BIOFIRE® Joint Infection (JI) Panel Guidance

What is it?

The BIOFIRE® Joint Infection (JI) Panel is a multiplex polymerase chain reaction test that amplifies DNA targets directly from synovial fluid to permit rapid identification of 39 pathogens and 8 antimicrobial resistance genes. The local turnaround time for testing results is about 4 hours. The JI Panel is highly sensitive and specific to detect pathogens included as targets on the panel. The JI panel should be considered in patients with suspected native joint septic arthritis or prosthetic joint infection and can be used to inform decision making when transitioning to targeted antimicrobial therapy.

What does it identify?

Table 1. Pathogens and Resistance Genes Detected

<table>
<tr><th>Gram Positive (+) Bacteria</th><th>Gram Negative (-) Bacteria</th></tr>
<tr><td>

Anaerococcus prevotii/vaginalis*
Clostridium perfringens*
Cutibacterium avidum/granulosum*
Enterococcus faecalis
Enterococcus faecium
Finegoldia magna*
Parvimonas micra*
Peptoniphilus*
Peptostreptococcus anaerobius*
Staphylococcus aureus
Staphylococcus lugdunensis
Streptococcus spp.

Streptococcus agalactiae
Streptococcus pneumoniae
Streptococcus pyogenes

</td><td>

Bacteroides fragilis*
Citrobacter
Enterobacter cloacae complex
Escherichia coli
Haemophilus influenzae
Kingella kingae
Klebsiella aerogenes
Klebsiella pneumoniae group
Morganella morganii
Neisseria gonorrhoeae
Proteus spp.
Pseudomonas aeruginosa
Salmonella spp.
Serratia marcescens

</td></tr>
<tr><th>Yeast</th><th>Gram Negative (-) Resistance Genes</th></tr>
<tr><td>

Candida spp.

Candida albicans

</td><td rowspan="3">
<u>Carbapenemases:</u>

IMP
KPC
NDM
OXA-48-like
VIM

<u>Extended Spectrum Beta-Lactamases (ESBL):</u>

CTX-M

</td></tr>
<tr><th>Gram Positive (+) Resistance Genes</th></tr>
<tr><td>
<u>Methicillin Resistance:</u>
mecA/C and MREJ (MRSA)

<u>Vancomycin Resistance:</u>
vanA/B
</td></tr>
</table>

*anaerobic targets

Table 1. Note: The JI panel is ONLY capable of detecting organisms and resistance genes included in the list above. Organisms not included on the panel as targets cannot be detected, and a negative JI panel does not necessarily indicate that there is not an infectious pathogen present. Notable potential pathogens that are **NOT** included in the joint panel include ***Cutibacterium acnes*** and coagulase-negative Staphylococci other than *Staphylococcus lugdunensis* such as ***Staphylococcus epidermidis***.

Specimen collection:

