing for Zika virus in asymptomatic pregnant patients is not recommended, but NAAT testing may still be considered for asymptomatic pregnant women with recent travel to an area with risk of Zika outside the U.S. and its territories. Symptomatic pregnant patients should receive NAAT testing if they have recently traveled to areas with a risk of Zika virus or if they have had sex with someone who lives in or recently traveled to areas with risk of Zika virus. If a pregnant woman (with risk of Zika virus exposure) has a fetus with prenatal ultrasound findings consistent with congenital Zika virus infection, Zika virus NAAT and IgM testing should be performed on maternal serum and NAAT on maternal urine. If amniocentesis is being performed as part of clinical care, Zika virus NAAT testing of amniocentesis specimens should also be performed.

1.4 In 2017, the CDC updated its guidelines on norovirus gastroenteritis outbreak management and disease prevention. Real-time reverse transcription-PCR assays, specifically, TaqMan-based real-time assays, which can contain multiple probes, is considered the effective laboratory diagnostic protocol for testing suspected cases of viral gastroenteritis.

1.5 In 2015, the CDC made recommendations for the use in NAATs in diagnosing numerous sexually transmitted infections. These recommendations were most recently updated in 2021, with the publication of new guidelines and the following recommendations:

1.5.1 For Candida species:

- "The majority of PCR tests for yeast are not FDA [U.S. Food and Drug Administration] cleared, and providers who use these tests should be familiar with the performance characteristics of the specific test used."

1.5.2 For Gonococcal Infections:

- "Culture, NAAT, and POC [point of care] NAAT, such as GeneXpert (Cepheid), are available for detecting genitourinary infection with N. gonorrhoeae"
- "NAATs and POC NAATs allow for the widest variety of FDA-cleared specimen types, including endocervical and vaginal swabs and urine for women, urethral swabs and urine for men, and rectal swabs and pharyngeal swabs for men and women. However, product inserts for each NAAT manufacturer should be consulted carefully because collection methods and specimen types vary."

1.5.3 For Chlamydial Infection:

- "NAATs are the most sensitive tests for these specimens and are the recommended test for detecting C. trachomatis infection. NAATs that are FDA cleared for use with vaginal swab specimens can be collected by a clinician or patient in a clinical setting. Patient collected vaginal swab specimens are equivalent in sensitivity and specificity to those collected by a clinician using NAATs, and this screening strategy is highly acceptable among women. Optimal urogenital specimen types for chlamydia screening by using NAAT include firstcatch urine (for men) and vaginal swabs (for women). Recent studies have demonstrated that among men, NAAT performance on self-collected meatal swabs is comparable to patient-collected urine or provider-collected urethral swabs."

1.5.4 For Gardnerella vaginalis:

- "Multiple BV [bacterial vaginosis] NAATs are available for BV diagnosis among symptomatic women. These tests are based on detection of specific bacterial nucleic acids and have high sensitivity and specificity for BV (i.e., G. vaginalis, A. vaginae, BVAB2, or Megasphaera type 1) and certain lactobacilli (i.e., Lactobacillus crispatus, Lactobacillus jensenii, and Lactobacillus gasseri)...Five quantitative multiplex PCR assays are available...Two of these assays are FDA cleared (BD Max Vaginal Panel and Aptima BV), and the other three are laboratory-developed tests."

1.5.5 For hepatitis C infection (HCV):

- In addition, “testing for HCV infection should include use of an FDA-cleared test for antibody to HCV…followed by NAAT to detect HCV RNA for those with a positive antibody result. Persons with HIV infection with low CD4+ T-cell count might require further testing by NAAT because of the potential for a false-negative antibody assay.”

1.5.6 For diseases characterized by genital, anal, or perianal ulcers (eg., herpes simplex virus [HSV], syphilis):

- "Specific evaluation of genital, anal, or perianal ulcers includes syphilis serology tests and darkfield examination from lesion exudate or tissue, or NAAT if available; NAAT or culture for genital herpes type 1 or 2; and serologic testing for type-specific HSV antibody. In settings where chancroid is prevalent, a NAAT or culture for Haemophilus ducreyi should be performed;" and
- "PCR is also the test of choice for diagnosing HSV infections affecting the central nervous system (CNS) and systemic infections (e.g., meningitis, encephalitis, and neonatal herpes). HSV PCR of the blood should not be performed to diagnose genital herpes infection, except in cases in which concern exists for disseminated infection (e.g., hepatitis)."

1.5.7 For Human immunodeficiency virus 1 (HIV-1):

- The use of NAAT is not mentioned; serologic tests are recommended for detecting antibodies against HIV-1 and by virologic tests that detect HIV antigens or RNA.

