Recommendations Regarding the Use of Blood Culture Identification 2 (BCID2) Panel Data

The Clinical Microbiology laboratory at Nebraska Medicine utilizes an FDA approved test called the BioFire® FilmArray® Blood Culture Identification Panel 2 (BCID2) This test uses a PCR-based approach to amplify DNA targets directly from positive blood cultures allowing rapid identification of pathogens and earlier transition to most appropriate therapy. This test identifies 30 different gram-negative, gram-positive, and yeast pathogens (**Table 1**). It also detects 10 genes associated with antimicrobial resistance, including those responsible for methicillin resistance in staphylococci, vancomycin resistance in enterococci, carbapenem-resistance in gram-negative bacteria, and one of the genes encoding an extended-spectrum β-lactamase. Additionally, the BCID2 detects some pathogens as a complex (*A. baumanii* complex), group (*K. pneumoniae* group), or genus (*Proteus* spp).

Table 1: List of Pathogens and Resistance Genes Detected

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

The microbiology lab notifies clinicians of positive blood culture gram-stain results immediately after they are performed. The BCID2 assay is subsequently performed, and results are typically available within One Chart in <2 hours. The rapid reporting of these data allows for early adjustment of antimicrobials to the most appropriate therapy. A list of recommended antibiotic treatment choices is outlined in **Table 3**. The Antimicrobial Stewardship Team developed these recommendations based on an analysis of the institutional antibiogram. Relevant information on susceptibility is provided for gram-negative pathogens where the activity of agents is variable. When blood culture Gram stain and BCID results are known, current antimicrobial therapy should be evaluated considering the clinical picture and adjusted to the most appropriate single agent if

possible. In addition, when full susceptibility results become available, therapy should be adjusted to the narrowest spectrum appropriate agent.

Final pathogen susceptibilities are usually available in 24-72 hours and should always be reviewed to determine if therapy adjustments should be made.

Evidence Demonstrating the Benefit of BCID Use

IDSA guidelines advocate for the use of rapid diagnostic testing on blood specimens to optimize antibiotic therapy and improve clinical outcomes.[2] Multiple studies, including a large meta-analysis, have shown that rapid pathogen identification when coupled with stewardship interventions can result in improved antibiotic use, shorter hospital stays, reduced cost, and decreased patient mortality (OR 0.64; 95% CI 0.51-0.79; NNT 17).[2-4] Review of BCID implementation at Nebraska Medicine demonstrated earlier implementation of active therapy (6 hours earlier) and more rapid transition to the narrowest spectrum effective therapy (12 hours earlier). The utility and cost-effectiveness of such testing is dependent upon clinicians reacting to the data. The antimicrobial stewardship team currently reviews these data during business hours and contacts the treating team if they feel adjustments in therapy are needed, but it is strongly recommended that these data be utilized in making treatment decisions at the time it is available.

BCID2 Performance

The clinical performance of the BCID2 Panel was established with a prospective multi-center study (comparator was standard manual and automated microbiological/biochemical identification methods) that was supplemented with archived and seeded positive blood culture specimens. Aggregate data suggests that BCID2 has 99% sensitivity and 99.8% specificity. The BCID2 test is highly accurate in monomicrobial bacteremia but in the rare incidence of polymicrobial bacteremia it may suffer from some degradation in accuracy. Polymicrobial Gram stain results and BCID2 results with multiple organisms detected should be interpreted with caution.

Certain infections may be polymicrobial in nature and the isolation of a single pathogen from the blood culture, while allowing narrowing of therapy, should not result in over-narrowing. An example would be complicated intra-abdominal infections where anaerobes are frequently present and therapy active against these pathogens should generally be included until definitive cultures of the site of infection have returned.

