

Interpretation of Positive Blood Cultures When PCR Blood Culture Identification (BCID2) Results are “Not Detected”

Nebraska Medicine currently utilizes a multiplex PCR-based blood culture identification (BCID2) system capable of identifying 30 potential pathogens and 10 genes associated with antimicrobial resistance. The BCID2 system detects over 90% of the causative agents in bloodstream infections either at a species level or a group level (i.e. Enterobacterales). For detailed guidance based on specific organism or organism groups, please refer to the appropriate UNMC guidance document. When microbes not included in the panel are present in a blood culture, the result will indicate “Not Detected.” This document aims to provide guidance in these scenarios based on the Gram stain characteristics and which bottles are showing growth (aerobic vs. anaerobic). This is based on data collected at Nebraska Medicine from January 2022 to July 2024.

Table 1: Management Recommendations Result of “Not Detected” on BCID2

Orange text = Cocci, Blue text = Bacilli (rods), Green text = Yeast

Gram Stain/Preliminary Culture Result	Likely Organism *	Recommended Treatment
Gram-positive: (% total Gram-positive BCID2 negative)		
Aerobic bottle (most organisms detected can also grow in anaerobic bottle)	<i>Micrococcus</i> sp. (35%) <i>Corynebacterium</i> sp. (19%)	1 of 2 blood cultures positive Hold antibiotics, do not repeat BCX 2 of 2 blood cultures positive Consider Vancomycin 15 mg/kg (renally dose adjusted)
Anaerobic bottle only	<i>Clostridium</i> sp. (15%) <i>Cutibacterium</i> sp. (12%) <i>Gemella</i> sp. (9%) <i>Actinomyces</i> sp. (9%) <i>Bacillus</i> sp., non-anthraxis (9%)	1 of 2 blood cultures positive Hold antibiotics, do not repeat BCX 2 of 2 blood cultures positive Consider Vancomycin 15 mg/kg (renally dose adjusted)
Gram-negative: (% total Gram-negative BCID2 negative)		
Aerobe (many can also grow in anaerobic bottles)	<i>Pseudomonas</i> sp. (non-aeruginosa) (25%) <i>Acinetobacter</i> sp. (non-baumannii) (13%) <i>Roseomonas</i> sp. (13%) <i>Neisseria</i> sp. (non-meningitidis) (13%)	Levofloxacin 750 mg IV/PO q24h
Anaerobe bottle only	<i>Bacteroides</i> sp. (38%) <i>Fusobacterium</i> sp. (24%)	Metronidazole 500 mg IV/PO q8h
Yeast: (% total Yeast BCID2 negative)		
Aerobe	<i>Candida</i> sp. (67%) <i>Malassezia</i> sp. (33%)	Fluconazole 800 mg x 1 followed by 400 mg q24h

*A full list of isolated organisms can be found below in Table 2

Gram-Positives

When a blood culture is positive, but the BCID results as “Not Detected” Gram-positive rods and cocci are most common (74%). The most common organisms isolated were *Micrococcus* sp., *Clostridium* sp., *Bacillus* sp., and *Corynebacterium* sp. making up 34% of all organisms detected and over three quarters of the Gram-positive organisms. These organisms can grow in either aerobic or anaerobic bottles. They are skin flora and usually considered contaminants and do not require treatment, but clinical judgment should be used. Treatment may be warranted in specific situations, such as when 2 of 2 blood cultures are positive or if the patient has a documented history of infection with the organism at another site. Typically, when multiple cultures yield these organisms and an infection is present, the cause is device-related, and the primary course of action is the removal of the device, when possible.

Anaerobic Gram-positive organisms are isolated less frequently, with the most common being *Cutibacterium* sp., *Actinomyces* sp., *Gemella* sp., and *Clostridium* sp. When they are detected in only 1 of 2 blood culture sets, they are generally considered contaminants and do not require treatment. However, clinical judgment should be exercised in these cases as with Gram-positive cocci.

Clostridium sp. are Gram-positive anaerobic bacilli that may appear “Gram-variable” or “Gram-negative” due to their propensity to decolorize during the Gram stain procedure. Metronidazole is appropriate therapy in cases of anaerobic Gram-variable or Gram-negative rod as it will typically be active against these pathogens.

Gram-Negatives

When all targets on the BCID2 indicate “Not Detected” but Gram-negative organisms are observed on the Gram stain, these organisms are usually anaerobes. The most common among them are members of the *Bacteroides fragilis* group and *Fusobacterium* sp. While *Bacteroides fragilis* is included on the BCID2 panel, other members of this group, such as *Bacteroides ovatus*, *Bacteroides vulgatus*, and *Bacteroides thetaiotaomicron* are not. When detected, these Gram-negative organisms suggest an underlying infection, often intra-abdominal, and can be associated with high mortality rates. Metronidazole is the preferred treatment for these organisms due to its strong efficacy and low resistance rates. Alternatively, beta-lactam/beta-lactamase inhibitor combinations (e.g., ampicillin-sulbactam or piperacillin-tazobactam) and carbapenems are also highly active.

Aerobic Gram-negative rods that are “Not Detected” are rarer and typically include non-*baumannii* *Acinetobacter* sp., *Pseudomonas fluorescens-putida* group, and *Roseomonas* sp. These organisms can be associated with true infection and should be treated with an appropriate agent in most cases. Levofloxacin has reliable activity against these and other aerobic Gram-negatives, making it an appropriate empiric choice until identification. Aerobic Gram-negative cocci that are “Not Detected” are most likely to be non-*meningitidis*-*Neisseria* sp., which usually do not require antibiotic therapy.