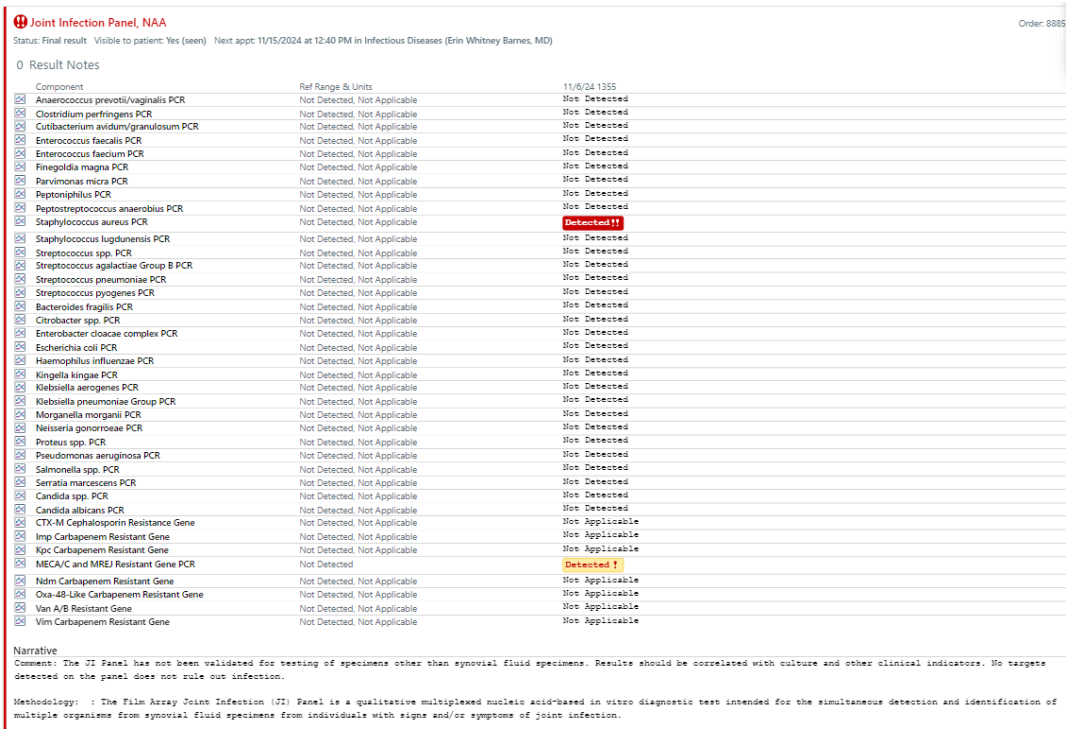
The only acceptable specimen type is synovial fluid. Synovial fluid specimens can be collected via arthrocentesis or during surgery. Synovial fluid specimens must be collected in a sterile container or non-heparinized syringe. The JI panel cannot be performed on specimens sent in preservative tubes, blood culture bottles, or viral transport medium. Additionally, the JI panel order may be canceled for insufficient quantity (requires at least 0.2 mL), invalid results from the BIOFIRE® FILMARRAY ® TORCH instrument, or if the synovial fluid specimen is too viscous, which may impede performance of the assay.

Ordering JI panel and synovial fluid culture:

The JI panel (LAB8783 Joint Infection Panel, NAAT) **must be ordered** in conjunction with or as an add on to synovial fluid culture (LAB5563 Synovial Culture (Aerobic)). The JI panel is not automatically added to synovial fluid cultures. JI panel orders are canceled if a corresponding synovial culture is not ordered. Synovial fluid culture is especially important to recover organisms for susceptibility testing, identify organisms not included in the JI panel, and further identify organism species when the JI panel only identifies the genus, complex, or group. Synovial fluid culture (aerobic) specimens are incubated for up to 14 days for detection of other aerobic organisms including other coagulase-negative Staphylococci and other anaerobic organisms such as *Cutibacterium acnes.* Other synovial cultures may be appropriate to order based on the suspected causative organism (e.g. anaerobic, acid-fast, fungal).

How are results reported?

Results can be viewed in chart review under the labs section in Encompass, with the lab order titled “Joint Infection Panel, NAA”. Results of the JI panel are **not** pulled into the micro tab in Encompass or the corresponding synovial culture result. Example:



Joint Infection Panel, NAA — Order: 8885

Status: Final result Visible to patient: Yes (seen) Next appt: 11/15/2024 at 12:40 PM in Infectious Diseases (Erin Whitney Barnes, MD)