1.5.8 For human papillomavirus (HPV):

- There are several FDA-cleared HPV tests that detect viral nucleic acid or messenger RNA; however, there are currently no algorithms for HPV 16/18/45 testing in the clinical guidelines;
- Testing for nononcogenic HPV (types 6 and 11) is not recommended; and
- "HPV assays should be FDA-cleared and used only for the appropriate indications" and should not be performed if the patient is "deciding whether to vaccinate against HPV;" when "providing care to persons with genital warts or their partners;" when "testing persons aged <25 years as part of routine cervical cancer screening;" or when "testing oral or anal specimens."

1.5.9 For Trichomonas vaginalis:

- NAAT is recommended for detecting T vaginalis in women due to its high sensitivity and specificity. Multiple assays are FDA-cleared to detect T vaginalis from vaginal, endocervical, or urine specimens for women.
- Although there is not a currently FDA-cleared assay test available for use in men, assays "...should be internally validated in accordance with CLIA [Clinical Laboratory Improvement Amendments] regulations before use with urine or urethral swabs from men."

1.6 In 2014, the CDC published recommendations regarding the laboratory-based detection of C. trachomatis and N. gonorrhoeae infections. It stated:

- NAATs are superior other available diagnostic tests in "overall sensitivity, specificity, and ease of specimen transport;"
- The use of "NAAT to detect chlamydia and gonorrhea except in cases of child sexual assault involving boys and rectal and oropharyngeal infections in prepubescent girls" is supported by evidence; and
- Only NAATs that have been cleared by the FDA for detection of C. trachomatis and N. gonorrhoeae should be used "as screening or diagnostic tests because they have been evaluated in patients with and without symptoms."

1.7 In 2009, the CDC published updated guidelines for the use of NAATs in diagnosing Mycobacterium tuberculosis bacteria. The CDC recommended that "NAA testing be performed on at least one respiratory specimen from each patient with signs and symptoms of pulmonary TB [tuberculosis] for whom a diagnosis of TB is being considered but has not yet been established, and for whom the test result would alter case management or TB control activities." Although it noted that "culture remains the gold standard for laboratory confirmation of TB and is required for isolating bacteria for drug-susceptibility testing and genotyping," the guideline stated that "NAA testing should become standard practice for patients suspected to have TB, and all clinicians and public health TB programs should have access to NAA testing for TB to shorten the time needed to diagnose TB from 1 to 2 weeks to 1 to 2 days."

National Institute of Health et al

2.1 The National Institute of Health (NIH), CDC, and HIV Medicine Association of the Infectious Diseases Society of America (IDSA) published guidelines for the prevention and

treatment of opportunistic infections in adults and adolescents with HIV The most recent update took place in 2024. In these guidelines, NAATs are discussed in the following situations:

2.1.1 Bartonella species

- For patients with suspected bacillary angiomatosis, serologic tests are the standard of care and the most accessible test for diagnosing Bartonella infection. There are PCR methods that have been developed for identification and speciation of Bartonella and are becoming increasingly available through private laboratories, as well as the CDC and may aid in diagnosis of Bartonella in freshly biopsied tissue samples or whole blood.

2.1.2 Clostridioides (Clostridium) difficile

- Detection of either the C. difficile toxin B gene, using NAAT, or the C. difficile toxin B protein, using an enzyme immunoassay, is required for diagnosis. PCR assays have high sensitivity and can detect asymptomatic carriers.

2.1.3 Cytomegalovirus

- For patients with suspected CMV disease, diagnosis is based on clinical symptoms and the presence of CMV in cerebral spinal fluid (CSF) or brain tissue. “In rare cases, the diagnosis may be unclear, and PCR of aqueous or vitreous humor specimens for CMV and other pathogens—especially herpes simplex virus, varicella zoster virus, and Toxoplasma gondii—can be useful for establishing the diagnosis."

2.1.4 Hepatitis B

- The CDC, the United States Preventive Services Task Force, and the American Association for the Study of Liver Disease (AASLD) recommend that patients with HIV infection should be tested for hepatitis B; however, NAATs are not recommended for initial testing in patients with HIV.

2.1.5 Hepatitis C

- Patients with HIV are recommended to undergo routine hepatitis C screening, initially “performed using the most sensitive immunoassays licensed for detection of antibody to HCV in blood.” The use of NAATs are not mentioned for initial testing in patients with HIV.

2.1.6 Herpes Simplex Virus

- “HSV DNA PCR and viral culture are preferred methods for diagnosis of mucocutaneous lesions potentially caused by HSV.”

2.1.7 Mycobacterium tuberculosis infection and disease

- “ NAA tests provide rapid diagnosis of TB, and some assays also provide rapid detection of drug resistance.”
- "NAA assays, if positive, are highly predictive of TB disease when performed on Acid-Fast Bacillus (AFB) smear-positive specimens. However, because nontuberculous mycobacterial infections (NTM) may occur in people with HIV with advanced

immunodeficiency, negative NAA results in the setting of smear-positive specimens may indicate NTM infection and can be used to direct therapy and make decisions about the need for respiratory isolation."

