BioFire® Blood Culture Identification 2 Panel (BCID2)®

What is it?

A multiplex PCR test that detects 33 pathogens and 10 genetic resistance markers directly from positive blood culture bottles. Results are available about an hour after the test is initiated. This technology informs decision making when moving from empiric to targeted antimicrobial therapy earlier in treatment.

What does it identify?

<table>
<tr><th>Gram Positive (+) Bacteria</th><th colspan="2">Gram Negative (-) Bacteria</th></tr>
<tr><td>Enterococcus faecalis
Enterococcus faecium
Listeria monocytogenes
Staphylococcus species
• Staphylococcus aureus
• Staphylococcus epidermidis
• Staphylococcus lugdunensis
Streptococcus species
• Streptococcus agalactiae
• Streptococcus pyogenes
• Streptococcus pneumoniae</td><td>Enterobacterales
• Enterobacter cloacae complex
• Escherichia coli
• Klebsiella aerogenes
• Klebsiella oxytoca
• Klebsiella pneumoniae group
• Proteus species
• Salmonella species
• Serratia marcescens</td><td>Acinetobacter calcoaceticus-baumannii complex
Bacteroides fragilis
Haemophilus influenzae
Neisseria meningitidis
Pseudomonas aeruginosa
Stenotrophomonas maltophilia</td></tr>
<tr><th>Gram Positive (+) Resistance Genes</th><th colspan="2">Gram Negative (-) Resistance Genes</th></tr>
<tr><td><u>Methicillin Resistance:</u>
mecA/C
mecA/C and MREJ (MRSA)

<u>Vancomycin Resistance:</u>
vanA/B</td><td colspan="2"><u>Carbapenemases:</u>
IMP
KPC
OXA-48-like
NDM
VIM

<u>Colistin Resistance:</u>
mcr-1

<u>Extended Spectrum Beta-Lactamases (ESBL):</u>
CTX-M</td></tr>
<tr><th>Yeast</th><td colspan="2" rowspan="2"></td></tr>
<tr><td>Candida albicans
Candida auris
Candida glabrata
Candida krusei
Candida parapsilosis
Candida tropicalis
Cryptococcus neoformans/gattii</td></tr>
</table>

Table 1. <u>Note:</u> The BCID2 panel is **ONLY** capable of detecting organisms and resistance genes included in the list above. Absence of a detected organism does **NOT** indicate a false-positive culture or reporting error.

How is it performed?

The test is not ordered. It is performed <u>automatically</u> on **positive** blood samples meeting one of the following criteria:

- All positive blood cultures with a gram positive, gram negative, or fungal organism seen on gram stain

<u>Note</u>: The BCID2 panel will be performed on the first blood sample meeting testing criteria and will not be repeated on samples collected in the subsequent 72 hours. <u>All samples will receive standard culture testing as well.</u>

How are results reported?

Results will appear within the blood culture report or as **Rapid Blood Culture Identification** under the micro tab, indicating the genus or species identified by multiplex PCR. When the organism identification and susceptibilities from standard testing are available, the culture report will be updated with this new information below the BCID2 result as shown below:

Example:

Blood Culture — Escherichia coli ESBL !

ESBL Extended Spectrum Beta-lactamase Producer.

Component	Ref Range & Units	
Acinetobacter calcoaceticus -baumannii complex PCR	Not Detected	Not Detected
Bacteroides fragilis PCR	Not Detected	Not Detected
Enterobacterales PCR	Not Detected	Detected !
Enterobacter cloacae complex PCR	Not Detected	Not Detected
Escherichia coli PCR	Not Detected	Detected !
Klebsiella aerogenes PCR	Not Detected	Not Detected
Klebsiella oxytoca PCR	Not Detected	Not Detected
Klebsiella pneumoniae Group PCR	Not Detected	Not Detected
Proteus species PCR	Not Detected	Not Detected
Salmonella species PCR	Not Detected	Not Detected
Serratia marcescens PCR	Not Detected	Not Detected
Haemophilus influenzae PCR	Not Detected	Not Detected
Neisseria meningitidis PCR	Not Detected	Not Detected
Pseudomonas aeruginosa PCR	Not Detected	Not Detected
Stenotrophomonas maltophilia PCR	Not Detected	Not Detected
Enterococcus faecalis PCR	Not Detected	Not Detected
Enterococcus faecium PCR	Not Detected	Not Detected
Staphylococcus PCR	Not Detected	Not Detected
Staphylococcus aureus PCR	Not Detected	Not Detected
Staphylococcus epidermidis PCR	Not Detected	Not Detected
Staphylococcus lugdunensis PCR	Not Detected	Not Detected
Streptococcus PCR	Not Detected	Not Detected
Streptococcus agalactiae PCR	Not Detected	Not Detected
Streptococcus pneumoniae PCR	Not Detected	Not Detected
Streptococcus pyogenes PCR	Not Detected	Not Detected
Candida albicans PCR	Not Detected	Not Detected
Candida auris PCR	Not Detected	Not Detected
Candida glabrata PCR	Not Detected	Not Detected
Candida krusei PCR	Not Detected	Not Detected
Candida parapsilosis PCR	Not Detected	Not Detected
Candida tropicalis PCR	Not Detected	Not Detected
Cryptococcus neoformans/gatti PCR	Not Detected	Not Detected
Kpc Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Detected
MCR-1 Resistant Gene	Not Detected, Not Applicable	Not Detected
Imp Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Detected
Oxa-48-Like Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Detected
Ndm Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Detected
Vim Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Detected
CTX-M Cephalosporin Resistance Gene	Not Detected, Not Applicable	Detected !

