HNL Lab Medicine®

# Blood Culture Identification Panel 2 (BCID2)

## Guidance for Interpretation of Rapid Nucleic Acid Amplification (NAA) Blood Culture Results

1. Recommendation for Empiric Therapy Based on Nucleic Acid Amplification (NAA) Organism Detection
2. Resistance Marker Conditional Reporting
3. Gram Positive Bacteria Details
4. Gram Negative Bacteria Details
5. Yeast Details

### Recommendations for Empiric Therapy Based on Nucleic Acid Amplification (NAA) Organism Detection

| ORGANISM | EMPIRIC THERAPY* |
|---|---|
| **Gram Positive** | |
| *Staphylococcus aureus* mecA/C and MREJ **Not Detected** | Oxacillin or Cefazolin |
| *Staphylococcus aureus* mecA/C and MREJ **Detected** | Vancomycin |
| *Staphylococcal* species or *Staphylococcus epidermidis* (not *S. aureus, S. lugdunensis*) | Potential contaminant, particularly if 1 of 2 blood culture sets; Use clinical judgement; if treatment indicated, vancomycin |
| *Enterococcus faecalis* vanA/B **Not Detected** | Ampicillin |
| *Enterococcus faecium* vanA/B **Not Detected** | Vancomycin |
| *Enterococcus faecalis* or *faecium* vanA/B **Detected** | Linezolid or Daptomycin<br>ID consult recommended |
| *S. agalactiae*<br>and/or<br>*S. pyogenes* | Penicillin, Cefazolin, or Ceftriaxone |
| *S. pneumoniae* | Penicillin, Ampicillin, or Ceftriaxone |
| Streptococcus species (not *S. agalactiae, S. pyogenes, S. pneumoniae*) | Potential contaminant, particularly if 1 of 2 blood culture sets;<br>Use clinical judgement; if treatment indicated, ceftriaxone |
| Listeria | Ampicillin<br>ID consult recommended |

| Gram Negative | |
|---|---|
| Enterobacterales<br>*E. coli*<br>*K. pneumoniae/oxytoca*<br>Proteus spp.<br>Salmonella<br>**No Resistance Marker Detected** | Ceftriaxone |
| Enterobacterales<br>*E. coli*<br>*K. pneumoniae/oxytoca*<br>Proteus spp.<br>Salmonella<br>CTX-M **Detected** | Meropenem |
| Enterobacterales<br>Enterobacter cloacae complex<br>*Klebsiella aerogenes*<br>*Serratia marcescens*<br>CTX-M **Not Detected** | Cefepime or Piperacillin/Tazobactam |
| Enterobacterales<br>*Enterobacter cloacae complex*<br>*Klebsiella aerogenes*<br>*Serratia marcescense*<br>CTX-M **Detected** | Meropenem |
| *Pseudomonas aeruginosa* | Cefepime or Piperacillin/Tazobactam |
| mcr-1, KPC, VIM, IMP, NDM,<br>and/or OXA-48-like **Detected** | Consult ID |
| *Haemophilus influenzae* | Amp/Sulbactam or Ceftriaxone |
| *Neisseria menigitidis* | Penicillin or Ceftriaxone |
| *Stenotrophomonas maltophilia* | Bactrim or Ciprofloxacin |
| **Yeast** | |
| *Candida albicans*<br>*Candida parapsilosis* | Fluconazole |
| *Candida glabrata*<br>*Candida krusei*<br>*Candida tropicalis* | Micafungin |
| *Cryptococcus neoformans/gattii* | Amphotericin B + Flucytosine |
| *C. auris detected* | Consult ID and notify Infection Control |

**May vary based on local antibiogram.*

## Resistance Marker Conditional Reporting

Resistance genes are conditionally reported in the BCID2 panel. The resistance marker is reported as detected or not detected only in the case that an associated organism is detected.

