

**Supplemental Table 1: Antimicrobial Stewardship Consensus Recommendations for BCID2 Targets**

| BCID2 Organism Targets Detected      | BCID2 Resistance Targets Detected | Final Organism Identification Interpretation | First-line Antimicrobial Options (in order of preference) | Special Populations   | Notes   | ID consult |
|--------------------------------------|-----------------------------------|--|---|---|---|------------|
| Enterococcus faecalis                |                                   | Enterococcus faecalis (not VRE)              | 1) Ampicillin   | <ul style="list-style-type: none"> <li>• Consider adding gentamicin at synergistic dosing if concern for endocarditis</li> <li>• <i>Clinical concern for active intraabdominal infectious process:</i> Continue gram negative and anaerobic coverage</li> </ul>                   | <ul style="list-style-type: none"> <li>• E. faecalis isolates at our institution are 100% ampicillin susceptible</li> </ul>   |            |
| Enterococcus faecium                 |                                   | Enterococcus faecium (not VRE)               | 1) Vancomycin   | <ul style="list-style-type: none"> <li>• Consider adding gentamicin at synergistic dosing</li> <li>• <i>Clinical concern for active intraabdominal infectious process:</i> Continue gram negative and anaerobic coverage</li> </ul>   |   |            |
| Enterococcus faecalis or faecium     | vanA/B pos                        | VRE  | 1) Linezolid or daptomycin                                | <ul style="list-style-type: none"> <li>• <i>Oncology pt w/o lung disease:</i> daptomycin</li> <li>• <i>Clinical concern for active intraabdominal infectious process:</i> Continue gram negative and anaerobic coverage</li> </ul>  |   | Rec        |
| Gram positive cocci (BCID2 negative) |                                   |  | 1) vancomycin   | <ul style="list-style-type: none"> <li>• <i>Oncology or GI patient:</i> Add Ampicillin (for possible E. gallinarum or E. cassileflavus)</li> <li>• Consider daptomycin or adding clindamycin if history of leuconostoc or pediococcus (intrinsic vancomycin resistant)</li> </ul> | <ul style="list-style-type: none"> <li>• Possible organisms include: other Enterococcus species including gallinarum or cassileflavus (with intrinsic vancomycin resistance), Micrococcus, Rothia, Abiotrophia, (less commonly leuconostoc, pediococcus)</li> </ul> |            |

|  |                                |  |   |  |   |             |
|--|--------------------------------|--|---|--|---|-------------|
| Listeria monocytogenes                                   |                                | Listeria monocytogenes                     | 1) Ampicillin                             | • <i>Meningitis, endocarditis, or immunocompromised</i> : ampicillin + gentamicin  |   | Rec         |
| Staphylococcus sp.                                       | Note: no mecA will be reported | Coag Neg Staph                             | 1) Vancomycin                             |  | •Can narrow off vancomycin once susceptibilities finalized<br>•Nafcillin causes vein irritation, best used continuous or with central line  |             |
| Staphylococcus epidermidis                               | mecA NOT detected              | Staphylococcus epidermidis (without mec A) | 1) Cefazolin (nafcillin for certain foci) | • <i>Endocarditis</i> : nafcillin 1 <sup>st</sup> line although cefazolin is reasonable alternative, consider adding gentamicin<br>• <i>Endocarditis with prosthetic material</i> : add rifampin, gentamicin<br>• <i>CNS infection</i> : nafcillin | •Nafcillin causes vein irritation, best used continuous or with central line  |             |
| Staphylococcus lugdunensis                               | mecA NOT detected              | Staphylococcus lugdunensis (without mec A) | 1) Cefazolin (nafcillin for certain foci) | • <i>CNS infection</i> : nafcillin<br>• <i>Endocarditis</i> : consider adding gentamicin, nafcillin 1 <sup>st</sup> line although cefazolin is reasonable alternative<br>• <i>Endocarditis with prosthetic material</i> : add rifampin, gentamicin | •Rare resistance to beta-lactams<br>•Can narrow to penicillin once susceptibilities finalized (if Beta-lactamase negative), reports of lower MICs to PCN if susceptible<br>•Nafcillin causes vein irritation, best used continuous or with central line |             |
| Staphylococcus epidermidis or Staphylococcus lugdunensis | mecA pos                       | Coag Neg Staph (with mecA)                 | 1)Vancomycin                              | • <i>Endocarditis</i> : consider adding gentamicin<br>• <i>Endocarditis with prosthetic material</i> : add rifampin, gentamicin  |   |             |
| Staphylococcus sp. + Staph aureus                        | mecA NOT detected              | MSSA                                       | 1)Cefazolin (nafcillin for certain foci)  | • <i>CNS infection</i> : nafcillin<br>• <i>Endocarditis</i> : consider adding gentamicin, nafcillin 1 <sup>st</sup> line although cefazolin is reasonable alternative<br>• <i>Endocarditis with prosthetic material</i> : add rifampin, gentamicin | •Nafcillin causes vein irritation, best used continuous or with central line  | Rec, if MSK |

