INTRODUCTION/BACKGROUND
Infections of the central nervous system (CNS) are potentially life-threatening requiring urgent and appropriate treatment. One of the most common CNS infections, Enterovirus (EV), can be difficult to empirically diagnose as it presents with similar symptoms to more serious infections. Without accurate diagnosis, patients with EV infections may be unnecessarily treated with antibiotics and hospitalized until a more serious infection can be ruled out. A common method for detecting EV is PCR, either using Laboratory Developed Tests (LDT) or with an U.S. Food and Drug Administration (FDA) cleared test such as the Cepheid® Xpert® EV test.

BioFire Diagnostics has developed the FilmArray® (FA) Meningitis/Encephalitis (ME) panel to aid in the diagnosis of CNS infections. This rapid, user-friendly panel simultaneously tests for 6 bacterial, 8 viral and 2 fungal targets using approximately 200 µL of CSF, with a comprehensive result in about 1 hour.

The FilmArray System
The FilmArray is a lab-in-a-pouch medium-scale fluid manipulation test performed in a fully automated fashion. The FilmArray ME pouch has a fitment (B) containing freeze-dried reagents and plungers that plunge liquids to the film portion of the pouch. This portion consists of stations for cell lysis (C), magnetic bead-based nucleic acid purification (D & E), first-stage multiplex PCR (F & G) and an array of 102, second-stage nested PCRs (I).

PCR primers are dried into the wells of the array and each primer set amplifies a unique product of the first-stage multiplex PCR. The second-stage PCR product is detected in a melting analysis using a fluorescent double-stranded DNA binding dye, LCGreen®.

FilmArray Pouch Loading Instruction

1. Sample lysis and bead collection
2. Magnetic bead collection blaster
3. Elution Station
4. Multiplex Outer PCR blaster
5. Dilution blaster
6. Inner Nested PCR blaster

RESULTS
FA ME was concordant with the ARUP LDT and detected EV in all 50 samples (50/50). Results for Xpert EV were concordant with the ARUP LDT for EV. Residual specimens were then split and tested simultaneously using a research use only (RUO) FA ME panel and the Xpert EV test. Each sample was tested per the manufacturer’s instructions.

Sixty (60) CSF samples previously tested by the validated ARUP LDT were evaluated using the FA ME and Xpert EV tests. Of the 60 CSF samples, 50 were positive by the ARUP LDT for EV. Residual specimens were then split and tested simultaneously using a research use only (RUO) FA ME panel and the Xpert EV test. Each sample was tested per the manufacturer’s instructions.

The FilmArray ME Panel detected additional pathogens in some samples.

These data demonstrate similar performance for EV detection in clinical specimens between the ARUP LDT, the Xpert EV test and the FA ME system. Further, the FA ME system detected additional pathogens in some samples.

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Table 1. Enterovirus Detection in Frozen, Archived, De-Identified Patient CSF Samples

<table>
<thead>
<tr>
<th>Test</th>
<th>EV Detection</th>
<th>Error</th>
<th>Additional Detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARUP LDT</td>
<td>50/50</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>FA ME</td>
<td>50/50</td>
<td>0/0</td>
<td>S. pneumoniae (2), HSV2 (2), EBV (1)</td>
</tr>
<tr>
<td>GX-EV</td>
<td>47/48</td>
<td>2/0</td>
<td>NA</td>
</tr>
</tbody>
</table>

Discloser: “The FilmArray ME Panel has not been approved for in vitro diagnostic use by the FDA or any other regulatory agencies.”

Figure 1. EV Detection in sample EVcomp_20 with ARUP LDT, Cepheid Xpert EV, and FilmArray ME Panel

Figure 2. EV Detection in sample EVcomp_45 with ARUP LDT, Cepheid Xpert EV, and FilmArray ME Panel

Figure 3. EV and S. pneumoniae Detection in sample EVcomp_14 with FilmArray ME Panel

CONCLUSIONS
These data demonstrate similar performance for EV detection in clinical specimens between the ARUP LDT, the Xpert EV test and the FA ME system. Further, the FA ME system detected additional pathogens in some samples.

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VIRUSES
- Cryptosporidium
- Enterovirus
- Epstein-Barr virus
- HIV-1
- HIV-2
- Hepatitis B virus
- Hepatitis C virus
- Influenza virus
- Respiratory syncytial virus
- Varicella zoster virus

Yeast
- Cryptococcus neoformans/gattii

Bacteria
- Escherichia coli K1
- Haemophilus influenzae
- Listeria monocytogenes
- Neisseria meningitidis
- Streptococcus agalactiae
- Streptococcus pneumoniae