| BioFire® BCID2 Panel AMR Gene Results | | | | | |
|---|---|---|---|---|---|
| ***vanA/B*** | ***mecA/C*** | ***mecA/C* and MREJ (MRSA)** | ***mcr-1*** | **CTX-M, IMP, KPC, NDM, VIM** | **OXA-48-like** |
| *Enterococcus faecalis*<br>*Enterococcus faecium* | *Staphylococcus epidermidis*<br>*Staphylococcus lugdunensis* | *Staphylococcus aureus* | *Enterobacter cloacae complex*<br>*Escherichia coli*<br>*Klebsiella aerogenes*<br>*Klebsiella oxytoca*<br>*Klebsiella pneumoniae group*<br>*Salmonella spp.* | *Acinetobacter calcoaceticus-baumannii complex*<br>*Enterobacterales*<br>*Enterobacter cloacae complex*<br>*Escherichia coli*<br>*Klebsiella aerogenes*<br>*Klebsiella oxytoca*<br>*Klebsiella pneumoniae group*<br>*Proteus spp.*<br>*Salmonella spp.*<br>*Serratia marcescens*<br>*Pseudomonas aeruginosa* | *Enterobacterales*<br>*Enterobacter cloacae complex*<br>*Escherichia coli*<br>*Klebsiella aerogenes*<br>*Klebsiella oxytoca*<br>*Klebsiella pneumoniae group*<br>*Proteus spp.*<br>*Salmonella spp.*<br>*Serratia marcescens* |

## Gram Positive Bacteria

***Staphylococcus spp.*** are gram-positive cocci that are appear as irregular, clusters on a Gram stain. Staphylococcus species are common colonizers of the skin and mucous membranes. They are opportunistic pathogens that can cause infection following breaks in the cutaneous epithelial barrier through trauma or medical interventions. Diagnostically, the genus is divided between coagulase-positive staphylococci and coagulase-negative *staphylococci* (CoNS). Due to being commensal organisms, CoNS species are regularly isolated from clinical specimens the provider must differentiate between contamination, colonization, and true infection

***Staphylococcus aureus*** is capable of causing a wide range of diseases. It is estimated that approximately 40% of S. aureus isolates may be methicillin resistant (MRSA). The primary mediator of methicillin resistance in staphylococci is the acquisition of the mecA or mecC genes encoded on the staphylococcal chromosome cassette mec (SCCmec), a mobile genetic element that can transfer between *Staphylococcus* spp.

***mecA/C and MREJ (MRSA)*** –A combined molecular detection of mecA/C, MREJ, and S. aureus indicates MRSA.

Staphylococcus epidermidis is the major cause of infections associated with prosthetic vascular grafts, prosthetic orthopedic devices, and cerebrospinal fluid shunts.

***Staphylococcus lugdunensis*** is part of the normal skin. It similar to S. aureus in terms of pathogenicity and virulence. Unlike most other CoNS, S. *lugdunensis* remains susceptible to a wide array of antimicrobial agents, including β-lactams.

***mecA/C*** – indicates methicillin-resistant (MR) staphylococci (not *Staphylococcus aureus*). This resistance marker will be reported with *Staphylococcus epidermidis* or *lugdunesis*.

**Enterococcus faecalis and Enterococcus faecium** are leading etiologies of gram-positive bloodstream infections from urinary, intra-abdominal infections, and infectious endocarditis. While patterns of resistance may vary by region, *E. faecalis* is commonly susceptible to ampicillin, while *E. faecalis* is more commonly resistant to this agent. Detection of vanA/B in *Enterococcus* allows for rapid decision making on use of vancomycin or alternative agents

**vanA/B** confers vancomycin resistance in *Enterococcus* spp. The prevalence of vancomycin-resistant enterococci (VRE) has increased rapidly, with VRE accounting for 60% of *E. faecium* and 2% of *E. faecalis* isolated from the bloodstream. Enterococci carrying vanA or vanB are resistant to high levels of vancomycin.

***Streptococcus spp.*** are gram-positive cocci that appear in chains or pairs on a Gram stain. *Streptococcus* species are frequently found as commensal bacteria on mucous membranes and are occasionally present as transient skin microbiota.

***Streptococcus agalactiae*** (Group B *Streptococcus*) can cause both early-onset neonatal disease, characterized by sepsis and pneumonia within the first seven days of life, and late-onset disease with meningitis and sepsis between day seven and three months of age. In adult patients, the spectrum of *S. agalactiae* infections includes blood-stream infection (BSI), pneumonia, meningitis, and endocarditis.

***Streptococcus pneumoniae*** colonizes the upper respiratory tract and is the most frequently isolated respiratory pathogen in community-acquired pneumonia.

***Streptococcus pyogenes*** (Group A *Streptococcus*) colonizes the human skin and upper respiratory tract, with these sites serving as primary focal sites of infections and principal reservoirs of transmission of these gram-positive bacteria.