What decisions can be made based on the BCID2 panel results?

As with all diagnostic tests, results from the BCID2 panel need to be evaluated in view of the patient's unique clinical scenario, severity of illness, and source of infection. BCID2 results help to optimize antimicrobial therapy. However, treatment should be re-evaluated when standard organism identification and susceptibility testing results are reported.

Common Scenarios: In certain situations, BCID2 can be used to de-escalate antimicrobials. Examples of common situations where de-escalation may be reasonable include but are not limited to:

- If *Staphylococcus aureus* is identified in the absence of methicillin resistance genes (MecA/C, MREJ): MRSA-active empiric therapy (i.e. vancomycin) should be discontinued and therapy can be changed to cefazolin or oxacillin.
- If *Escherichia coli* or *Klebsiella pneumoniae* is identified in the absence of the CTX-M gene in patients on antipseudomonal coverage (i.e. cefepime or piperacillin/tazobactam): de-escalate to ceftriaxone
    - Internal microbiology data for *Escherichia coli* and *Klebsiella spp.* isolates:
        - When 60 *E. coli* isolates and 45 *Klebsiella spp.* isolates at Atrium Health Wake Forest Baptist were reviewed for detection of CTX-M by BCID2 and correlating ceftriaxone susceptibility by standard culture and susceptibility report, the positive predictive value (PPV) was 100% for *E. coli* and *Klebsiella spp.* and the negative predictive value (NPV) was 94% for *E. coli* and 100% for *Klebsiella spp.*
    - Patients in whom de-escalation may not be appropriate:
        - Lack of source control, suspected polymicrobial infection, ANC ≤500, other infection caused by resistant organism / recent culture history with known resistance, hemodynamic instability or metastatic infection
- If only gram-negative organism(s) identified: discontinue empiric anti-MRSA agent (i.e vancomycin, daptomycin, linezolid)
- Refer to Treatment Decision Algorithms (Table 2-5) below for more information

In certain situations, BCID2 can be used to escalate antimicrobial therapy. If an organism or resistance gene is identified that is not covered by current therapy, modify therapy to treat the pathogen(s). An example of a common situation where escalation is advised may include but is not limited to:

- If gram-negative with CTX-M gene is identified: escalation to a carbapenem may be appropriate
- Refer to Treatment Decision Algorithms (Table 2-5) below for more information

Other considerations:

- BCID2 is reported from blood cultures and will only detect what is present in the blood; therefore, source of infection should always be considered.
- Data suggest that BCID2 is highly sensitive (99%) and specific (99.8%) for monomicrobial bloodstream infections; however, in polymicrobial infections the capacity to correctly identify all present organisms is decreased.
- BCID2 can report to certain family (*Enterobacterales*) or genus (*Staphylococcus, Streptococcus*) levels, with or without identification of a species. These flags should not be confused with identification of a species.
    - When BCID2 is only able to identify *Enterobacterales* to the family level, the species is not one of the included *Enterobacterales* species on the BCID2 panel (i.e. *E. cloacae, E. coli, K. aerogenes, K. oxytoca, K. pneumoniae, Proteus* spp, *Salmonella* spp, *S. marcescens*). If any of the listed *Enterobacterales* organisms are detected, *Enterobacterales* will also report as detected.
    - When BCID2 only identifies *Staphylococcus* species to the genus level, (i.e. NOT *aureus, lugdunensis, epidermidis*), the species is likely to be a coagulase negative *Staphylococcus* other than *epidermidis*. If any of the *Staphylococcus* species included on the panel are detected, the *Staphylococcus* genus will also report as detected.