Interpreting Genotypic Resistance Data

The BCID2 detects common genetic markers associated with resistance to antibiotics. These are useful for determining if initial therapy is likely to be active and can assist in de-escalation of antibiotics as well. It should be noted that the detection of a resistance gene does not always equate to confirmation of resistance when susceptibility testing is performed. Additionally, the limited panel of resistance genes present does not encompass all mechanisms of resistance, particularly in gram-negative pathogens. Within the *Enterobacterales*, resistance to expanded spectrum cephalosporins is mediated via a variety of β-lactamases. While CTX-M is the most common extended-spectrum beta-lactamase (ESBL) encountered, even if it is not detected, the isolate can still be resistant to expanded-spectrum cephalosporins via other β-lactamases not detected by the BCID2 panel. To assist with this, we have developed a genotypic antibiogram for the organism where CTX-M is most common (*E. coli* and *Klebsiella pneumoniae*) which is below. These data as well as the antibiogram data have been incorporated into the recommendations found in Table 3. Finally, phenotypic susceptibility testing is required to determine final antimicrobial susceptibility and should be used to guide final therapy decisions.

Genotypic Gram Negative Blood Antibiogram† **Aug 1, 2021 - Nov 1, 2022** Inpatients only, first isolate per patient	**# Isolates**	Amikacin	Ampicillin (Amox)	Amp/Sulbactam	Amox/Clavulanate	Aztreonam	Cefazolin (1st gen)	Cefuroxime-PO (2nd)	Cefoxitin (2nd)	Ceftriaxone (3rd)	Ceftazidime (3rd)	Cefepime (4th)	Ertapenem	Gentamicin	Levofloxacin	Meropenem	Piperacillin/Tazo	Sulfa/Trim	Tetracycline	Tobramycin
Escherichia coli	**249**	99	44	58	86	82	62	69	94	81	83	85	100	87	73	100	98	72	70	86
CTX-M Detected	41	95	0			5	0	0		0	17	12	100	63	17	100		59	44	56
No CTX-M Detected	208	100	52	64	88	98	74	83	94	97	96	100	100	91	84	100	99	75	75	91
Klebsiella pneumoniae	**64**	98	R	84	88	91	81	80	94	91	91	92	98	95	94	100	94	84	77	89
CTX-M Detected	6*	83	R			0	0	0		0	0	17	83	50	67	100		0	17	0
No CTX-M Detected	58	100	R	93	97	100	90	88	95	100	100	100	100	100	97	100	97	93	83	98
*Use caution interpreting results with < 30 isolates							R = intrinsically resistant													
Green background = most likely susceptible, Yellow = possibly susc, Red = unlikely to be susceptible (avoid empirically)																				
†For use in blood stream infections with BCID2 results																				

Common Misinterpretation of Results from Rapid Blood Culture Identification Panel

The BCID2 identifies pathogens to the genus (*Staphylococcus, Streptococcus*) or family-level (*Enterobacterales* order, formerly *Enterobacteriaceae*). Some confusion has been noted with interpretation of these analytes as well as markers of antimicrobial resistance. A genus includes numerous bacterial species. For example, the *Staphylococcus* genus PCR detects multiple species of staphylococci including *S. aureus*, *S. epidermidis*, *S. hominis*, and others. When *S. aureus* is present, the *Staphylococcus* genus and *S. aureus* analytes will both be detected. Similarly, when *S. epidermidis* is present, both the *Staphylococcus* genus and the *S. epidermidis* markers will be positive. But when a coagulase-negative staphylococcus such as *S. hominis* is present, only the *Staphylococcus* genus analyte will be detected. Further, the *mecA/C* genes confer resistance to β-lactam antibiotics such as oxacillin in staphylococci and therapy should be adjusted to account for these results. However, for oxacillin resistance to be detected in *S. aureus* (MRSA), both the *mecA/C* gene and the MREJ target (which detects the far-right extremity of *SCCmec* and *orFX* and is a *S. aureus* specific target) need to be

detected. Thus, detection of *mecA/C*/MREJ suggests MRSA is present and vancomycin or daptomycin should be used (see **Table 2**). The detection of only *mecA* without MREJ when *Staphylococcus* genus and *S. aureus* are positive indicates that a Coagulase-negative Staphylococci (e.g. MRSE) may also be present in addition to *S. aureus*. The *mecA/C* result is only reported when one of the specific Staphylococcal species is detected (*S. aureus*, *S. epidermidis*, or *S. lugdunensis*). Thus, if only the *Staphylococcus* genus is detected *mecA/C* will not be reported.