- "NAA tests are more sensitive than AFB smear, being positive in 50% to 80% of smear negative, culture-positive specimens and up to 90% when three NAA tests are performed. Therefore, it is recommended that for all patients with suspected pulmonary TB, a NAA test be performed on at least one specimen. NAA tests also can be used on extrapulmonary specimens with the caveat that the sensitivity is often lower than with sputum specimens."

Infectious Disease Society of America et al

Since 2008, the IDSA has partnered with various societies to publish nine recommendations regarding the use of NAATs to diagnose the viruses and infections discussed in this evidence review.

In 2024, the IDSA and the American Society for Microbiology published a guide on the diagnosis of infectious diseases. In this guideline, NAATs were recommended diagnostic procedures for Enterovirus, Hepatitis C, Hepatitis B, Cytomegalovirus, bacterial vaginosis, Herpes Simplex Virus, Human Herpesvirus 6, HIV, Influenza Virus, and Zika Virus. In addition to providing guidance on diagnosing these diseases, the guidelines also provided recommendations on testing for other conditions by testing for common etiologic agents. Table 3 describes selected conditions for which IDSA recommends NAATs for diagnosing etiologic agents.

Table 3. IDSA Recommended Conditions for Use of NAATs in Identifying Etiologic Agents of Other Conditions*

Etiologic Agents	Recommended Conditions for Use of NAATs in Diagnosis when Specific Etiologic Agents is Suspected
Bartonella spp	Bloodstream infections; encephalitis
Chlamydia pneumonia	Bronchiolitis, bronchitis, and pertussis; community-acquired pneumonia
Chlamydia trachomatis	Pre-septal and orbital cellulitis, lacrimal and eyelid infections, and conjunctivitis; pharyngitis; orbital and periorbital cellulitis, and acrimal and eyelid infections; proctitis; epididymitis and orchitis; pathogens associated with cervicitis/ urethritis; pathogens associated with pelvic inflammatory disease and endometritis
Clostridioides (Clostridium) difficile	Gastroenteritis, infectious, and toxin- induced diarrhea

Cytomegalovirus	Pericarditis and myocarditisa; encephalitis; pneumonia in the immunocompromised host; esophagitis; gastroenteritis, infectious, and toxin- induced diarrhea; burn wound infectionsb
Enterovirus	Meningitis; encephalitis; brochiolitis, bronchitis, and pertussis; community- acquired pneumonia; gastroenteritis, infectious, and toxin-induced diarrhea; pre-septal and orbital cellulitis, lacrimal and eyelid infections, and conjunctivitis; infectious keratitis; endophthalmitis, panophtalmitis, uveitis, and retinitis
Herpes simplex virus	Meningitis; encephalitis; esophagitis; proctitis; pathogens associated with cervicitis/ urethritis; burn wound infectionb; periocular structure infections/conjunctivitis, orbital and periorbital cellulitis, and acrimal and eyelid infections; periocular structure infections/ keratitis; pharyngitis; genital lesions; endophthalmitis, panophthalmitis, uveitis, and retinitis; pneumonia in the immunocompromised host
HIV	Pericarditis and myocarditis; meningitisc; pharyngitisc
Human herpesvirus 6	Encephalitis
Influenza virus	Encephalitis; bronchiolitis, bronchitis, and pertussis; community- acquired pneumonia; hospital- acquired pneumonia and ventilator- associated pneumonia; pulmonary infections in cystic fibrosis
Legionella spp	Community- acquired pneumonia; hospital- acquired pneumonia and ventilator- associated pneumonia; surgical site infections
Mycobacteria species- both tuberculosis and NTM	Community- acquired pneumonia; infections of the pleural space; meningitis; osteomyelitis; encephalitis
Neisseria gonorrhoeae	Joint infection; pharyngitis; proctitis; native joint infection and bursitis; epididymitis and orchitis; pathogens associated with cervicitis/ urethritis; pathogens associated with pelvic inflammatory disease and endometritis
Staphylococcus aureus	Joint infection; trauma-associated cutaneous infection; surgical site infections; osteomyelitis
Streptococcus, group A	Pharyngitis; periprosthetic joint infection

Trichomonas vaginalis	Pathogens associated with cervicitis/ urethritis; pathogens associated with pelvic inflammatory disease and endometritis; epididymitis and orchitis

* The IDSA provided recommendations for many situations in which NAATs are recommended for diagnosing certain etiologic agents commonly seen, with the listed conditions noted under the Recommended Conditions for Use of NAATs in Diagnosis Column. HIV: human immunodeficiency virus; IDSA: Infectious Disease Society of America; MRSA: methicillin-resistant Staphylococcus aureus; NAAT: nucleic acid amplification test: NTM: nontuberculous mycobacteria.

a Recommended as first choice if available.

b Where applicable and laboratory-validated.

c The guidelines caution that NAAT is not 100% sensitive in individuals with established HIV infection due to viral suppression; therefore, if NAAT is used, subsequent serologic testing is recommended.