    - When BCID2 is only able to identify *Streptococcus* species to the genus level, the species is not one of the included *Streptococcus* species on the BCID2 panel (i.e. *agalactiae, pneumoniae, pyogenes*). If any of the *Streptococcus* species included on the panel are detected, the *Streptococcus* genus will also report as detected.
- *S. epidermidis* and other coagulase negative *Staphylococcus* species (CoNS) are normal skin flora and may contaminate cultures. In situations where a single blood culture is positive for a CoNS and there is an alternative explanation for the patient's symptoms or no concern for active infection, the sample may be considered contaminated. In cases where multiple sets of blood cultures or repeat cultures are positive with the same CoNS, true infection from CoNS should be considered.
- *S. aureus* and *S. lugdunensis* should not be considered contaminants. ID consultation is recommended for cases of bacteremia caused by these organisms.

Whom do I contact for questions about the BCID2 panel?

- Microbiology lab (6-2658) or CAUSE (secure chat group: WFMC CAUSE Antimicrobial Stewardship Approval)
- Rarely, discrepancies between the BCID2 and the antimicrobial susceptibility testing results occur (e.g. mecA/C is identified but oxacillin is susceptible by MIC). The microbiology lab or ID/CAUSE may be contacted for questions about these cases.

The following treatment decision algorithms outline potential options for revised empiric antimicrobial therapy in response to BCID2 panel results that would be reasonable in most situations. Response to the BCID2 results should consider the entire clinical picture and these recommendations should not supersede clinical judgement. If choosing an additional or alternative empiric antimicrobial than what is listed in the algorithms below, please utilize institutional antibiograms that provide local resistance data for decision making (found on the Atrium Health Wake Forest Baptist Intranet). If uncertain of optimal therapy, consult Infectious Diseases or message CAUSE.

Table 2. Gram-Positive Organism BCID2 Treatment Decision Algorithm		
BCID2 Result	**Revised Empiric Therapy**	**Comments**
***Staphylococcus* species**		
Staphylococcus aureus Negative mecA/C and MREJ	cefazolin or oxacillin	• MecA/C and MREJ detection indicates methicillin resistant *Staphylococcus aureus* (MRSA) • MREJ is specific for methicillin resistant *Staphylococcus aureus* (MRSA) • Recommend ID consult
Staphylococcus aureus Positive mecA/C and MREJ	vancomycin	
Staphylococcus lugdunensis Negative mecA/C	cefazolin or oxacillin	• MecA/C detection indicates methicillin resistant *Staphylococcus lugdunensis* • Recommend ID consult
Staphylococcus lugdunensis Positive mecA/C	vancomycin	
Staphylococcus epidermidis Negative mecA/C	cefazolin or oxacillin	• MecA/C detection indicates methicillin resistant *Staphylococcus epidermidis* (MRSE) • *S. epidermidis* and other coagulase negative *Staphylococcus* species (CoNS) are normal skin flora and may contaminate cultures. In situations where a single blood culture is positive for a CoNS and there is an alternative explanation for the patient's symptoms or no concern for active infection, the sample may be considered contaminated
Staphylococcus epidermidis Positive mecA/C	vancomycin	
Staphylococcus PCR only	vancomycin	• When BCID2 only identifies *Staphylococcus* species to the genus level, the species is NOT one of the included *Staphylococcus* species on the BCID2 panel • MecA/C detection is not assessed when a species is not identified
***Enterococcus* species**		
Enterococcus faecalis Negative vanA/B	ampicillin	• CAUSE/ID approval required for daptomycin and IV linezolid • Even when E. faecalis is vancomycin resistant, 90-92% or isolates remain susceptible to ampicillin
Enterococcus faecalis Positive vanA/B	ampicillin alternative: linezolid or daptomycin	
Enterococcus faecium Negative vanA/B	vancomycin	• CAUSE/ID approval required for daptomycin and IV linezolid
Enterococcus faecium Positive vanA/B	linezolid or daptomycin	
***Streptococcus* species**		
Streptococcus pyogenes (Group A)	penicillin	• *Streptococcus pyogenes* (Group A) is 100% susceptible to penicillin
Streptococcus agalactiae (Group B)	penicillin	• *Streptococcus agalactiae* (Group B) is 100% susceptible to penicillin
Streptococcus pneumoniae	ceftriaxone	• If meningitis is suspected, add vancomycin
Streptococcus PCR only	ceftriaxone	• When BCID2 is only able to identify *Streptococcus* species to the genus level, the species is not one of the included *Streptococcus* species on the BCID2 panel
Other Gram Positives		
Listeria monocytogenes	ampicillin	• Recommend ID consult