Another area of confusion is with the *Enterobacterales* order (formerly *Enterobacteriaceae*). Families within this order encompass many gram-negative organisms including *E. coli*, *Klebsiella* species, *Enterobacter* species, *Proteus* species and *Citrobacter* species, among others. Thus, when *E. coli* is present, both the *Enterobacterales* and *E. coli* analytes will be positive. If an *Enterobacterales* order member that does not have a species-specific PCR target is present (e.g. *Citrobacter* species), only the *Enterobacterales* analyte will be positive.

Occasionally the BCID2 panel will be completely negative. In those cases, please refer to the Negative BCID result document for potential pathogens and antibiotic recommendations.

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

Bacterial Marker	Result	Interpretation
Staphylococcus *S. aureus, S. epidermidis, S. lugdunensis*	Detected Not detected	Coagulase-negative *Staphylococcus* species (methicillin-resistance unknown)
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 pneumoniae** (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 5)

* There is very small chance that both the specific pathogen and another *Enterobacterales* which cannot be 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 Therapy

Use this table to select the most appropriate empiric therapy for treating a blood stream infection (BSI). Data on susceptibility for various gram-negative pathogens was derived from the 2023 institutional antibiograms including a bloodstream infection specific antibiogram (see **Table 4**).

- Patients who have responded clinically to a narrow spectrum agent do not need to have their antimicrobial therapy escalated and should continue their current therapy, even if this guideline recommends a broader spectrum agent.
- Patients who have not clinically responded to initial therapy (persistent fever, lack of improvement, etc.) may have their therapy adjusted to a more active regimen based on the guideline.
- Allergies, organ dysfunction, and risk factors for or personal history of antimicrobial resistance should be considered when choosing therapy.
- Double coverage of gram-negative pathogens is not generally recommended and if started can usually be discontinued based on pathogen identification although there are certain pathogens where it may be considered which are noted within the guideline.

BCID2 Result	Preferred Therapy	Comments
Gram Positive Pathogens		
Enterococcus faecalis *Van A/B* negative=vancomycin susceptible	<u>*Van A/B* Negative:</u> Ampicillin 2g IV q4h	Ampicillin: 100% susceptible Severe PCN allergy: Vancomycin
Van A/B positive= VRE (very uncommon)	<u>*Van A/B* Positive:</u> Ampicillin 2g IV q4h	Evaluation for endocarditis recommended with *E. faecalis* bacteremia
Enterococcus faecium *Van A/B* negative=vancomycin susceptible	<u>*Van A/B* Negative:</u> Vancomycin 15 mg/kg IV with pharmacy to dose	Vancomycin: 100% susceptible in Van A/B negative isolates
Van A/B positive= VRE (common)	<u>*Van A/B* Positive:</u> Linezolid 600 mg IV/PO q12h	**Consider ID consult.** Daptomycin 10 mg/kg IV q24h is an alternative, but less active, requires susceptibility confirmation, and ID consult.
Listeria monocytogenes	Ampicillin 2g IV q4h	Severe PCN allergy: TMP/SMX
***Staphylococcus* genus with other Staph species negative** <u>Blood Culture (BCX) result:</u> 1 of 2 sets positive	**Do not start antibiotics or draw repeat blood cultures** as likely contaminant.	In critically ill patients already on antibiotics, continue current therapy until more definitive results return
2 of 2 positive (*mecA* not reported when only *Staphylococcus* genus detected)	Vancomycin 15 mg/kg IV with pharmacy to assist in dosing	Daptomycin 6 mg/kg IV q24h is an alternative