Use of NAATs for diagnosing Candida species, Gardnerella vaginalis, Streptococcus Group B, and Vancomycin-resistant enterococcus as etiologic agents was not recommended.

In 2017, the IDSA published clinical practice guidelines for the management of healthcare-associated ventriculitis and meningitis. When making diagnostic recommendations, the IDSA notes cultures as the standard of care in diagnosing healthcare-associated ventriculitis and meningitis, but that "nucleic acid amplification tests, such as PCR, on CSF may both increase the ability to identify a pathogen and decrease the time to making a specific diagnosis (weak, low)." (Strength of recommendation and quality of evidence established using the GRADE [Grading of Recommendations Assessment, Development and Evaluation] methodology.)

In 2008, the IDSA published clinical practice guidelines for the management of encephalitis. The following recommendations were made:

- "Biopsy of specific tissues for culture, antigen detection, nucleic acid amplification tests (such as PCR), and histopathologic examination should be performed in an attempt to establish an etiologic diagnosis of encephalitis (A-III)." (Strength of recommendation level "A indicates good evidence to support recommendation for use." Quality of evidence level III indicates "evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.")
- "Nucleic acid amplification tests (such as PCR) of body fluids outside of the CNS may be helpful in establishing the etiology in some patients with encephalitis (B-III)." (Strength of recommendation level B indicates "moderate evidence to support recommendation." Quality of evidence level III indicates "evidence from opinions of respected authorities based on clinical experience, descriptive studies, or reports of expert committees.")
- "Nucleic acid amplification tests (such as PCR) should be performed on CSF specimens to identify certain etiologic agents in patients with encephalitis (A-III). Although a

positive test result is helpful in diagnosing infection caused by a specific pathogen, a negative result cannot be used as definitive evidence against the diagnosis."

- The use of NAATs was recommended for diagnosing CMV, herpes simplex virus 1 and 2, Human herpesvirus 6, Bartonella henselae, Mycoplasma pneumoniae, and Mycobacterium tuberculosis.

In 2018, the IDSA and the Society for Healthcare Epidemiology of America (SHEA) published weak recommendations with low quality evidence for the use of NAATs to diagnose Clostridioides (Clostridium) difficile.

- "The best-performing method (i.e., in use positive and negative predictive value) for detecting patients at increased risk for clinically significant C. difficile [CDI] infection" is use of a "stool toxin test as part of a multistep algorithm…rather than NAAT along for all specimens received in the clinical laboratory when there are no preagreed institutional criteria for patient stool submission."
- "The most sensitive method of diagnosis of CDI in stool specimens from patients likely to have CDI based on clinical symptoms" is use of "a NAAT alone or a multistep algorithm for testing…rather than a toxin test alone when there are preagreed institutional criteria for patient stool submission."

In 2017, the IDSA published clinical practice guidelines for the diagnosis and management of infectious diarrhea. The following recommendations were made:

- In situations where enteric fever or bacteremia is suspected, "culture-independent, including panel-based multiplex molecular diagnostics from stool and blood specimens, and when indicated, culture-dependent diagnostic testing should be performed" (GRADE: strong, moderate).
- In testing for Clostridioides (Clostridium) difficile in patients >two years of age, "a single diarrheal stool specimen is recommended for detection of toxin or toxigenic C. difficile strain (e.g., nucleic acid amplification testing)" (GRADE: strong, low).
- NAATs are not recommended for diagnosing CMV.
- It was also noted that "clinical consideration should be included in the interpretation of results of multiple-pathogen nucleic acid amplification tests because these assays detect DNA and not necessarily viable organisms" (GRADE: strong, low).

In 2016, the IDSA published updated clinical practice guidelines for managing candidiasis. The guideline noted many limitations of PCR testing. No formal recommendation was made, but the guidelines did state that "the role of PCR in testing samples other than blood is not established."

In 2020, the IDSA established a panel composed of eight members including frontline clinicians, infectious diseases specialists and clinical microbiologists who were members of the IDSA, American Society for Microbiology, Society for Healthcare Epidemiology of America (SHEA), and the Pediatric Infectious Diseases Society (PIDS). Panel members represented the disciplines of adult and pediatric infectious diseases, medical microbiology, as well as nephrology and gastroenterology. The panel created a coronavirus disease 2019 diagnosis guideline using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach for

evidence assessment; and, given the need for rapid response to an urgent public health crisis, the methodological approach was modified according to the GIN/McMaster checklist for the development of rapid recommendations. The panel published recommendations for COVID-19 diagnosis in an online format, as when substantive new information becomes available the recommendations will require frequent updating. The current recommendations (December 23, 2020) support severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid testing for the following groups:

- all symptomatic individuals suspected of having COVID-19;
- asymptomatic individuals with known or suspected contact with a COVID-19 case;
- asymptomatic individuals with no known contact with COVID-19 who are being hospitalized in areas with a high prevalence of COVID-19 in the community;
- asymptomatic individuals who are immunocompromised and being admitted to the hospital, regardless of COVID-19 exposure;
- asymptomatic individuals prior to hematopoietic stem cell transplant or solid organ transplantation, regardless of COVID-19 exposure;
- asymptomatic individuals without known exposure to COVID-19 undergoing major time-sensitive surgeries;
- asymptomatic individuals without a known exposure to COVID-19 who are undergoing a time-sensitive aerosol generating procedure (e.g., bronchoscopy) when personal protective equipment (PPE) is limited, and testing is available;
- asymptomatic individuals without known exposure when the results will impact isolation/quarantine/personal protective equipment (PPE) usage decisions, dictate eligibility for surgery, or inform administration of immunosuppressive therapy.