0 Result Notes

Component	Ref Range & Units	11/6/24 1355
Anaerococcus prevotii/vaginalis PCR	Not Detected, Not Applicable	Not Detected
Clostridium perfringens PCR	Not Detected, Not Applicable	Not Detected
Cutibacterium avidum/granulosum PCR	Not Detected, Not Applicable	Not Detected
Enterococcus faecalis PCR	Not Detected, Not Applicable	Not Detected
Enterococcus faecium PCR	Not Detected, Not Applicable	Not Detected
Finegoldia magna PCR	Not Detected, Not Applicable	Not Detected
Parvimonas micra PCR	Not Detected, Not Applicable	Not Detected
Peptoniphilus PCR	Not Detected, Not Applicable	Not Detected
Peptostreptococcus anaerobius PCR	Not Detected, Not Applicable	Not Detected
Staphylococcus aureus PCR	Not Detected, Not Applicable	Detected!!
Staphylococcus lugdunensis PCR	Not Detected, Not Applicable	Not Detected
Streptococcus spp. PCR	Not Detected, Not Applicable	Not Detected
Streptococcus agalactiae Group B PCR	Not Detected, Not Applicable	Not Detected
Streptococcus pneumoniae PCR	Not Detected, Not Applicable	Not Detected
Streptococcus pyogenes PCR	Not Detected, Not Applicable	Not Detected
Bacteroides fragilis PCR	Not Detected, Not Applicable	Not Detected
Citrobacter spp. PCR	Not Detected, Not Applicable	Not Detected
Enterobacter cloacae complex PCR	Not Detected, Not Applicable	Not Detected
Escherichia coli PCR	Not Detected, Not Applicable	Not Detected
Haemophilus influenzae PCR	Not Detected, Not Applicable	Not Detected
Kingella kingae PCR	Not Detected, Not Applicable	Not Detected
Klebsiella aerogenes PCR	Not Detected, Not Applicable	Not Detected
Klebsiella pneumoniae Group PCR	Not Detected, Not Applicable	Not Detected
Morganella morganii PCR	Not Detected, Not Applicable	Not Detected
Neisseria gonorroeae PCR	Not Detected, Not Applicable	Not Detected
Proteus spp. PCR	Not Detected, Not Applicable	Not Detected
Pseudomonas aeruginosa PCR	Not Detected, Not Applicable	Not Detected
Salmonella spp. PCR	Not Detected, Not Applicable	Not Detected
Serratia marcescens PCR	Not Detected, Not Applicable	Not Detected
Candida spp. PCR	Not Detected, Not Applicable	Not Detected
Candida albicans PCR	Not Detected, Not Applicable	Not Detected
CTX-M Cephalosporin Resistance Gene	Not Detected, Not Applicable	Not Applicable
Imp Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Applicable
Kpc Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Applicable
MECA/C and MREJ Resistant Gene PCR	Not Detected	Detected !
Ndm Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Applicable
Oxa-48-Like Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Applicable
Van A/B Resistant Gene	Not Detected, Not Applicable	Not Applicable
Vim Carbapenem Resistant Gene	Not Detected, Not Applicable	Not Applicable

Narrative

Comment: The JI Panel has not been validated for testing of specimens other than synovial fluid specimens. Results should be correlated with culture and other clinical indicators. No targets detected on the panel does not rule out infection.

Methodology: : The Film Array Joint Infection (JI) Panel is a qualitative multiplexed nucleic acid-based in vitro diagnostic test intended for the simultaneous detection and identification of multiple organisms from synovial fluid specimens from individuals with signs and/or symptoms of joint infection.

Making antimicrobial decisions based on JI panel results:

The JI panel may be used to revise empiric therapy for suspected native joint septic arthritis and prosthetic joint infection. However, the JI panel results should be evaluated in conjunction with patient-specific criteria such as severity of illness, clinical syndrome, risk factors for antimicrobial resistance or history of antimicrobial resistance, allergies, organ dysfunction, and other factors. Additionally, the diagnosis of native joint septic arthritis and prosthetic joint infection should be made in conjunction with other clinical and laboratory findings including synovial fluid testing (cell count and differential, crystal identification), histological evaluation of tissue, intraoperative inspection, and radiographic results if available.

The following treatment decision recommendations describe potential options for revised empirical antimicrobial therapy in response to the JI panel results. Synovial fluid cultures should continue to be monitored for pathogens which may not be detected from the JI panel and antimicrobial therapy should be adjusted if needed. Additionally, it is possible that pathogens detected on the panel may not be isolated in subsequent culture. For example, this may occur when samples are collected after initiation of antibiotic therapy. Antimicrobial therapy should also be re-evaluated when organism identification and susceptibility results return. The recommendations below are reasonable for most clinical situations but should not supersede clinical judgement. When making antimicrobial therapy decisions, it is recommended to consider local resistance data using institutional antibiograms when available. If optimal antimicrobial therapy remains uncertain, consult Infectious Diseases or secure chat CAUSE with questions. Infectious Diseases consultation is recommended to guide management of native joint septic arthritis or prosthetic joint infection.