Staphylococcus aureus *(Staph species +)* *mecA/C* and MREJ negative = MSSA *mecA/C* and MREJ positive = MRSA	 <u>*mecA/C* and MREJ Negative:</u> Cefazolin 2g q8h <u>*mecA/C* and MREJ Positive:</u> Vancomycin 15 mg/kg IV with pharmacy to dose	**ID consult required by hospital policy** Oxacillin 2g IV q4h is an alternative Daptomycin 6 mg/kg IV q24h is an alternative to vancomycin
Staphylococcus epidermidis *(Staph species +)* <u>Blood Culture (BCX) result:</u> 1 of 2 positive 2 of 2 positive *mecA* negative = oxacillin susceptible *mecA* positive = oxacillin resistant	 **Do not start antibiotics or draw repeat blood cultures as likely contaminant.** <u>*mecA* Negative</u>: Cefazolin 2g IV q8h <u>*mecA* Positive:</u> Vancomycin 15 mg/kg IV with pharmacy to dose	 In critically ill patients already on antibiotics, continue current therapy until more definitive results return. Oxacillin 2g q4h is an alternative Daptomycin 6 mg/kg q24h is an alternative to vancomycin
Staphylococcus lugdunensis *(Staph species +)* *mecA* negative = oxacillin susceptible *mecA* positive = oxacillin resistant	 <u>*mecA* Negative</u>: Cefazolin 2g IV q8h <u>*mecA* Positive:</u> Vancomycin 15 mg/kg IV with pharmacy to dose	 Oxacillin 2g q4h IV is an alternative **Consider ID Consult.** While a coagulase-negative species, infections are similar to *S. aureus*. If 1 of 2 blood cultures positive, may still be a contaminant, but favor treatment and repeating blood cultures.
Streptococcus **genus detected, with other Strep species negative** <u>Blood Culture (BCX) result:</u> 1 of 2 positive 2 of 2 positive	 **Do not start antibiotics or draw repeat blood cultures as likely contaminant.** Ceftriaxone 2g IV q24h	 In critically ill patients already on antibiotics, continue current therapy until more definitive results return. Vancomycin is an alternative in severe beta-lactam allergy
Streptococcus pyogenes (Group A Strep) and ***Streptococcus agalactiae*** (Group B Strep)	Penicillin 3 million units IV q4h **OR** Ampicillin 2g IV q4h **OR** Cefazolin 2g IV Q8h	Beta-hemolytic strep are routinely susceptible to beta-lactam antibiotics. If in shock consult ID to determine if combination therapy needed Severe PCN allergy: Cefazolin (or Ceftriaxone) based on patient assessment
Streptococcus pneumoniae <u>Source of Infection:</u> Pneumonia	 Penicillin 3 million units IV q4h **OR** Ampicillin 2g IV q4h	 PCN highly active against pneumococcus Severe PCN allergy: Ceftriaxone

CNS Infection	Ceftriaxone 2g IV q12h **PLUS** Vancomycin 15 mg/kg IV with pharmacy to dose	Continue vancomycin until susceptibilities return
Gram Negative Pathogens		
***Enterobacterales* order only** *CTX-M* detected = Extended-Spectrum Beta-Lactamase (ESBL) present *KPC, IMP, VIM, NDM,* or *OXA-48* detected = Carbapenemase present	CTX-M Negative: Cefepime 1g IV q6h **OR** Piperacillin/tazobactam 4.5 g IV q8h over 4 hours CTX-M Positive or Nosocomial Onset: Ertapenem 1g IV q24h **OR** Meropenem IV 500mg q6h **Carbapenemase positive: Consult ID**	Formerly *Enterobacteriaceae*. Note: this is a group of possible enteric Gram-negative organisms, not a specific bacterial genus. See Table 5 for potential pathogens included in this group.
***Acinetobacter baumannii* complex** CTX-M and Carbapenemase genes are uncommon. If detected consult ID.	Meropenem 500 mg IV q6h **OR** Ampicillin/Sulbactam 4.5g IV q6h	Meropenem: 91-100% susceptible (cumulative) Levofloxacin: 92-100% susceptible (cumulative) Cefepime: 84-91% susceptible (cumulative) Ampicillin/Sulbactam: 91% susceptible (cumulative) If critically ill or non-responding, consult ID
Bacteroides fragilis	Metronidazole 500 mg IV/PO q8h	Anerobic organism usually part of polymicrobial infections (i.e. intra-abdominal, etc.) Piperacillin/tazobactam alternative to metronidazole
***Enterobacter cloacae* complex** *CTX-M* detected = ESBL present (Uncommon in this pathogen) *KPC, IMP, VIM, NDM, or OXA-48* detected = Carbapenemase present	CTX-M Negative: Cefepime 1 g IV q6h CTX-M Positive or Nosocomial-onset: Meropenem 500 mg IV q6h **Carbapenemase positive: Consult ID**	Cefepime: 91% susceptible (cumulative) • 95% CO susceptible (blood) • 90% NO susceptible (blood) Meropenem: 100% susceptible Levofloxacin: 94-100% susceptible Ertapenem: 85% susceptible (cumulative) • 90% CO susceptible (blood) • 76% NO susceptible (blood) Piperacillin/tazobactam: 81% susceptible (cumulative) • 90% CO susceptible (blood) • 71% NO susceptible (blood)
Escherichia coli *CTX-M* detected = ESBL present *KPC, IMP, VIM, NDM,* or *OXA-48* detected = carbapenemase present	*CTX-M is the primary mechanism of resistance and takes precedence over antibiogram data. Use genotypic antibiogram to determine therapy.* CTX-M Negative: Ceftriaxone 2g IV q24h CTX-M Positive: Ertapenem 1g IV q24h **OR** Meropenem 500mg IV q6h **Carbapenemase positive: Consult ID**	**Genotypic Antibiogram CTX-M negative:** • Ceftriaxone, Piperacillin/tazobactam, and Cefepime: 97-100% susceptible Ceftriaxone: 81% susceptible (cumulative) • 84% CO susceptible (blood) • 68% NO susceptible (blood) Pip/tazo: 80% susceptible (cumulative) • 83% CO susceptible (blood) • 68% NO susceptible (blood) Cefepime: 83% susceptible (cumulative) • 85% CO susceptible (blood) • 71% NO susceptible (blood) Levofloxacin: 76% susceptible (cumulative) • 78% CO susceptible (blood) • 57% NO susceptible (blood) Ertapenem/Meropenem: 99-100% susceptible