The IDSA panel further recommends the following:

- collecting nasopharyngeal swab, mid-turbinate swab, anterior nasal swab, saliva or a combined anterior nasal/oropharyngeal swab rather than oropharyngeal swabs alone for SARS-CoV-2 RNA testing in symptomatic individuals with upper respiratory tract infection or influenza-like illness suspected of having COVID-19 (conditional recommendation, very low certainty of evidence).
- nasal and mid-turbinate swab specimens may be collected for SARS-CoV-2 RNA testing by either patients or healthcare providers, in symptomatic individuals with upper respiratory tract infection or influenza-like illness suspected of having COVID-19 (conditional recommendation, low certainty of evidence).
- a strategy of initially obtaining an upper respiratory tract sample (e.g., nasopharyngeal swab) rather than a lower respiratory sample for SARS-CoV-2 RNA testing in hospitalized patients with suspected COVID-19 lower respiratory tract infection. If the initial upper respiratory sample result is negative, and the suspicion for disease remains high, the IDSA panel suggests collecting a lower respiratory tract sample (e.g., sputum, bronchoalveolar lavage fluid, tracheal aspirate) rather than collecting another upper respiratory sample (conditional recommendations, very low certainty of evidence)

- performing a single viral RNA test and not repeating testing in symptomatic individuals with a low clinical suspicion of COVID-19 (conditional recommendation, low certainty of evidence).
- repeating viral RNA testing when the initial test is negative (versus performing a single test) in symptomatic individuals with an intermediate or high clinical suspicion of COVID-19 (conditional recommendation, low certainty of evidence).
- using either rapid RT-PCR or standard laboratory-based NAATs over rapid isothermal NAATs in symptomatic individuals suspected of having COVID-19 (conditional recommendation, low certainty of evidence).

American Society of Transplantation

4.1 In 2019, the American Society of Transplantation Infectious Diseases Community of Practice published guidelines which addressed vancomycin-resistant enterococci (VRE) infections in solid organ transplant patients. The guidelines noted the cost-effectiveness and accuracy of "emerging molecular diagnostics for VRE colonization, including multiplexed PCR performed after culture on selective media," compared with culture alone.

American Academy of Pediatrics

5.1 The thirty-second edition of the American Academy of Pediatrics (AAP) Red Book (2021) describes the diagnostic and treatment options for many infectious diseases in the pediatric population. Their recommendations for appropriate diagnostic tests for the viruses and infections discussed in this policy are detailed in Table 4.

Table 4. Red Book Diagnostic Test Recommendations for the Pediatric Population

Infection	Diagnostic Test Recommendation
Bartonella henselae	EIA IFA NAAT (PCR)
Candida species	Clinical evaluation microscopy PNA FISH probes and PCR assays developed for rapid detection directly from positive blood cultures
Chlamydia pneumoniae	NAATs (PCR) are the preferred method for diagnosis of acute infection. Serologic antigen test is an option, but is technically complex and interpretation is subjective
Chlamydia trachomatis	NAATs are recommended for C trachomatis urogenital infections and in post pubescent individuals. They are not recommended for diagnosing C trachomatis conjunctivitis or pneumonia or in the evaluation of prepubescent children for possible sexual assault.

Clostridioides (Clostridium) difficile	NAATs detect genes responsible for the production of toxins A and B, rather than free toxins A and B in the stool, which are detected by EIA NAAT could be considered alone if a policy in place to screen symptoms; if no policy in place, multi-step algorithms involving EIA, GDH, NAAT plus toxin is recommended
Coronaviruses (including SARS-CoV-2 and MERS-CoV)	RT-PCR Direct antigen testing
Cytomegalovirus	Saliva PCR is the preferred diagnostic tool for screening.
Enterovirus	RT-PCR and culture from a variety of specimens
Gardnerella vaginalis	Microscopy Numerous NAATs have been recommended when microscopy is unavailable
Hepatitis B	Serologic antigen tests NAATs
Hepatitis C	IgG antibody enzyme immunoassays NAATs
Herpes simplex virus	Cell culture NAATs- diagnostic method of choice for neonates with CNS infections, older children, and adults with HSE
Human herpesvirus 6	Few developed assays are available commercially and do not differentiate between new, past, and reactivated infection. Therefore, these tests "have limited utility in clinical practice:" Serologic tests; PCR- the assays are not sensitive in younger children.
HIV 1	HIV DNA PCR or RNA PCR-preferred test to diagnose HIV infection in infants and children younger than 18mo; highly sensitive and specific by 2 weeks of age and available
Human papillomavirus	"Detection of HPV infection is based on detection of viral nucleic acid."

