Reactivity and Specificity of a Research Use Only (RUO) Prototype of a Highly Multiplexed Sample-to-Answer PCR System for the Detection of Pathogens from Positive Blood Culture

Background
Rapid diagnosis of causative agents of bloodstream infections improves patient outcomes and antibiotic stewardship. BioFire Diagnostics, LLC, is developing the BioFire® Blood Culture Identification 2 (BCID2) Panel, increasing the coverage of the BioFire® FilmArray® Blood Culture Identification (BCID) Panel for key pathogens and antimicrobial resistance (AMR) markers in aerobic and anaerobic positive blood culture (PBC). This revision expands the menu from 27 to 43 targets, with 26 bacterial (14 revised, 6 new) and 7 fungal analytes (2 revised, 2 new), as well as 9 AMR markers (1 revised, 6 new). Notable additions include the anaerobe Bacteroides fragilis, the emerging fungal pathogen Candida auris, and the multiresistant bacteria strain, mcr-1. This study details the reactivity and specificity of a RUO BioFire BCID2 panel.

Methods
The prototype panel was tested with fungal and bacterial isolates, some carrying AMR markers, at two sites by multiple operators. Reactivity was assessed at 10^6-10^8 colony-forming units/mL (CFU/mL) for 368 analytes, and specificity at 10^3 CFU/mL for 31 on-panel and 160 off-panel strains. Evaluation included multiple strains for species level assays and AMR marker assays, as well as multiple species for family/genus level assays. Concordance with standard of care (SoC) results was examined for 157 archived PBC.

Preliminary Concordance of BioFire BCID and BCID2 Panels with SoC in Archived Clinical Samples

Exclusivity
- Panel exclusivity assessment against 191 species
  - On-panel organisms (intrapanel cross-reactivity)
  - Phylogenetic-neighbors
  - Representative subset of normal skin flora
  - Off-panel organisms likely to be encountered in PBC
- Bacteria tested at 10^6 CFU/mL
  - 100% specificity observed for 43/45 assays
  - 2/45 assays were found to cross-react with non-target species
- Endotoxin assays not evaluated

Conclusions
Performance of the RUO BioFire BCID2 Panel shows that many key pathogens implicated in bloodstream infections can be identified with high sensitivity and specificity, and highlights the utility of the updated assays and the expanded menu to aid in the diagnosis of etiological agents of bloodstream infections.

All data points were obtained with a Research Use Only (RUO) version of the panel. The BioFire BCID2 Panel has not been evaluated by the FDA or other regulatory agencies for In Vitro Diagnostic use.