Klebsiella (Enterobacter) aerogenes *CTX-M* detected = ESBL present (Uncommon in this pathogen) *KPC, IMP, VIM, NDM,* or *OXA-48* detected= Carbapenemase present	CTX-M Negative: Cefepime 1 g IV q6h CTX-M Positive OR Nosocomial: Meropenem 500mg IV q6h **Carbapenemase positive: Consult ID**	Cefepime: 92% susceptible (cumulative) • 89% CO susceptible (blood) • 76% NO susceptible (blood) Piperacillin/tazobactam: 82% susceptible • 73% CO susceptible (blood) • 54% NO susceptible (blood) Ertapenem: 97% susceptible (cumulative) • 100% CO susceptible (blood) • 72% NO susceptible (blood) Meropenem: 100% susceptible Levofloxacin: 98% susceptible (cumulative) • 100% CO susceptible (blood) • 90% NO susceptible (blood)
Klebsiella oxytoca *CTX-M* detected = ESBL present (Uncommon in this pathogen) *KPC, IMP, VIM, NDM, or OXA-48* detected = Carbapenemase present	CTX-M Negative **AND** Community-onset: Ceftriaxone 2gIV daily **OR** Levofloxacin 750mg IV/PO daily CTX-M Positive **OR** Nosocomial-onset: Ertapenem 1g IV q24h **OR** Meropenem 500mg IV q6h **Carbapenemase positive: Consult ID**	Cefepime: 80% susceptible (cumulative) • 92% CO susceptible (blood) • 57% NO susceptible (blood) Piperacillin/tazobactam: 75% susceptible (cumulative) • 92% CO susceptible (blood) • 50% NO susceptible (blood) Ertapenem/Meropenem: 92-96% susceptible Levofloxacin: 96% susceptible (cumulative) • 100% CO susceptible (blood) • 85% NO susceptible (blood) Ceftriaxone: 75% susceptible (cumulative) • 92% CO susceptible (blood) • 50% NO susceptible (blood)
***Klebsiella pneumoniae* group** *CTX-M* detected = ESBL present *KPC, IMP, VIM, NDM, or OXA-48* detected = Carbapenemase present	*CTX-M is the primary mechanism of resistance and takes precedence over antibiogram data. Use genotypic antibiogram to determine therapy.* CTX-M Negative: Ceftriaxone 2g IV q24 **OR** Levofloxacin 750mg IV/PO daily CTX-M Positive: Ertapenem 1g IV q24h **OR** Meropenem 500mg IV q6h **Carbapenemase positive: Consult ID**	Ceftriaxone: 84% susceptible (cumulative) • 92% CO susceptible (blood) • 67% NO susceptible (blood) Piperacillin/tazobactam: 82% susceptible (cumulative) • 92% CO susceptible (blood) • 58% NO susceptible (blood) Cefepime: 85% susceptible (cumulative) • 92% CO susceptible (blood) • 67% NO susceptible (blood) Levofloxacin: 91% susceptible (cumulative) • 96% CO susceptible (blood) • 80% NO susceptible (blood) Ertapenem/Meropenem: 98-100% susceptible
***Proteus* spp.** *CTX-M* detected = ESBL present *KPC, IMP, VIM, NDM, or OXA-48* detected = Carbapenemase present	CTX-M Negative: Ceftriaxone 2g IV q24 **OR** Ampicillin/Sulbactam 3g IV q6h CTX-M Positive: Ertapenem 1g IV q24h **OR** Meropenem 500mg IV q6h **Carbapenemase positive: Consult ID**	Ceftriaxone: 94% susceptible (cumulative) • 92% susceptible (blood) Ampicillin/sulbactam: 90% cumulative • 90% susceptible (blood) Pip/tazo: 94% cumulative • 97% susceptible (blood) Ertapenem/Meropenem: 100% susceptible