Yeast

Detection of non-identifiable yeast is rare and are most commonly *Candida* sp. not included on the BCID2 panel, including *Candida dubliniensis*, *Candida lusitanae*, and *Candida kefyr*. Fluconazole can be used to treat these organisms. Rarely *Malassezia* sp. are also present. Echinocandins such as micafungin do not have activity against *Malassezia* sp. and therefore an azole is preferred empiric therapy. Consultation with Infectious Diseases should be considered when treating disseminated fungal infections.

Table 2: Organism Groups Identified by Culture and “Not Detected” by BCID2

Specific Organism Stratified by Gram Stain					
Gram Stain	Aerobe/Anaerobe	Genus/Grouping	n	% of Total BCID Negative	% of Gram Stain by Bottle
Gram Positive			163	76.17%	76.17%
Aerobe Total			89	44.39%	58.28%
		<i>Micrococcus</i> species	33	15.42%	34.74%
		<i>Corynebacterium striatum</i> group	11	5.14%	11.58%
		<i>Enterococcus</i> species	7	3.27%	7.37%
		<i>Corynebacterium</i> species, not <i>C. striatum</i>	7	3.27%	7.37%
		<i>Rothia</i> species	6	2.80%	6.32%
		<i>Bacillus</i> species	6	2.80%	6.32%
		<i>Aerococcus</i> species	5	2.34%	5.26%
		<i>Staphylococcus</i> species	5	2.34%	5.26%
		<i>Lactobacillus</i> species	5	2.34%	5.26%
		<i>Microbacterium</i> species	3	1.40%	3.16%
		<i>Brevibacterium</i> species	2	0.93%	2.11%
		<i>Kocuria</i> species	2	0.93%	2.11%
		<i>Rhodococcus</i> species	1	0.47%	1.05%
		<i>Janibacter</i> species	1	0.47%	1.05%
		<i>Leuconostoc</i> species	1	0.47%	1.05%
Anaerobe Total			74	31.78%	41.72%
		<i>Clostridium</i> species	10	4.67%	14.71%
		<i>Cutibacterium acnes</i>	8	3.74%	11.76%
		<i>Gemella</i> species	6	2.80%	8.82%
		<i>Bacillus</i> species	6	2.80%	8.82%
		<i>Actinomyces</i> species	6	2.80%	8.82%
		<i>Eggerthella</i> species	4	1.87%	5.88%
		<i>Parvimonas</i> species	4	1.87%	5.88%
		<i>Fingoldia magna</i>	4	1.87%	5.88%
		<i>Anaerococcus</i> species	2	0.93%	2.94%
		<i>Globicatella</i> species	2	0.93%	2.94%
		<i>Paenibacillus</i> species	2	0.93%	2.94%
		<i>Eubacterium limosum</i>	2	0.93%	2.94%
		<i>Atopobium</i> species	2	0.93%	2.94%
		<i>Pediococcus</i> species	2	0.93%	2.94%
		<i>Peptococcus</i> species	1	0.47%	1.47%
		<i>Streptococcus</i> species	1	0.47%	1.47%
		<i>Cutibacterium</i> species	1	0.47%	1.47%
		<i>Propionibacterium</i> species	1	0.47%	1.47%
		<i>Peptostreptococcus</i> species	1	0.47%	1.47%
		<i>Dermabacter hominis</i>	1	0.47%	1.47%
		<i>Facklamia</i> species	1	0.47%	1.47%

Gram Negative		45	21.03%	21.03%
Aerobe Total		16	7.48%	35.56%
	<i>Pseudomonas</i> (non-aeruginosa) species	4	1.87%	25.00%
	<i>Acinetobacter</i> (non-baumannii) species	2	0.93%	12.50%
	<i>Roseomonas</i> species	2	0.93%	12.50%
	<i>Neisseria</i> (non-meningitidis) species	2	0.93%	12.50%
	<i>Cardiobacterium hominis</i>	1	0.47%	6.25%
	<i>Haemophilus parainfluenzae</i>	1	0.47%	6.25%
	<i>Achromobacter xylosoxidans</i>	1	0.47%	6.25%
	<i>Kingella</i> species	1	0.47%	6.25%
	<i>Stenotrophomonas maltophilia</i>	1	0.47%	6.25%
	<i>Moraxella</i> species	1	0.47%	6.25%
Anaerobe Total		29	13.55%	64.44%
	<i>Bacteroides fragilis</i> group	11	5.14%	37.93%
	<i>Fusobacterium</i> species	7	3.27%	24.14%
	<i>Prevotella</i> species	4	1.87%	13.79%
	<i>Pasteurella</i> species	2	0.93%	6.90%
	<i>Desulfovibrio</i> species	2	0.93%	6.90%
	<i>Campylobacter</i> species	1	0.47%	3.45%
	<i>Parabacteroides</i> species	1	0.47%	3.45%
	<i>Enterobacter cloacae</i>	1	0.47%	3.45%
Yeast		6	2.80%	2.80%
	<i>Candida</i> species	4	1.87%	66.67%
	<i>Malassezia</i> species	2	0.93%	33.33%
Grand Total		214	100.00%	100.00%

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