|  |  |   |   |  |   |                |
|--|--|---|---|--|---|----------------|
| Staphylococcus sp.<br>+ Staph aureus       | mecA pos   | Mixed Coag Neg<br>Staph (with mecA)<br>+ MSSA               | 1)Vancomycin  | <ul style="list-style-type: none"> <li>•<i>CNS infection or Endocarditis</i>: consider adding gentamicin</li> <li>•<i>Endocarditis with prosthetic material</i>: add rifampin, gentamicin</li> </ul>   |   | Rec, if<br>MSK |
| Staphylococcus sp.<br>+ Staph aureus       | mecA pos<br>AND MREJ<br>pos                          | MRSA  | 1)Vancomycin<br>2) Ceftaroline,<br>particularly for<br>very ill patients at<br>renal risk | <ul style="list-style-type: none"> <li>•<i>CNS infection or Endocarditis</i>: consider adding gentamicin</li> <li>•<i>Endocarditis with prosthetic material</i>: add rifampin, gentamicin</li> <li>•<i>MSK infection</i>: consider ceftaroline first line</li> </ul> |   | Rec, if<br>MSK |
| Streptococcus sp.                          |  | Strep species (Not<br>pneumococcus,<br>GAS, GBS)            | 1)Vancomycin  | <ul style="list-style-type: none"> <li>• <i>Endocarditis</i>: consider adding gentamicin</li> </ul>  | <ul style="list-style-type: none"> <li>•Narrow to ampicillin, penicillin, or cefazolin if susceptible</li> <li>•Possible species include (but not limited to): Strep viridans group (including Strep mitis), Strep anginosus, alpha-Streptococcus, beta-Streptococcus (not A or B)</li> </ul> |                |
| Streptococcus sp. +<br>Strep agalactiae    |  | Group B Strep   | 1)Ampicillin  | <ul style="list-style-type: none"> <li>•<i>Neonates</i>: consider synergistic gentamicin for first 5 days</li> </ul>   |   | Rec            |
| Streptococcus sp. +<br>Strep pyogenes      |  | Group A Strep   | 1) Ampicillin (or<br>any beta-lactam)   | <ul style="list-style-type: none"> <li>•<i>Toxin ds</i>: consider adding clindamycin</li> </ul>  | <ul style="list-style-type: none"> <li>•Can stop 2nd agent when improving</li> </ul>  | Rec            |
| Streptococcus sp. +<br>Strep pneumoniae    |  | Pneumococcus  | 1)Ceftriaxone<br>2)Ampicillin   | <ul style="list-style-type: none"> <li>•<i>Meningitis</i>: Vancomycin + Ceftriaxone</li> <li>•<i>Pneumonia</i>: High-Dose Ampicillin</li> </ul>  |   |                |
| <b>BCID2 Organism<br/>Targets Detected</b> | <b>BCID2<br/>Resistance<br/>Targets<br/>Detected</b> | <b>Final Organism<br/>Identification<br/>Interpretation</b> | <b>First-line<br/>Antimicrobial<br/>Options (in<br/>order of<br/>preference)</b>          | <b>Special Populations</b>   | <b>Notes</b>  | <b>ID c/s?</b> |

