ANMC Adult Rapid Blood Pathogen Identification Panel Guideline

(Last Updated: 5/2024)

ANMC utilizes an FDA approved test called the Blood Culture Identification 2 (BCID2) Panel performed on the FILMArray instrument. The test uses polymerase chain reaction (PCR) to amplify DNA targets from 3 groups of pathogens (gram positive bacteria, gram negative bacteria and yeast). It is performed directly following a positive blood culture and with an expansion in 2020 now allows rapid identification of 30 different pathogens (**Table 1**), including 10 genes responsible for vancomycin-resistant *Enterococci*, methicillin-resistant *Staphylococci,* CTX-M gene (ESBL), mcr-1 gene (colistin resistance), and five of the genes responsible for carbapenem-resistant *Enterobacterales*. In addition to detecting multiple species-specific assays, the panel also contains 3 genus specific assays (*Staphylococcus*, *Streptococcus* and *Enterobacterales*) that allows detection of pathogens for which there are no specific targets. A comprehensive list of all pathogens detected by BCID can be found in **Table 3**.

Table 1: List of Pathogens/Resistance Genes Detected by Blood Pathogen Panel 2 (panel updated December 2021)

Gram-Positive Bacteria	Gram-Negative Bacteria	Yeast	Resistance Markers
*Enterococcus faecalis**	*Acinetobacter calcoaceticus- baumannii*	*Candida albicans*	Cabapenemases
*Enterococcus faecium**	*Bacteroides fragilis**	*Candida auris**	*KPC*
Listeria monocytogenes	*Enterobacterales* family	*Candida glabrata*	IMP*
Staphylococcous species	*Enterobacter cloacae* complex	*Candida krusei*	OXA-48-like*
Staphylococcus aureus	*Escherichia coli*	*Candida parapsilosis*	NDM*
*Staphylococcus epidermidis**	*Klebsiella aerogenes**	*Candida tropicalis*	VIM*
*Staphylococcus lugdunensis**	*Klebsiella oxytoca*	*Cryptococcus neoformans/gattii**	Colistin Resistance
Streptococcus species	*Klebsiella pneumoniae* group		mcr-1*
Streptococcus agalactiae	*Proteus* species		ESBL
Streptococcus pneumonia	*Salmonella* species*		CTX-M*
Streptococcus pyogenes	*Serratia marcescens*		Methicillin (oxacillin) resistances
	Haemophilus influenzae		*mecA/C*
	Neisseria meningitidis		mecA/C & MREJ* (MRSA)
	Pseudomonas aeruginosa		Vancomycin resistance
	*Stenotrophomonas maltophilia**		*vanA/B*

*Indicates new target on BCID2 panel

Immediately following a positive blood culture, the ANMC microbiology lab performs the BCID2. The results are typically available within 2 hours. It is important to note, that this test is NOT a standalone test. Blood samples with bacterial growth are still cultured and proper MIC testing is performed. The rapid reporting of pathogen identification allows for early escalation or de-escalation of antimicrobials to the most appropriate therapy while waiting for susceptibilities. A list of recommended antimicrobial treatment choices are outlined in **Table 3**.

The ANMC Antimicrobial Stewardship Program (ASP) developed these recommendations based upon the institutional antibiogram and national guidelines issued by the Infectious Diseases Society of America (IDSA). Relevant local susceptibility data is provided for gram-negative pathogens if activity for the antimicrobial is available. When both blood culture gram-stain and BCID2 results are available, current antimicrobial therapy should be evaluated in light of the clinical picture and adjusted to the most appropriate regimen. Additionally, when full susceptibility results become available therapy should again be evaluated and adjusted to the most appropriate narrow spectrum agent. It is important to note that certain infections are often polymicrobial in nature. In most cases, isolation of a single pathogen from the BCID2 should warrant narrowing of antimicrobial therapy, but should never result in over-narrowing. An example would be in complicated intra-abdominal infections where anaerobes are frequently present and therapy against these pathogens should generally be included until definitive cultures of the site of infection are available. Providers must use clinical judgment on a case-by-case basis.