***Salmonella* spp.** *CTX-M* detected = ESBL present *KPC, IMP, VIM, NDM, or OXA-48* detected = Carbapenemase present	CTX-M Negative: Ceftriaxone 2g IV q24 CTX-M Positive: Ertapenem 1g IV q24h **OR** Meropenem 500mg IV q6h **Carbapenemase positive: Consult ID**	Ceftriaxone: 94% susceptible Ampicillin: 86% susceptible Ciprofloxacin: 81% susceptible TMP/SMX: 92% susceptible
Serratia marcescens *CTX-M* detected = ESBL present (Uncommon in this pathogen) *KPC, IMP, VIM, NDM, or OXA-48* detected= carbapenemase present	CTX-M Negative: Cefepime 1g IV q6h CTX-M Positive: Ertapenem 1g IV q24h **OR** Meropenem 500mg IV q6h **Carbapenemase positive: Consult ID**	Cefepime: 100% susceptible Levofloxacin: 89-95% susceptible TMP/SMX: 95-100% susceptible Ertapenem: 93-100% susceptible Meropenem: 100% susceptible
Haemophilus influenzae	Ampicillin/sulbactam 3g IV q6h **OR** Ceftriaxone 2g IV q24h	
Neisseria meningitidis	Ceftriaxone 2g IV q12h	Can change to Q24h if CNS infection ruled out
Pseudomonas aeruginosa CTX-M and Carbapenemase genes are uncommon. If detected consult ID. *Consider tobramycin combination therapy or Ceftolozane/tazobactam in critically ill, nosocomial, or non-responding patients*	Piperacillin/tazobactam 4.5 g IV q8h infused over 4h +/- Tobramycin 7 mg/kg IV q24h (pharmacy to dose) **OR** Ceftolozane/tazobactam 3g IV q8h infused over 3 hours (ID consult required)	Cefepime: 87% susceptible (cumulative) • 86% CO susceptible (blood) • 78% NO susceptible (blood) Piperacillin/tazobactam: 88% susceptible (cumulative) • 86% CO susceptible (blood) • 80% NO susceptible (blood) Meropenem: 88% susceptible (cumulative) • 92% CO susceptible (blood) • 82% NO susceptible (blood) Ceftolozane/tazobactam: 97-100% susceptible Levofloxacin: 73-88% susceptible Tobramycin: 95-100% susceptible
Stenotrophomonas maltophilia	Sulfamethoxazole/trimethoprim 8-12 mg/kg (TMP component) IV/PO in three divided doses daily	TMP/SMX: 98-100% susceptible Levofloxacin: 90-100% susceptible
Yeast Pathogens		
Candida albicans	Micafungin 100mg IV q24h	Micafungin: 99% susceptible Fluconazole: 92% susceptible (could consider in stable patient without previous azole exposure)
Candida auris	Micafungin 100 mg IV q24h	**Consult ID** Emerging yeast pathogen that is often drug resistant, requires enhanced contact isolation
Candida glabrata	Micafungin 100mg IV q24h	Micafungin: 93% susceptible
Candida krusei	Micafungin 100mg IV q24h	Micafungin: 100% susceptible