Table 2. Gram-Positive (+) Organisms JI Panel Treatment Decision Algorithm

Organism	Revised Empiric Therapy	Comments
*Anaerococcus prevotii/vaginalis**	Penicillin	• Alternative: Metronidazole
*Clostridium perfringens**	Penicillin	• Alternative: Metronidazole
*Cutibacterium avidum/granulosum**	Penicillin	• Metronidazole is not active • Alternative: Vancomycin
Enterococcus faecalis Negative *van*A/B	Ampicillin	• CAUSE/ID approval needed for daptomycin, IV linezolid • 99% of *E. faecalis* isolates are ampicillin susceptible, including 90-92% of vancomycin resistant isolates
Enterococcus faecalis Positive *van*A/B (VRE)	Ampicillin Alternative: Daptomycin or linezolid	
Enterococcus faecium Negative *van*A/B	Vancomycin	• CAUSE/ID approval needed for daptomycin, IV linezolid
Enterococcus faecium Positive *van*A/B (VRE)	Daptomycin or linezolid	
*Finegoldia magna**	Penicillin	• Alternative: Metronidazole
*Parvimonas micra**	Penicillin	• Metronidazole resistance has been described though resistance rates are low

*Peptoniphilus**	Penicillin	• Alternative: Metronidazole
*Peptostreptococcus anaerobius**	Penicillin	• Resistance with metronidazole has been described
Staphylococcus aureus Negative *mec*A/C and MREJ (MSSA)	Cefazolin or Oxacillin	• *mec*A/C and MREJ detection indicates methicillin resistant *Staphylococcus aureus* (MRSA) • MREJ is specific for MRSA • **Recommend ID consult**
Staphylococcus aureus Positive *mec*A/C and MREJ (MRSA)	Vancomycin	
Staphylococcus lugdunensis Negative *mec*A/C	Cefazolin or Oxacillin	• *mec*A/C detects methicillin resistant *Staphylococcus lugdunensis* • **Recommend ID consult**
Staphylococcus lugdunensis Positive *mec*A/C	Vancomycin	
Streptococcus spp.	Ceftriaxone	• When the JI panel only detects *Streptococcus* spp at the genus level, the species is one that is not included on the JI panel
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	Penicillin or Ceftriaxone	• Both ceftriaxone and penicillin are highly active against *Streptococcus pneumoniae* locally in non-meningitis isolates

Table 3. Gram-Negative (-) Organisms JI Panel Treatment Decision Algorithm

Organism (without resistance gene detected)	Revised Empiric Therapy	Comments
*Bacteroides fragilis**	Metronidazole	• In most cases, polymicrobial infection should be suspected with detection of *Bacteroides fragilis*, and culture results should be monitored for identification of pathogens not detected by the JI panel • Alternatives when polymicrobial infection is suspected:

		piperacillin/tazobactam, ampicillin/sulbactam (additional anaerobic coverage with metronidazole is not needed for these agents)
Citrobacter	Cefepime	• *Citrobacter freundii* is more common species and has high rates of ampC production • *Citrobacter koseri* does not harbor chromosomal ampC beta-lactamases and if identified on culture, may be treated with any susceptible beta-lactam
Enterobacter cloacae complex	Cefepime	• High rates of ampC production
Escherichia coli	Ceftriaxone	
Haemophilus influenzae	Ceftriaxone	• Recommend further de-escalation if beta-lactamase negative on culture results
Kingella kingae	Ceftriaxone	• Recommend further de-escalation if beta-lactamase negative on culture results
Klebsiella aerogenes	Cefepime	• High rates of ampC production
Klebsiella pneumoniae group	Ceftriaxone	
Morganella morganii	Cefepime	• 94% susceptible on local antibiogram
Neisseria gonorrhoeae	Ceftriaxone	• Consider evaluating for additional STIs such as chlamydia
Proteus spp.	Ceftriaxone	
Pseudomonas aeruginosa	Cefepime or piperacillin/tazobactam	
Salmonella spp.	Ceftriaxone	
Serratia marcescens	Ceftriaxone	
Gram Negative (-) Resistance Genes Detected		
CTX-M (ESBL)	Carbapenem	• Indicates an extended-spectrum beta-lactamase (ESBL) producing organism • CAUSE/ID approval required for carbapenems