Table 2: Interpretations of *Staphylococcus* and *Enterobacterales* BCID2 Results

Bacterial Marker	Result	Interpretation
Staphylococcus *S. aureus, S. epidermidis, S. lugdunensis*	Detected Not detected	Presumed Methicillin-resistant Coagulase-negative *Staphylococcus species* The mecA analyte is not reported for non-*S. epidermidis* and *S. lugdunensis* coagulase-negative species (e.g. *S. hominis, S. simulans, S. capitis*, among others). Presume beta-lactam resistance.
Staphylococcus detected *S. epidermidis* *S. aureus, S. lugdunensis* *mecA*	Detected Detected Not Detected Not Detected	Methicillin-susceptible *Staphylococcus epidermidis*
Staphylococcus *S. aureus* *S. epidermidis, S. lugdunensis* MREJ and *mecA*	Detected Detected Not Detected Detected	Methicillin-resistant *S. aureus* (MRSA)
Staphylococcus *S. aureus* *S. epidermidis, S. lugdunensis* MREJ and *mecA*	Detected Detected Not Detected Not Detected	Methicillin-susceptible *S. aureus* (MSSA)
Enterobacterales *E. coli* *CTX-M*	Detected Detected Detected	Presumed ESBL producing *E. coli**
Enterobacterales *Klebsiella pneumoniae* *CTX-M*	Detected Detected Not Detected	*Klebsiella pneumonia** (unlikely to have ESBL present)
Enterobacterales *Enterobacter cloacae* *KPC*	Detected Detected Detected	Presumed Carbapenem Resistant *Enterobacter cloacae**
Enterobacterales All other species	Detected Not Detected	*Enterobacteriaceae species* lacking specific marker on the BCID2 panel (see Table 4)

* There is very small chance that both the specific pathogen and another Enterobacteriaceae which cannot be not detected specifically by the BCID are present, but the therapy recommended should generally cover these pathogens as well

Table 3: Blood Pathogen Panel Results and Recommended Empiric Therapy

The table below contains interpretations of BCID2 data and recommended empiric antibiotic therapy for treating blood stream infections (BSIs) at ANMC. When the clinical picture and judgement dictates, patients who respond to narrow spectrum therapy do not always need to be escalated, even if this guideline recommends a broader spectrum agent. Similarly, patients who continue to deteriorate or are not clinically responding despite appropriate empirical antimicrobial therapy may require broader coverage. Allergies, organ dysfunction and history of multi-drug resistant organisms (MDROs) should always be considered prior to selecting empiric antimicrobial therapy.

Gram Positive Organisms				
Pathogen Detected		**Preferred Empiric Therapy**	**Alternative Therapy**	**Comments/Considerations**
Enterococcus faecalis		Ampicillin (regardless of VanA/B result)	Vancomycin (per pharmacy) If Van A/B positive- Linezolid or Daptomycin	Consider ID consult.
Enterococcus faecium	*Van A/B* Negative	Vancomycin (per pharmacy)	Linezolid	Consider ID consult. *High dose daptomycin (10mg/kg q24h) should be utilized for VRE blood stream infections
	Van A/B Positive (VRE)	Linezolid	Daptomycin*	
Listeria monocytogenes		Ampicillin	TMP/SMX in patients with severe beta-lactam allergy	Consider ID consult. GPR will not be run on BCID automatically. Please discuss with microbiology staff if concern for *Listeria* is present.
Staphylococcus aureus	*mecA/MREJ* Negative (MSSA)	Cefazolin	Nafcillin	Repeat Blood cultures (BCx) and formal ID consult recommended. Daptomycin should not be utilized when pneumonia is the primary source of infection.
	mecA/MREJ Positive (MRSA)	Vancomycin (per pharmacy)	Daptomycin	
Staphylococcus sp.* & *Staphylococcus epidermidis (<u>NOT</u> aureus or lugdunensis)	1 of 2 Positive	Probable contaminant. Consider withholding therapy. Do <u>not</u> need to routinely repeat BCx		*Staphylococcus epidermidis* mecA negative should be treated with cefazolin or naficillin.
	2 of 2 Positive	Vancomycin (per pharmacy)	Daptomycin	
Staphylococcus lugdunensis	*mecA Negative*	Cefazolin	Nafcillin	Consider ID consult.
	mecA Positive	Vancomycin (per pharmacy)	Daptomycin	
Streptococcus pyogenes (Group A, Beta hemolytic Strep) and ***Streptococcus agalactiae*** (Group B, Beta hemolytic Strep)		Penicillin G <u>*or*</u> Ampicillin <u>*or*</u> Cefazolin	Vancomycin (per pharmacy)	Beta-hemolytic strep are routinely susceptible to penicillin
Streptococcus pneumoniae	Pneumonia	Ampicillin	Cefazolin Ceftriaxone	Continue vancomycin in patients with suspected CNS infection until susceptibilities are available.
	CNS Infection	Vancomycin (per pharmacy) + Ceftriaxone		
Streptococcus species (NOT Group A, NOT Group B, NOT *pneumonia*e)	1 of 2 Positive	Possible contaminant, if no other source of infection, consider discussing with ID provider.		In severely ill or immunocompromised patients consider starting/continuing therapy until more definitive results are available.
	2 of 2 Positive	Ampicillin	Vancomycin (per pharmacy)	