Candida parapsilosis	Fluconazole 12mg/kg load, then 6mg/kg IV q24h **OR** Micafungin 100mg IV q24h	Consider micafungin if previous azole exposure
Candida tropicalis	Micafungin 100mg IVq24h	Micafungin: 93% susceptible
Cryptococcus neoformans/gattii	Liposomal amphotericin B 3mg/kg IV q24h	**Consult ID to determine need for flucytosine**
Gram Negative Resistance Genes		
IMP, KPC, NDM, VIM, or OXA-48-like	**Consult ID**	Markers for carbapenem-resistance in gram negative pathogens (i.e. CRE)
mcr-1	**Consult ID**	Marker for colistin resistance, a drug used in multi-drug-resistant gram-negative infections
CTX-M	Ertapenem 1g IV q24h **OR** Meropenem 500mg IV q6h	Marker for most common extended spectrum β-lactamase (ESBL) found in gram-negative pathogens (esp. *E. coli* and *Klebsiella* sp.) ESBLs hydrolyze expanded spectrum cephalosporins (ceftriaxone, cefepime) and piperacillin/tazobactam A negative result does not exclude the presence of other ESBL enzymes or other beta-lactamases although in organisms such as *E. coli* and *K. pneumoniae* other beta-lactamases are very unlikely
Gram Positive Resistance Genes		
mecA/C ***mecA/C and* MREJ**	Vancomycin	*mecA/C* is a marker for methicillin/oxacillin-resistance and is reported alone in non-*S. aureus Staphylococci (*i.e.= MRSE). MREJ is only evaluated in *S. aureus* and when present with *mecA/C* is specific for MRSA.
vanA/B	Linezolid 600mg IV/PO q12h **Consider ID consult**	Marker for vancomycin-resistant Enterococcus (i.e.= VRE)

Abbreviations: CO= community onset, NO= nosocomial onset

Table 4: Nebraska Medicine Bloodstream Infection Antibiograms

Data generated over 2 years (2022-3) for Nebraska Medical Center location only. Gram negative organisms presented for community-onset (BSI within 72 hours admission) and nosocomial-onset (BSI >72 hours after admission)

Cumulative Blood Culture Antibiogram **Nebraska Medical Center** **Jan 1 2022 - Dec 31, 2023** Admitted patients only, first isolate per patient	Isolates	Ampicillin	Cefazolin	Ceftriaxone	Cefepime	Clindamycin	Daptomycin	Erythromycin	Levofloxacin	Linezolid	Meropenem	Oxacillin	Penicillin	Tetracycline	TMP/SMX	Vancomycin
GRAM POSITIVE ORGANISMS																
Staphylococcus aureus	400	R	72			77	99	57	76	100		72	R	93	98	100
Methicillin-resistant Staphylococcus aureus	111	R	R	R	R	66	99	22	29	100	R	0	R	92	94	100
CoNS	284	R	100			49	100	37	54	100		33	R	85	49	100
Staphylococcus epidermidis	250	R	26			44	100	31	51	100		26	R	84	43	100
Staphylococcus lugdunensis	13	R	100			84	100	76	81	100		84	R	84	92	100
Enterococcus faecalis	124	100	R	R	R	R	99	31	89	99			100	37	R	100
Enterococcus faecium	71	11	R	R	R	R	67	15	11	98			11	19	R	36
Vancomycin-resistant Enterococcus faecium	47	0	R	R	R	R	72	14	2	100			0	10	R	R
Viridans Strep	106	74		95	92	91		39	81		100		73	71		98
Streptococcus pneumoniae	50	100		100	100	100		93	98		98		94	90	93	100