Influenza virus	"RT-PCR, viral culture tests, and rapid influenza molecular assays are available options for testing; optimal choice of influenza test depends on the clinical setting."
Legionella pneumophila	BCYE media Legionella antigen in urine Direct IFA Genus-specific PCR reaction-based assays
Meningitis	Cultures of blood and CSF NAATs- "useful in patients who receive antimicrobial therapy before cultures are obtained."
Mycobacteria species	M tuberculosis disease: Chest radiography and physical examination Several NAATs are cleared for rapid detection of M tuberculosis, but expert consultation is recommended for interpretation of results. NTM: "definite diagnosis of NTM disease requires isolation of the organism."
Mycoplasma pneumoniae	"PCR tests for M pneumonia are available commercially and increasing replacing other tests, because PCR tests performed on respiratory tract specimens have sensitivity and specifically between 80% and 100%, yield positive results earlier in the course of illness than serologic tests, and are rapid."
Neisseria gonorrhoeae	"NAATs are far superior in overall performance compared with other N gonorrhoeae culture and nonculture diagnostic methods to test genital and nongenital specimens, but performance varies by NAAT type."
Staphylococcus aureus	"NAATS are approved for detection and identification of S aureus, including MRSA, in positive blood cultures."
Streptococcus, group A	"Children with pharyngitis and obvious viral symptoms should not be tested or treated for group A streptococcal infection. Laboratory confirmation is required for cases in children without viral symptoms… culture on sheep blood agar can confirm group A streptococcal infection."
Streptococcus, group B	"Gram-positive cocci in pairs or short chains from a normally sterile body fluid provides presumptive evidence of infection."

Trichomonas vaginalis	Microscopy NAATs are “the most sensitive mean of diagnosing T vaginalis infection and is encouraged for detection in females and males.”
Vancomycin-resistant Enterococcus	"Selective agars are available for screening of vancomycin-resistant enterococcus from stool specimens. Molecular assays are available for direct detection of vanA and vanB genes from rectal and blood specimens to identify vancomycin-resistant enterocci"
Zika virus	NAATs Trioplex real-time PCR assay Serologic testing

BCYE: buffered charcoal yeast extract; CNS: central nervous system; CSF: cerebrospinal fluid; DNA: deoxyribonucleic acid; EIA: enzyme immunoassay; FDA: Food and Drug Administration; GDH: glutamate dehydrogenase; HIV: human immunodeficiency virus; HPV: human papillomavirus; HSE: herpes simplex encephalitis; IFA: indirect fluorescent antibody; MERS-CoV: Middle East respiratory syndrome coronavirus; MSRA: methicillin-resistant Staphylococcus aureus; NAAT: nucleic acid amplification test; NTM: nontuberculous mycobacteria; PCR: polymerase chain reaction; PNA FISH: peptide nucleic acid fluorescent in situ hybridization; RNA: ribonucleic acid; RT: reverse transcriptase; SARS-CoV-2: severe acute respiratory syndrome coronavirus 2.

In 2019, the AAP published guidelines on managing infants at risk for group B streptococcus (GBS). It recommends antenatal vaginal-rectal culture performed by using a broth enrichment “followed by GBS identification by using traditional microbiologic methods or by NAAT-based methods.” However, point-of-care NAAT-based screening should not be the primary method of determining maternal colonization status due to reported variable sensitivity as compared with traditional culture, as well as “because most NAAT-based testing cannot be used to determine the antibiotic susceptibility of colonizing GBS isolates among women with a penicillin allergy.”

American College of Gastroenterology

6.1 In 2016, the American College of Gastroenterology published clinical guidelines on the diagnosis, treatment, and prevention of acute diarrheal infections in adults. It recommended that, given that “traditional methods of diagnosis (bacterial culture, microscopy with and without special stains and immunofluorescence, and antigen testing) fail to reveal the etiology of the majority of cases of acute diarrheal infection,… the use of FDA-approved culture-independent methods of diagnosis can be recommended at least as an adjunct to traditional methods. (Strong recommendation, low level of evidence).” These are described in the rationale as multiplex molecular testing.

American College of Obstetricians and Gynecologists
Published in 2020, the ACOG has issued a Practice Bulletin on vaginitis in nonpregnant patients. The Bulletin made the following recommendations on the initial evaluation of patients with symptoms of vaginitis, citing CDC guidelines:

"A complete medical history, physical examination of the vulva and vagina, and clinical testing of vaginal discharge (i.e., pH testing, a potassium hydroxide "whiff test," and microscopy) are recommended for the initial evaluation of patients with vaginitis symptoms."