Gram Negative Organisms (No resistance genes detected)			
Pathogen Detected	**Preferred Empiric Therapy**	**Alternative Therapy**	**Comments/Considerations** (Susceptibility data from 2023)
Acinetobacter calcoaceticus-baumannii complex	Meropenem 500mg IV q6h	Ampicillin/Sulbactam 3g IV q4h	Consider ID consult.
Bacteroides fragilis	Metronidazole	Piperacillin/Tazobactam	Usually part of underlying infection (i.e. intra-abdominal)
***Enterobacterales* order ONLY**	Cefepime 2g IV q8h (extended infusion over 4 hours)	Levofloxacin Meropenem	See list of potential pathogens in **Table 4** Contact microbiology, ID, or Antimicrobial Stewardship with questions
Enterobacter cloacae*	Cefepime 2g IV q8h (extended infusion over 4 hours)	Levofloxacin Meropenem	Cefepime: 97% susceptible Levofloxacin: 93% susceptible Meropenem: 96% susceptible
Escherichia coli	Ceftriaxone	Piperacillin/Tazobactam	Ceftriaxone: 95% susceptible Pip/Tazo: 98% susceptible
Klebsiella aerogenes*	Cefepime 2g IV q8h (extended infusion over 4 hours)	Levofloxacin Meropenem	Cefepime: 100% susceptible Levofloxacin: 98% susceptible Meropenem: 100% susceptible
Klebsiella oxytoca	Ceftriaxone	Piperacillin/Tazobactam Levofloxacin	Ceftriaxone: 100% susceptible Pip/Tazo: 100% susceptible Levofloxacin: 100% susceptible
***Klebsiella pneumoniae* group**	Ceftriaxone	Piperacillin/Tazobactam Levofloxacin	Ceftriaxone: 98% susceptible Pip/Tazo: 96% susceptible Levofloxacin: 92% susceptible
***Proteus* species**	Ceftriaxone	Piperacillin/Tazobactam Levofloxacin	Ceftriaxone: 96% susceptible Pip/Tazo: 100% susceptible Levofloxacin: 94% susceptible
***Salmonella* species**	Ceftriaxone		
Serratia marcescens	Ceftriaxone	Levofloxacin Meropenem	Ceftriaxone: 100% susceptible Levofloxacin: 100% susceptible Meropenem: 100% susceptible
Haemophilus influenza	Ampicillin/sulbactam *or* Ceftriaxone		De-escalate to ampicillin if beta-lactamase negative
Neisseria meningitidis	Ceftriaxone 2g IV q12h		*N. meningitidis* is associated with CNS infection. Rule out meningitis. Consider ID consult.
Pseudomonas aeruginosa	Cefepime 2g IV q8h (extended infusion over 4 hours)	Piperacillin/Tazobactam Ciprofloxacin	Cefepime: 99% susceptible Pip/Tazo: 96% susceptible Ciprofloxacin: 95% susceptible
Stenotrophomonas maltophilia	Sulfamethoxazole/Trimethoprim 15-20 mg/kg/day (TMP) in three divided doses	Levofloxacin	

*AmpC chromosomal and inducible organisms may develop resistance during prolonged therapy with third-generation cephalosporins. Therefore, isolates that are initially susceptible may become resistant within three to four days after initiation of therapy.

Yeast Organisms		
Pathogen Detected	**Preferred Empiric Therapy**	**Comments/Considerations**
Candida albicans	Micafungin	Repeat Blood cultures (BCx) and formal ID consult recommended.
Candida auris	Micafungin	
Candida glabrata	Micafungin	
Candida krusei	Micafungin	
Candida parapsilosis	Micafungin	
Candida tropicalis	Micafungin	
Cryptococcus neoformans/gattii	Liposomal amphotericin B 3mg/kg daily	