***Listeria monocytogenes***, the causative agent of listeriosis, is a gram-positive bacillus that is ubiquitous in soil and water and can be found in the gastrointestinal tract of up to 5% of healthy adults. Listeriosis is considered the most severe bacterial foodborne infection due to its high mortality rate, despite early antibiotic treatment (11 – 60%). Populations at risk for developing invasive listeriosis include the immunosuppressed, pregnant women, neonates, fetuses, and the elderly.

## Gram-Negative Bacteria

***Acinetobacter calcoaceticus-baumannii* complex** organisms (*A. baumannii*, *A. calcoaceticus*, *A. dijkshoorniae*, *A. nosocomialis*, *A. pittii*, and *A. seifertii*) are related *Acinetobacter* species not reliably differentiated from one another by some manual or automated phenotypic microbial identification systems. These organisms are ubiquitous, non-fermentative, and gram-negative coccobacilli that primarily act as opportunistic pathogens infecting critically ill patients. Multi-drug resistant strains demonstrate resistance to most antibiotic classes, including carbapenems.

***Bacteroides fragilis*** is an obligately anaerobic, gram-negative, non-spore-forming rod. *Bacteroides* species, of which *B. fragilis* is the most common, are part of the normal microbiota of the human colon. However, they can cause significant infection if displaced into the bloodstream or surrounding tissue.

**Enterobacterales** is an order composed of seven families (*Budviciaceae, Enterobacteriaceae, Erwiniaceae, Hafniaceae, Morganellaceae, Pectobacteriaceae, and Yersiniaceae*), many genera, and over 250 species of gram-negative, facultatively anaerobic rods and coccobacilli. The spread of antimicrobial resistance in Enterobacteriaceae has increased the complexity of treating BSI associated with the gram-negative bacteria. Resistance to third- and fourth-generation cephalosporins is mediated primarily by the production of extended-spectrum β-lactamases (ESBLs) and overproduction of AmpC β-lactamases. While the majority of Enterobacteriaceae remain susceptible to carbapenems, KPC-type carbapenemases are emerging and spreading (carbapenem-resistant Enterobacteriaceae; CRE) in certain locations within the United States and worldwide.

***Enterobacter cloacae complex*** organisms (*E. cloacae, E.asburiae, E. hormaechei, E. kobei, E. ludwigii, and E. mori*) are gram-negative, rod-shaped bacteria. *E. cloacae* complex organisms have been implicated in numerous nosocomial infections.

***Escherichia coli*** are gram-negative bacteria that are part of the normal flora of the intestines of humans and animals. Most pathogenic *E. coli* infections are associated with gastrointestinal illness, but may also cause urinary tract infections, BSIs, and meningitis. As with other Enterobacteriaceae, extended-spectrum β-lactamases (ESBLs), including CTX-M and AmpC β-lactamases, and *Klebsiella pneumoniae*-carbapenemase (KPC) pose a significant antibiotic resistance problem.

***Klebsiella aerogenes***, previously known as *Enterobacter aerogenes*, is a gram-negative, facultatively anaerobic, rod-shaped bacterium. It is a nosocomial and opportunistic pathogen generally found in the gastrointestinal tract, urine, and skin of colonized patients.

***Klebsiella oxytoca*** is an aerobic gram-negative, rod-shaped bacterium that is carried on mucosal surfaces (nasopharynx and bowel) and found in agricultural environments. Opportunistic infections due to *K. oxytoca* include soft tissue infections, urinary tract infections, pneumonia, and BSIs.

***Klebsiella pneumonia* group** includes three phylogroups classified as distinct species; *K. pneumoniae*, *K. quasipneumoniae*, and *K. variicola*. *K. pneumoniae* is associated most often with nosocomial infections in the elderly or immunocompromised.

***Proteus spp.*** are commonly isolated, with *Proteus mirabilis* observed most frequently. Most infections (approximately 85%) are thought to be community acquired; however, nosocomial outbreaks have also occurred.

***Salmonella spp.*** are motile, gram-negative, facultatively anaerobic rods that are associated with infection following the consumption of contaminated meat, fresh produce, and manufactured products. Strains of Salmonella are categorized as typhoidal and non-typhoidal.

***Serratia marcescens*** is a common nosocomial pathogen and colonizer. *S. marcescens* is the primary pathogenic species of the Serratia genus. It is of particular concern due to its emerging antibiotic resistance to commonly used agents like β-lactams, aminoglycosides, carbapenems, and fluoroquinolones.