Daptomycin not corrected for E-Test Yet

Cumulative Blood Culture Antibiogram **Nebraska Medical Center** **Jan 1 2022 - Dec 31, 2023** Admitted patients only, first isolate per patient (time after admission <72 (community) or >72 hours (nosocomial))	Isolates	Amikacin	Amoxicillin/Clavulanate	Ampicillin	Ampicillin/Sulbactam	Aztreonam	Cefazolin	Ceftriaxone	Ceftazidime	Cefepime	Ceftolozane/Tazobactam	Ceftazidime-Avibactam	Ertapemen	Gentamicin	Levofloxacin	Meropenem	Meropenem/Vaborbactam	Pip/Tazo	Tetracycline	Tigecycline	TMP/SMX	Tobramycin
GRAM NEGATIVE ORGANISMS																						
Escherichia coli (community)	347	99	77	47	55	85	66	84	84	85	99	99	99	87	78	99	99	83	69	100	72	86
Escherichia coli (nosocomial)	73	100	58	35	43	69	53	68	67	71	98	100	100	86	57	100	100	68	76	100	72	89
Klebsiella pneumoniae (community)	98	100	92	0	90	93	89	92	92	92	98	98	98	96	96	98	100	92	85	98	85	95
Klebsiella pneumoniae (nosocomial)	31	96	51	0	48	67	48	67	67	67	100	100	100	90	80	100	100	58	61	90	61	87
Pseudomonas aeruginosa (community)	51	98	R	R	R	80	R	R	90	86	100	94	R	92	88	92		86	R	R	R	100
Pseudomonas aeruginosa (nosocomial)	41	97	R	R	R	73	R	R	80	78	97	97	R	92	73	82		80	R	R	R	97
Enterobacter cloacae (community)	43	100	R	R	R	93	R	81	93	95			90	97	97	100	100	90	90	95	95	97
Enterobacter cloacae (nosocomial)	21	100	R	R	R	71	R	66	71	90			76	100	100	100	100	71	95	100	95	100
Proteus mirabilis (community)	36	100	91	86	91	100	77	94	100	100	100	100	100	97	88	100	100	100	R		88	97
Proteus mirabilis (nosocomial)	5	100	80	80	80	80	80	80	80	80	100	100	100	60	80	100	100	80	R		80	60
Klebsiella oxytoca (community)	28	100	92	0	78	92	32	92	92	92	100	100	96	96	100	96	100	92	96	100	92	96
Klebsiella oxytoca (nosocomial)	14	92	35	0	21	50	14	50	57	57	78	100	92	71	85	92	100	50	50	100	57	57
Serratia marcescens (community)	23	100	R	R	R	91	R	73	78	100	100	100	100	100	95	100	100	95	21	100	95	95
Serratia marcescens (nosocomial)	10	100	R	R	R	90	R	70	80	100	100	100	100	100	90	100	100	90	30	100	100	100
Klebsiella aerogenes (community)	15	100	R	R	R	100	R	66	73	100		100	100	100	100	100	100	73	86	100	93	100
Klebsiella aerogenes(nosocomial)	11	100	R	R	R	63	R	27	45	90		100	72	100	90	100	100	54	81	90	90	100
Morganella morganii (community only)	8	100	R	R	R	87	R	75	75	100	87	100	100	75	62	100	100	100	62	R	75	87
Citrobacter freundii complex (community)	5	100	R	R	R	100	R	100	100	100		100	100	100	100	100		100	100	100	60	100
Citrobacter freundii complex (nosocomial)	10	100	R	R	R	50	R	40	40	90		100	100	100	80	100		100	90	100	80	100

Table 5: Pathogens Detected by BCID2

Genus Specific Assay	Pathogens Detected		Pathogens Not Detected
Enterococcus	*E. faecium* *E. faecalis*		All other Enterococcus species including: *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 Viridians group species and non-Group A/B beta-hemolytic streptococci.	All species within the *Streptococcus* genus should be amplified by one of the assays on the panel 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.	*Providencia* spp. *Proteus* spp. *Pseudoescherchia* spp. *Rahnella* spp. *Raoultella* spp. *Salmonella* spp. *Serratia* spp. *Sodalis* spp. *Shigella* spp. *Tatumella* spp. *Trabulsiella* spp. *Yersinia* spp. *Serratia* spp. *Sodalis* spp. *Shigella* spp. *Tatumella* spp. *Trabulsiella* spp. *Yersinia* spp. *Yokanella* spp.	*Providencia heimbachae* *Photorhabdus asymbiotica* *Arsenophonus nasoniae*

	Plesiomonas spp. *Pluralibacter* spp.		

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