|                              |      |                              |                               |  |  |     |
|------------------------------|------|------------------------------|-------------------------------|--|--|-----|
| Acinetobacter baumannii      |      | Acinetobacter baumannii      | 1)Meropenem                   | <ul style="list-style-type: none"> <li>•High level resistance is rare at our center, so if patient is improving on cephalosporin may continue pending susceptibilities</li> </ul>  | <ul style="list-style-type: none"> <li>•Often carries constitutive (not inducible) AmpC, so can rely on MIC</li> <li>•Variable carbapenem-resistance mechanisms that are not detected (including efflux pumps and porin mutations)</li> </ul>  | Rec |
| Haemophilus influenza        |      | Haemophilus influenza        | 1)Ceftriaxone                 |  | <ul style="list-style-type: none"> <li>•Narrow to ampicillin if beta-lactamase neg. Beta-lactamase does not affect cephalosporins.</li> </ul>  | Rec |
| Neisseria meningitidis       |      | Neisseria meningitidis       | 1)Ceftriaxone<br>2)Ampicillin |  | <ul style="list-style-type: none"> <li>•May narrow once susceptibilities finalize</li> </ul>   | Rec |
| Pseudomonas aeruginosa       | none | Pseudomonas aeruginosa       | 1)Cefepime<br>2)Meropenem     | <ul style="list-style-type: none"> <li>•<i>Very ill or immunocompromised:</i> meropenem or double coverage with beta-lactam PLUS (fluoroquinolone or aminoglycoside) during hi-inoculum period to assure at least one active agent</li> </ul>                            | <ul style="list-style-type: none"> <li>•Dose cefepime on high end, shortest interval (50mg/kg q8h) as intermediate MICs may be susceptible, dose-dependent</li> <li>•Variable carbapenem-resistance mechanisms that are not detected (including efflux pumps and porin mutations)</li> </ul> | Rec |
| Bacteroides fragilis         |      | Bacteroides fragilis         | 1)Metronidazole               | <ul style="list-style-type: none"> <li>•<i>GI patients or GI abscess:</i> Plus ceftriaxone or cefepime (or single-agent meropenem)</li> <li>• <i>immunocompromised:</i> Plus cefepime (or single-agent meropenem)</li> </ul>   |  |     |
| Stenotrophomonas maltophilia |      | Stenotrophomonas maltophilia | 1)TMP/SMX                     | <ul style="list-style-type: none"> <li>•<i>Very ill or immunocompromised:</i> Dual coverage with TMP/SMX plus levofloxacin or ceftazidime until susceptibility results are known</li> <li>•Consider aztreonam-avibactam (or aztreonam + ceftaz-avibactam) for</li> </ul> | <ul style="list-style-type: none"> <li>•Has intrinsic MBL (metallo-beta-lactamase), intrinsic resistance to carbapenems</li> </ul>   | Rec |

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|   |  |  |                             | severely ill patients or those with MDR isolates.<br>•Could also consider eravacycline for MDR isolates |  |  |
| Enteric bacteria                                |  | Enteric bacteria of species not listed below | 1)Cefepime<br>2)Meropenem   | • <i>GI abscess</i> : Add anaerobic coverage  | •Potential for IBL<br>•Possible species include (but not limited to): Citrobacter spp, Enterobacter spp (other than cloacae), Cronobacter spp, Providencia spp, Yersinia spp, Serratia spp (other than marcescens), Morganella spp, Pantoea spp, Hafnia spp. |  |
| Enteric bacteria + Enterobacter cloacae complex |  | Enterobacter cloacae                         | 1)Cefepime<br>2)Meropenem   | • <i>GI abscess</i> : Add anaerobic coverage  | •Potential for IBL   |  |
| Enteric bacteria + Escherichia coli             |  | E Coli or Shigella                           | 1)Ceftriaxone               | • <i>GI abscess</i> : Add anaerobic coverage<br>• <i>Concern for ESBL</i> : meropenem                   | •if on pressor support consider meropenem  |  |
| Enteric bacteria + Klebsiella oxytoca           |  | Klebsiella oxytoca                           | 1)Ceftriaxone               | • <i>GI abscess</i> : Add anaerobic coverage<br>• <i>Concern for ESBL</i> : meropenem                   | • if on pressor support consider meropenem   |  |
| Enteric bacteria + Klebsiella pneumoniae        |  | Klebsiella pneumoniae                        | 1) Ceftriaxone              | • <i>GI abscess</i> : Add anaerobic coverage<br>• <i>Concern for ESBL</i> : meropenem                   | •if on pressor support consider meropenem  |  |
| Enteric bacteria + Klebsiella aerogenes         |  | Klebsiella aerogenes                         | 1) Cefepime                 | •Meropenem if critically ill  | •High likelihood for IBL or ESBL (TEM-24, not CTX-M type)<br>•Dose cefepime on high end, shortest interval as intermediate MICs may be susceptible, dose-dependent   |  |
| Enteric bacteria + Proteus spp.                 |  | Proteus                                      | 1) Cefepime<br>2) Meropenem | • <i>GI abscess</i> : Add anaerobic coverage  | •Potential for IBL (Indole pos species such as P. vulgaris or P. penneri)  |  |