The Bulletin noted that single-swab multiplex PCR testing "may be a promising alternative to microscopy," but that its clinical utility is still under evaluation.

American Society for Microbiology
7.1 In 2020, the American Society for Microbiology updated the 2010 guidelines on detecting and identifying GBS that were originally published by the CDC, with plans to continue updating regularly. The most recent update took place July 2021. The guidelines state that "intrapartum NAAT without enrichment has an unacceptably high false negative rate...As such we do not recommend the use of intrapartum NAAT without enrichment to rule out the need for prophylaxis." All GBS screening specimens should be incubated in selective enrichment broth prior to agar media plating or NAAT. "Nucleic acid amplification-based identification of GBS from enrichment broth is acceptable" for GBS screening, "but not sufficient for all patients" due to high false-negative rates.

U.S. Preventive Services Task Force Recommendations
See previous section for Hepatitis B USPSTF recommendations.

KEY WORDS:
Bartonella henselae or quintana, Borrelia burgdorferi, Candida species, Chlamydia pneumonia or trachomatis, Clostridium difficile, Cytomegalovirus (CMV), Enterovirus, Vancomycin-resistant Enterococcus, Gardnerella vaginalis, Hepatitis B, Hepatitis C, Hepatitis G, Herpes simplex virus, Herpes virus-6, Human immunodeficiency virus 1 (HIV-1), Human immunodeficiency virus (HIV-2), Human papillomavirus (HPV), Influenza virus, Legionella pneumophila, Mycobacterium species, Mycobacterium tuberculosis, Mycobacterium avium, Mycobacterium intracellulare, Mycoplasma pneumonia, Neisseria gonorrhoeae, Respiratory Viral Panel, Staphylococcus aureus, Methicillin-resistant Staphylococcus aureus, Streptococcus, Group A, Streptococcus, Group B, Trichomonas vaginalis, Human Herpes virus-6, MicroGenDX, MYCODART, BioFire, FilmArray GI Panel, FilmArray Respiratory Panel, GI panel, Respiratory Panel, ePlex, GIPP, Zika Virus, COVID-19, Severe acute respiratory syndrome coronavirus 2, SARS-CoV-2, Multitarget, Orthopoxvirus, Monkeypox, cowpox virus, vaccinia virus, Xpert® Xpress MVP, Xpert® CT/NG, Cepheid®, PreTect HPV-Proofer' 7, tick borne bacteria, GI Assay, Lab Genomics, Thermo Fischer, Lesion Infection, Qlear, Qlear UTI, Lifescan Labs, Qlear UTI-Reflex ABR, Respiratory Pathogens with ABR, Urogenital Pathogen with Rx Panel, UPX, GENETWORx, GENETWORx UTI with ABR, mycoplasma genitalium, BK polyomavirus, BKPyV, Human polyomavirus 1, Alinity™ m STI Assay, Proofer 7 HPV

mRNA E6 and E7 Biomarker Test, PANNAT STEC Test, Biocode Gastrointestinal Pathogen Panel (GPP), Great Basin Stool Bacterial Pathogens Panel, Curetis Unyvero Lower Respiratory Panel, BIOFIRE SPOTFIRE Respiratory (R) Panel, BIOFIRE SPOTFIRE Respiratory (R) Panel Mini, QIAstat-Dx Respiratory Panel; QIAstat-Dx Analyzer, NxTAG Respiratory Pathogen Panel v2 (NxTAG RPP v2)

APPROVED BY GOVERNING BODIES:

The U.S. Food and Drug Administration maintains a list of nucleic acid amplification tests (NAATs) that have been cleared by the Center for Devices and Radiological Health. These NAATs have been cleared for many of the microorganisms discussed in this review and may be reviewed on this site.

The table below summarizes the NAATs cleared for central nervous system panels when diagnosing meningitis and/or encephalitis, for panels when diagnosing gastroenteritis, and for respiratory panels.

Table 5. FDA Cleared Nucleic Acid Amplification Tests for Central Nervous System, Gastrointestinal, and Respiratory Panels

NAAT	Manufacturer	510(k) Number	Product Code
Meningitis/Encephalitis (CNS) Pathogen Panels			
FilmArray Meningitis/Encephalitis Panel	BioFire Diagnostics, LLC (Salt Lake City, UT)	DEN150013, K160462	PLO
Gastroenteritis Pathogen Panels			
xTAG Pathogen Panel (GPP)	Luminex Molecular Diagnostics, Inc. (Toronto, Ontario, CA)	DEN130003, K121454	PCH
PANNAT STEC Test	Micronics, Inc. (Redmond, WA)	K173330	PCH
Progastro SSCS Assay	Gen-Probe Prodesse, Inc.(Waukesha, WI)	K123274	PCH
Biocode Gastrointestinal Pathogen Panel (GPP)	Applied Biocode (Santa Fe Springs, CA)	K180041	PCH