KPC, OXA-48-like	Consult ID/CAUSE to discuss preferred therapy Ceftazidime/avibactam	• Indicates carbapenem-resistant organism • CAUSE/ID approval required for ceftazidime/avibactam
IMP, NDM, VIM	Consult ID/CAUSE to discuss preferred therapy Cefiderocol	• Indicates carbapenem-resistant organism producing a metallo-beta-lactamase • CAUSE/ID approval required for cefiderocol

Table 4. Yeast Organisms JI Panel Treatment Decision Algorithm		
Organism	Revised Empiric Therapy	Comments
Candida spp. (without *Candida albicans* detected)	Micafungin	• Recommend ID consult • Indicative of Candida species other than *Candida albican*s • *Candida parapsilosis* can have relatively higher micafungin MICs Consider sequencing therapy to fluconazole • *Candida auris* may have high rates of resistance
Candida albicans	Micafungin	• Recommend ID consult • Candida albicans is typically susceptible to fluconazole, but recommend starting with echinocandin for invasive candidiasis

Limitations and Considerations:

The JI panel may result negative due to a joint infection with pathogens that are not detected on the panel or if the pathogen quantity is below the limit of detection. A negative JI panel result does not rule out joint infection, as other pathogens can be implicated that are not detected on the panel including other bacteria, viruses, and fungi depending on the clinical scenario.

Rarely, polymicrobial specimens with four or more organisms detected are possible. In this instance, retesting of the sample is recommended to confirm the polymicrobial result. The JI panel has not been validated for testing specimens other than synovial fluid and cannot be used on swabs or tissue samples. The JI panel is not intended to monitor effectiveness of treatment and should not be performed as a test of cure.

Questions about the panel?

Contact Microbiology lab (6-2658) or CAUSE (secure chat group: WFMC CAUSE Antimicrobial Stewardship Approval) for questions about the panel or discrepancies between the panel and antimicrobial susceptibility results.

References:

1. BioFire® Joint Infection Panel [product labeling: instructions for use]. bioMérieux. Salt Lake City, UT. Updated August 2023

2. Esteban J, Salar-Vidal L, Schmitt BH, et al. Multicenter evaluation of the BIOFIRE Joint Infection Panel for the detection of bacteria, yeast, and AMR genes in synovial fluid samples. *J Clin Microbiol.* 2023;61(11):e0035723. doi:10.1128/jcm.00357-23

3. Rams TE, Sautter JD, van Winkelhoff AJ. Antibiotic Resistance of Human Periodontal Pathogen *Parvimonas micra* Over 10 Years. *Antibiotics (Basel)*. 2020;9(10):709. Published 2020 Oct 17. doi:10.3390/antibiotics9100709

4. Veloo AC, Welling GW, Degener JE. Antimicrobial susceptibility of clinically relevant Gram-positive anaerobic cocci collected over a three-year period in the Netherlands. *Antimicrob Agents Chemother.* 2011;55(3):1199-1203. doi:10.1128/AAC.01771-09

5. Achermann Y, Liu J, Zbinden R, et al. Propionibacterium avidum: A Virulent Pathogen Causing Hip Periprosthetic Joint Infection. *Clin Infect Dis.* 2018;66(1):54-63. doi:10.1093/cid/cix665

6. Beredaki MI, Pournaras S, Meletiadis J. A new PK/PD target for assessing efficacy of micafungin against Candida parapsilosis. *J Antimicrob Chemother.* 2024;79(1):157-165. doi:10.1093/jac/dkad360