Table 3. Gram-Negative Organism BCID2 Treatment Decision Algorithm		
BCID2 Result	**Revised Empiric Therapy**	**Comments**
Enterobacterales with <u>NO resistance genes detected</u>		
Escherichia coli	ceftriaxone	
Klebsiella pneumoniae group	ceftriaxone	
Klebsiella oxytoca	ceftriaxone	
Klebsiella aerogenes (formerly known as *Enterobacter aerogenes*)	cefepime	• High rates of AmpC production – cefepime preferred
Proteus species	ceftriaxone	
Enterobacter cloacae complex	cefepime	• High rates of AmpC production – cefepime preferred
Serratia marcescens	ceftriaxone	
Salmonella species	ceftriaxone	
Enterobacterales (WITHOUT species identification)	cefepime or piperacillin/tazobactam	• Enterobacterales is the name of a family of gram-negative bacteria, it is not the *Enterobacter* genus • When BCID2 is only able to identify Enterobacterales to the family level, the species is not one of the included Enterobacterales species on the BCID2 panel • Consider source when choosing between cefepime or piperacillin-tazobactam (e.g. piperacillin-tazobactam for intra-abdominal infection due to additional anaerobic coverage)
Other Gram-Negative Organisms with <u>NO resistance genes detected</u>		
Acinetobacter calcoaceticus-baumannii complex	ampicillin/sulbactam	• Refer to CAUSE antimicrobial dosing guide for high dose ampicillin-sulbactam dosing
Pseudomonas aeruginosa	cefepime or piperacillin/tazobactam	
Stenotrophomonas maltophilia	sulfamethoxazole/ trimethoprim	• Refer to CAUSE antimicrobial dosing guide for optimal dosing
Haemophilus influenzae	ampicillin/sulbactam or ceftriaxone	
Neisseria meningitidis	ceftriaxone	• Recommend ID consult
Bacteroides fragilis	metronidazole	•For polymicrobial infections requiring additional coverage, piperacillin/tazobactam will treat *B. fragilis* (additional anaerobic coverage (e.g. metronidazole) is not needed)
Resistance Genes Detected		
Positive CTX-M (ESBL)	carbapenem*	• Indicates an extended-spectrum beta-lactamase (ESBL) producing organism • In clinically stable patients with a suspected or confirmed urinary source, piperacillin/tazobactam is usually an appropriate alternative* • CAUSE/ID approval required for carbapenems
Positive KPC or OXA48-like	Consult ID/CAUSE to discuss preferred therapy ceftazidime/avibactam	• Indicates a carbapenem resistant organism • CAUSE/ID approval required for ceftazidime/avibactam
Positive IMP, NDM, VIM	Consult ID/CAUSE to discuss preferred therapy cefiderocol	• Indicates a carbapenem resistant organism producing a metallo-beta-lactamase • CAUSE/ID approval required for cefiderocol
Positive mcr-1	Treat as indicated above	• Indicates a colistin reistant organism

Table 4. Fungal Organism BCID2 Treatment Decision Algorithm		
BCID2 Result	**Revised Empiric Therapy**	**Comments**
Candida species		
Candida albicans	micafungin	• Recommend ID consult
Candida auris	Consult ID/CAUSE to discuss preferred empiric therapy micafungin	• Recommend ID consult • High rates of resistance possible
Candida glabrata	micafungin	• Recommend ID consult
Candida krusei	micafungin	• Recommend ID consult • Intrinsically resistant to fluconazole
Candida parapsilosis	micafungin	• Recommend ID consult • Isolates can have higher MICs to echinocandins, consider fluconazole as alternative if concerned for echinocandin resistance or non-response
Candida tropicalis	micafungin	• Recommend ID consult
Other Fungal Organisms		
Cryptococcus (C. neoformans/C. gattii)	Consult ID/CAUSE to discuss preferred empiric therapy liposomal amphotericin B + flucytosine	• CAUSE/ID approval required for liposomal amphotericin B

Table 5. What to do when no organisms are detected on BCID2?
The BCID2 panel is **ONLY** capable of detecting organisms and resistance genes included in table 1. Absence of a detected organism does **NOT** indicate a false-positive culture or reporting error. When no organisms are detected on BCID2 consider the blood culture gram stain results (e.g. gram positive or negative), growth environment (e.g. aerobic, anaerobic, or both), gaps in antimicrobial coverage, past culture history, suspected source of bacteremia and clinical stability of patient when deciding on an appropriate empiric regimen.