Biocode Pathogen Panel	Applied Biocode (Santa Fe Springs, CA)	K190585	PCH
EntericBio Dx Assay	Serosep, Ltd (Annacotty, IE)	K182703	PCH
Filmarray Panel	BioFire Diagnostics, LLC (Salt Lake City, UT)	K140407, K160459	PCH
ProGastro SSCS	Hologic/Genprobe (Waukesha, WA)	K123274	PCH
BD MAX Enteric Bacterial Panel (EBP)	BD Diagnostics (Sparks, MD)	K170308	PCH
Verigene Enteric Pathogen Panel (EP)	Nanosphere, Inc. (Northbrook, IL)	K142033, K140083	PCH
xTAG Gastroenterology Pathogen Panel(GPP) Multiplex Nucleic Acid-Based Assay System	Luminex Molecular Diagnostics, Inc. (Toronto, Ontario, CA)	K121894	PCH
FilmArray GI Panel	BioFire Diagnostics, Inc. (Salt Lake City, UT)	K140407	PCH
Great Basin Stool Bacterial Pathogens Panel	Great Basin Scientific, Inc. (Salt Lake City, UT)	K163571	PCH
Respiratory Viral Panels			
Curetis Unyvero Lower Respiratory Panel	Opgen		
BIOFIRE SPOTFIRE Respiratory (R) Panel	BioFire Diagnostics, Inc (Salt Lake City, UT)	K213954	QOF
BIOFIRE SPOTFIRE Respiratory (R) Panel Mini	BioFire Diagnostics, Inc (Salt Lake City, UT)	K230719	QOF
QIAstat-Dx Respiratory Panel; QIAstat-Dx Analyzer	QIAGEN GmbH (Germantown, MD)	K183597	OCC

ID-TAG Respiratory Viral Panel Nucleic Assay System	Luminex Molecular Diagnostics, Inc. (Toronto, Ontario, CA)	DEN070013, K063765	PCH
Biocode Respiratory Pathogen Panel	Applied BioCode, Inc. (Santa Fe Springs, CA)	K192485	PCH
Nxtag Respiratory Pathogen Panel	Luminex Molecular Diagnostics, Inc. (Toronto, Ontario, CA)	K193167	PCH
NxTAG Respiratory Pathogen Panel v2 (NxTAG RPP v2)	Luminex Molecular Diagnostics, Inc(Toronto, Ontario, CA)	K231758	QOF
xTAG Respiratory Virus Panel (RVP)	Luminex Molecular Diagnostics, Inc. (Toronto, Ontario, CA)	K081483	PCH
Qiastat-Dx Respiratory Panel	QIAGEN GmbH (Germantown, MD)	K183597	PCH
xTAG Respiratory Virus Panel FAST	Luminex Molecular Diagnostics, Inc. (Toronto, Ontario, CA)	K103776	PCH
eSensor® Respiratory Virus Panel (RVP)	Clinical Micro Sensors, Inc.(Carlsbad, CA)	K113731	PCH
Verigene Respiratory Pathogens Plus Nucleic Acid Test	Nanosphere, Inc. (Northbrook, IL)	K103209	PCH
BioFire FilmArray Respiratory Panel (RP)	BioFire Diagnostics, Inc. (Salt Lake City, UT)	K123620	PCH

CNS: central nervous system; DEN: de novo; FDA: Food and Drug Administration. NAAT: nucleic acid amplification tests.

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group-specific policy will supersede this policy when applicable.

CURRENT CODING:

*See Policy Section.

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POLICY HISTORY:

Adopted for Blue Advantage, November 12, 2018.
Medical Policy Group, January 2020
Medical Policy Group, March 2021
Medical Policy Group, June 2021

Medical Policy Group, November 2021: 2022 Annual Coding Update. Added new CPT Codes 0301U, 0302U, and 87154 to the policy section.
Medical Policy Group, December 2021
Medical Policy Group, March 2022: Quarterly coding update.
Medical Policy Group, June 2022
Medical Policy Group, October 2022: Quarterly coding update.
Medical Policy Group, December 2022
Medical Policy Group, June 2023
UM Committee, December 2023: Policy approved by UM Committee for use for Blue Advantage business.
Medical Policy Group, January 2024: Policy statement updated to include BK polyomavirus as medically necessary for renal transplant recipients receiving immunosuppressive therapy and in persons with renal failure in the setting of an immunosuppressed state. Available for comment from February 1, 2024, through March 1, 2024.
UM Committee, January 2024: January policy update approved by UM Committee for use for Blue Advantage business.
Medical Policy Group, March 2024: Quarterly Coding Update: CPT codes 0354U and 0416U deleted effective 03/31/24.
Medical Policy Group, May 2024: Quarterly Coding Update: CPT codes 0455U and 0463U added to Current Coding section as medically necessary effective 07/01/24. CPT code 0353U deleted effective 6/30/24.
Medical Policy Group, July 2024
UM Committee, July 2024: Annual review of policy approved by UM Committee for use for Blue Advantage business.