|   |                                      |   |  |  |  |            |
|---|--------------------------------------|---|--|--|--|------------|
| Enteric bacteria + Salmonella spp.                                  |                                      | Salmonella                                  | 1) Ceftriaxone                                       |  | •Requires higher dosing 75mg/kg/day  | Rec        |
| Enteric bacteria + Serratia marcescens                              |                                      | Serratia marcescens                         | 1) Cefepime<br>2) Meropenem                          | • <i>GI abscess</i> : Add anaerobic coverage   | •Potential for IBL   |            |
| <i>Any Gram Negative Rod</i> (except Pseudomonas and Acinetobacter) | *KPC pos                             | Carbapenem resistant gram-negative rod      | 1) Ceftazidime-avibactam<br>2) Meropenem-vaborbactam | •Consider aztreonam-avibactam if available (ceftolozane-tazobactam not as effective)   | • <b>Call epi to notify and isolate</b><br>•Note resistance to ceftaz-avi emerges on therapy (observed 10% of the time)                                    | <b>Req</b> |
| <i>Any Gram-Negative Rod</i> (except Pseudomonas and Acinetobacter) | *IMP, NDM, or VIM pos                | MBL-producing gram negative rod             | 1) Aztreonam PLUS ceftazidime-avibactam              | •Consider adding colistin/polymyxin B or tigecycline   | • <b>Call epi to notify and isolate</b><br>•Consider aztreonam-avibactam if available (ceftolazone-tazo and ceftaz-avi alone not shown to be as effective) | <b>Req</b> |
| <i>Any Gram Negative Rod</i> (except Pseudomonas and Acinetobacter) | *OXA-48-like                         | Carbapenem resistant gram-negative rod      | 1) Ceftazidime-avibactam                             |  | • <b>Call epi to notify and isolate</b>  | <b>Req</b> |
| <i>Any Gram Negative Rod</i>  | *CTX-M pos                           | ESBL-producer                               | 1) Meropenem   |  | •Call epi to notify and isolate  | Rec        |
| <i>Any Gram Negative Rod</i>  | *Mcr-1 pos                           | Colistin-resistant                          | <b>Call ID</b>                                       | Resistant to almost all antimicrobials, call ID and CDC for recommendations  | • <b>Call epi to notify and isolate immediately</b><br>•Typically found with additional resistance genes   | <b>Req</b> |
| Pseudomonas aeruginosa  | *KPC, IMP, Oxa-like, NDM, or VIM pos | Carbapenem-resistant Pseudomonas aeruginosa | 1) Ceftolozane-tazobactam                            | Consider the following new agents if available:<br>•Imipenem-relebactam<br>•Cifiderocol<br>Could consider colistin/polymyxin B (Note: tigecycline not effective) | • <b>Call epi to notify and isolate</b><br>•Variable resistance mechanisms are not detected (including efflux pumps and porin mutations)                   | <b>Req</b> |
| Acinetobacter baumannii   | *KPC, IMP, Oxa-like,                 | Carbapenem-resistant                        | 1) Cifiderocol (if available)                        | Consider the following new agents if first-line agents not available:  | • <b>Call epi to notify and isolate</b>  | <b>Req</b> |