***Pseudomonas aeruginosa*** is an opportunistic, gram-negative pathogen that rarely causes disease in healthy individuals but can cause sepsis in patients with burn wounds, malignancies, immunodeficiency, or in preterm infants. *P. aeruginosa* is a leading cause of nosocomial infections and is responsible for 10% of all hospital-acquired infections. *P. aeruginosa* is susceptible to a limited number of antibiotics (antipseudomonal penicillins and cephalosporins, carbapenems, fluoroquinolones, and ciprofloxacin), and multi-drug resistant (MDR).

***CTX-M*** is a class A extended-spectrum β-lactamase (ESBL) resistance enzyme. CTX-M ESBLs are predominantly found in the Enterobacteriaceae family. However, they have also been reported in other non-enteric, gram-negative bacteria such as *Pseudomonas aeruginosa, Stenotrophomonas maltophilia, Acinetobacter baumannii, Vibrio spp.* and *Aeromonas spp*. Over the last decade, CTX-M has become the most prominent ESBL in the United States.

**Carbapenemase Genes (IMP, KPC, NDM, VIM, OXA-48-like)** confer resistance to beta-lactam antibiotics including cephalosporins and carbapenems. Depending on the resistance marker detected, some of the new beta-lactam/beta-lactamase inhibitor combos may also be clinically ineffective. Treatment with ceftazidime-avibactam or meropenem-vaborbactam is recommended when KPC and/or OXA-48-like markers are detected. Detection of IMP, NDM, and/or VIM may necessitate combination treatment. Consultation with an ID physician and/or pharmacist are recommended in the event any of these markers are detected.

**mcr-1** is an emerging marker of public health importance. It is associated with elevated MICs to colistin, a last-resort drug for some multidrug-resistant infections.

***Haemophilus influenzae*** is a gram-negative coccobacillus, isolated exclusively from humans, that can be present as normal flora of the oropharynx and can cause infections when introduced into the lower respiratory tract. Approximately 20-35% of isolated strains are resistant to amoxicillin.

***Neisseria meningitidis*** is a fastidious, aerobic, gram-negative diplococcus that is spread by mucus or respiratory droplets, often from asymptomatic carriers. This organism may progress quickly and is associated with BSI and meningitis with fever and a characteristic hemorrhagic rash.

***S. maltophilia*** can infect both children and adults. Hospital-acquired infections associated with substantial morbidity and mortality are increasing, particularly in the immunocompromised patient population. In addition, community-acquired *S. maltophilia* infections have been reported from patients that often presented some form of comorbidity (trauma, central venous catheter, prior antibiotic use, malignancy, HIV infection, etc.). *S. maltophilia* is intrinsically resistant to multiple classes of antibiotics.

## Yeast

***Candida* species** are yeasts that are ubiquitous in the environment and as members of the normal human microbiota, especially in the digestive tract and on mucous membranes. These fungi are important agents of opportunistic nosocomial infections ranging from superficial (e.g. oral thrush) to systemic (e.g. BSI). They often occur in combination with other bacteria or a second Candida spp. The five most common species causing BSIs are ***C. albicans, C. glabrata, C. parapsilosis, C. tropicalis,*** and ***C. krusei***. *C. albicans* accounted for over 65% of all Candida BSI cases reported in North America. Among the non-C. albicans species, *C. glabrata* is the most common cause of BSI in the United States, while *C. parapsilosis* and *C. tropicalis* are the major players in other countries. *Candida krusei* is well known as a fungal pathogen among patients with hematologic malignancies and among blood and marrow transplant recipients.

***Candida auris*** was first reported in 2009 as an isolate from the external ear canal of a patient from Japan. This report was followed by the first three cases of nosocomial BSI caused by *C. auris* in 2011 from South Korea. A collaborative project led by the US Centers for Disease Control and Prevention (CDC) described the multidrug-resistant (MDR) nature of C. auris and its global emergence as a nosocomial pathogen: 93% of the 54 isolates from this study were reported to be resistant to fluconazole, the standard antifungal drug of choice in many countries, 41% were resistant to two antifungal classes, and 4% were resistant to three classes.

***Cryptococcus neoformans/gattii*** are fungi found in soil and bird droppings that can become pathogenic following their inhalation and hematogenous spread to the brain and meninges. *C. neoformans* is considered an opportunistic pathogen of immunocompromised individuals. It is the AIDS-defining illness in up to 50% of AIDS patients. *C. gattii* infections are relatively rare but appear to be increasing. In addition to those with reduced immune function, *C. gattii* can also cause disease in the immunocompetent, particularly in persons with underlying health conditions.

*Information above adapted from the Instruction for Use from BioFire Diagnostics Blood Culture Identification Panel 2*