Resistance Genes		
IMP, KPC, OXA-48-like, NDM, VIM	ID consult Ceftazidime/avibactam 2.5g IV q8h (infused over 3 hours) **PLUS** aztreonam 2g IV q8h (infused over 3 hours) **at the same time** as ceftazidime/avibactam	Markers for carbapenem-resistance in gram negative pathogens
mcr-1	Consider ID consult	Marker for colistin resistance
CTX-M	Meropenem 500 mg IV q6h preferred therapy	Marker for most common extended spectrum β-lactamase (ESBL) found in gram-negative pathogens ESBLs hydrolyze expanded spectrum cephalosporins (ceftriaxone, cefepime) and piperacillin/tazobactam Negative results do not exclude the presence of other ESBL enzymes or other beta-lactamases
mecA/C	Vancomycin (pharmacy to dose)	mecA/C is a marker for methicillin/oxacillin resistance in non-*S. aureus Staphylococci*. Reported for *S. epidermidis* and *S. lugdunensis*.
mecA/C and MREJ	Vancomycin (pharmacy to dose)	MREJ is only evaluated in *S. aureus* and when present with mecA/C is specific for MRSA.
vanA/B	Linezolid 600 mg IV/PO q12h	Marker for vancomycin-resistant Enterococcus (VRE)

Table 4: Pathogens Detected by Blood Culture Identification Panel 2

Genus Specific Assay	Pathogens Detected by BCID2	Pathogens Not Detected By BCID2
Enterococcus BCID included a genus level assay for *Enterococcus*. BCID2 does not include this genus assay, only including species specific detection for the 2 major species associated with blood stream infections.	• E. faecium* • E. faecalis*	• *E. avium* • *E. casseliflavus* • *E. durans* • *E. gallinarum* • *E. hirae* • *E. dispar* • *E. saccharolyticus* • *E. raffinosus* • *E. mundtii*
Staphylococcus genus	It is predicted that only 5 species will not be detected. Of those, only *S. equorum* has been reported in a clinical setting.	• *S. equorum* • *S. fluerettii* • *S. lentus* • *S. muscae* • *S. rostri*
Streptococcus genus Designed to detect most Viridans group species and non-Group A/B beta hemolytic streptococci.	All species within the *Streptococcus* genus should be amplified by one or more of the assays on the panel at positive blood culture levels. Some species may not be detected if present in a blood culture at low levels or if they have variant sequences (see right).	• *S. equi* • *S. entericus* • *S. halitosis* • *S.hyovaginalis* • *S. minor* • *S. pantholopis* • *S. oralis* • *S. sobrinus* • *S. suis* • *S. uberis*
Enterobacterales Designed to detect less common gram-negative bacteria within multiple families of the order Enterobacterales. Information about the detection of specific subspecies, strains, isolates, or serotypes of gram-negative bacteria is provided in the product instructions for use (Table 98 – Table 112) available at www.biofiredx.com/support/documents.	• Cedeceae spp. • Citrobacter spp. • Cosenzaea spp. • Cronobacter spp. • Edwardsiella spp (In silico predication) • Enterobacter spp. • Escherichia spp. • Erwinia spp. • *Hafnia spp.* • *Klebsiella spp.* • *Kluyvera spp.* • *Kosakonia spp.* • *Leclercia spp.* • *Lelliottia spp.* • *Mixta spp.* • *Morganella spp.** • *Pantoea spp.* • *Phytobacter spp.* • *Plesiomonas spp.* • *Pluralibacter spp.* • *Providencia spp.** • *Proteus spp.* • *Pseudoescherchia spp* • *Rahnella spp.** • *Raoultella spp.* • *Salmonella spp.** • *Serratia spp.* • *Sodalis spp.* • *Shigella spp.* • *Tatumella spp.** • *Trabulsiella spp.* • *Yersinia spp.** • *Yokanella spp.*	• *Providencia heimbachae* • *Photorhabdus asymbiotica* • *Arsenophonus nasoniae*

***Indicates new species group detected by the BCID2 panel

References:

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2. Timbrook TT, Morton JB, McConeghy KW, Caffrey AR, Mylonakis E, LaPlante KL. The Effect of Molecular Rapid Diagnostic Testing on Clinical Outcomes in Bloodstream Infections: A Systematic Review and Meta-analysis. Clin Infect Dis. 2017;64(1):15-23. doi:10.1093/cid/ciw649
3. Pardo J, Klinker KP, Borgert SJ, Butler BM, Giglio PG, Rand KH. Clinical and economic impact of antimicrobial stewardship interventions with the FilmArray blood culture identification panel. Diagn Microbiol Infect Dis. 2016;84(2):159-164. doi:10.1016/j.diagmicrobio.2015.10.023
4. Messacar K, Hurst AL, Child J, et al. Clinical Impact and Provider Acceptability of Real-Time Antimicrobial Stewardship Decision Support for Rapid Diagnostics in Children With Positive Blood Culture Results. J Pediatric Infect Dis Soc. 2017;6(3):267-274. doi:10.1093/jpids/piw047
5. BioFire® Blood Culture Identification 2 (BCID2) Panel [product labeling: instructions for use]. BioFire Diagnostics, Salt Lake City, UT; updated June 2020.