|   | NDM, or VIM pos   | Acinetobacter baumannii   | 2) Eravacycline (if available) | <ul style="list-style-type: none"> <li>•Colistin/polymyxin B</li> <li>•Tigecycline</li> </ul>   | <ul style="list-style-type: none"> <li>•Note: Combination B-lactam/B-lactamase inhibitors are NOT reliable</li> <li>•Variable resistance mechanisms are not detected (including efflux pumps and porin mutations)</li> </ul> |  |
|---|---|---|--------------------------------|---|--|--|
| BCID2 Organism Targets Detected/ Interpretation | First-line Antimicrobial Options (in order of preference) | Special Populations   |                                | Notes   | ID consult   |  |
| Candida albicans                                | 1) IV fluconazole   | <ul style="list-style-type: none"> <li>•Extensive Azole Exposure: IV micafungin</li> <li>•Neonate: IV liposomal amphotericin B</li> </ul>   |                                | •Discuss line removal.  | Rec  |  |
| Candida auris                                   | 1) IV micafungin  | <ul style="list-style-type: none"> <li>•Ill or immunocompromised: Consider dual IV micafungin + IV liposomal amphotericin B</li> <li>•Extensive Echinocandin Exposure: IV liposomal amphotericin B</li> <li>•Neonate: IV liposomal amphotericin B</li> <li>•CNS/Eye Disease: IV liposomal amphotericin B</li> </ul> |                                | <ul style="list-style-type: none"> <li>•Call epi to notify and isolate immediately</li> <li>•High fluconazole resistance. Reports of isolates resistant to all classes</li> <li>•Discuss line removal.</li> </ul> | Req  |  |
| Candida glabrata                                | 1) IV micafungin  | <ul style="list-style-type: none"> <li>•Extensive Echinocandin Exposure: IV liposomal amphotericin B</li> <li>•Neonate: IV liposomal amphotericin B</li> <li>•CNS/Eye Disease: IV liposomal amphotericin B</li> </ul>   |                                | <ul style="list-style-type: none"> <li>•Variable fluconazole resistance.</li> <li>•Discuss line removal.</li> </ul>   | Rec  |  |
| Candida krusei                                  | 1) IV micafungin  | <ul style="list-style-type: none"> <li>•Extensive Echinocandin Exposure: IV liposomal amphotericin B or IV voriconazole</li> <li>•Neonate: IV liposomal amphotericin B</li> <li>•CNS/Eye Disease: IV liposomal amphotericin B</li> </ul>  |                                | <ul style="list-style-type: none"> <li>•Intrinsic fluconazole resistance.</li> <li>•Discuss line removal.</li> </ul>  | Rec  |  |
| Candida parapsilosis                            | 1) IV fluconazole   | <ul style="list-style-type: none"> <li>•Extensive fluconazole exposure: IV liposomal amphotericin B or IV Voriconazole</li> <li>•Neonate: IV liposomal amphotericin B</li> </ul>  |                                | <ul style="list-style-type: none"> <li>•Higher MICs to echinocandins.</li> <li>•Discuss line removal.</li> </ul>  | Rec  |  |
| Candida tropicalis                              | 1) IV fluconazole   | <ul style="list-style-type: none"> <li>•Extensive fluconazole exposure: IV micafungin</li> <li>•Neonate: IV liposomal amphotericin B</li> </ul>   |                                | •Discuss line removal.  | Rec  |  |
| Cryptococcus neoformans/gattii                  | 1) IV liposomal amphotericin B                            | <ul style="list-style-type: none"> <li>•CNS: IV liposomal amphotericin B +flucytosine</li> <li>•Mild pulmonary disease or asymptomatic: Consider IV fluconazole</li> </ul>  |                                |   | Req  |  |

**Supplemental Table 2: non-BCID2 targets isolated in culture**

| <u>Organism</u>                | <u>Number isolated</u> |
|--------------------------------|------------------------|
| <i>Acinetobacter species</i>   | 1                      |
| <i>Micrococcus species</i>     | 5                      |
| <i>Rothia species</i>          | 3                      |
| <i>Corynebacterium</i>         | 3                      |
| <i>Moraxella species</i>       | 1                      |
| <i>Morganella species</i>      | 1                      |
| <i>Bacillus species</i>        | 2                      |
| <i>Abiotrophia species</i>     | 2                      |
| <i>Enterococcus gallinarum</i> | 1                      |