Supplementary Table 4. Major studies evaluating the performance of the FDA approved/cleared multiplex meningitis and encephalitis panel

Study	**Leber et al.** (1)			**Messacar et al.** (2)		**Hanson et al.** (3)			**Graf et al.** (4)			**Rhein et al.** (5)
	Sensitivity compared to conventional testing, before discrepant analysis	Specificity compared to conventional testing before discrepant analysis	Results after discrepant analysis: Concordant +/ discordant false +/ discordant False -	Number identified by: conventional testing/ multiplex panel	Percent positive agreement, n = 138	Number identified by: conventional testing/ multiplex panel (baseline agreement)	Sensitivity after discrepant analysis	Specificity after discrepant analysis	Number of samples positive by laboratory-developed tests	Number of samples positive by multiplex panel	Positive agreement between the multiplex panel and laboratory-developed tests	Performance compared to culture for cerebrospinal fluid collected on admission from patients with meningitis n = 36 (18 positive and 24 negative)
Cytomegalovirus	3/3 (100%)	1,554/1557 (99.8%)	4/2/0			7/4 (4)	57%	100%				
Enterovirus	44/46 (95.7%)	1,507/1,514 (99.5%)	49/2/2	33/36	96%	37/37 (36)	97%	100%	38	36	95%	
Herpes simplex virus 1	2/2 (100%)	1,556/1,558 (99.9%)	2/2/0	4/5	99%	12/13 (11)	93%	98%	4	2	50%	
Herpes simplex virus 2	10/10 (100%)	1,548/1,550 (99.9%)	11/1/0			29/29 (29)	100%	100%	1	1	100%	
Human herpes virus 6	18/21 (85.7%)	1,532/1,536 (99.7%)	19/3/2			13/18 (12)	95%	100%	2	2	100%	
Human parechovirus	9/9 (100%)	1,548/1,551 (99.8%)	12/0/0			0/1 (0)	100%	100%	16	15	94%	
Varicella zoster virus	4/4 (100%)	1,553/1,556 (99.8%)	6/1/0			32/32 (32)	100%	100%				
Escherichia coli K1	2/2 (100%)	1,557/1,558 (99.9%)	2/1/0	1/1	100%	1/1 (1)	100%	100%				
Haemophilus influenzae	1/1 (100%)	1,558/1,559 (99.9%)	2/0/0	1/1	100%	4/5 (4)	100%	100%	1	1	100%	
Listeria monocytogenes	0/0	1,560/1,560 (100%)	0/0/0			0/0	NA	100%				
Neisseria meningitidis	0/0	1,560/1,560 (100%)	0/0/0			1/1 (1)	100%	100%				
Streptococcus agalactiae	0/1 (0%)	1,544/1,559 (99.9%)	0/1/1	3/3	100%	1/5 (1)	67%	99%	1	1	100%	
Streptococcus pneumoniae	4/4 (100%)	1,544/1,556 (99.2%)	9/7/0			3/6 (3)	100%	99%	4	4	100%	
Cryptococcus neoformans/gattii	1/1 (100%)	1,555/1,559 (99.7%)	3/2/0			14/9 (8)	64%	NA				100% sensitivity and 100% specificity compared to culture upon initial patient presentation
Comparison methods	Fresh and frozen cerebrospinal fluid was studied. Viral and fungal targets were compared to PCR with bidirectional sequencing. Bacterial targets were compared to culture. Discrepant analysis was done by re-testing samples by conventional methods or the multiplex panel. In some cases an additional, independent molecular testing was used.			Frozen cerebrospinal fluid was studied. Bacterial testing was done by culture on solid plates and in blood culture bottles. Enterovirus testing was performed using the Xpert EVV RT-PCR (Cepheid). HSV was performed on the Multicode-RTx HSV RT-PCR (Luminex Corporation). Discrepant analysis was by repeat testing with the original method.		Frozen cerebrospinal fluid was studied and was included if previously positive by cryptococcal antigen (IMMY), laboratory-developed viral PCR assay, and/or bacterial culture. Discrepant analysis was with Associated Regional and University Pathologists (ARUP) laboratory-developed PCRs.			Frozen cerebrospinal fluid was selected based on positivity by laboratory-developed PCRs or culture (n=67). Additionally frozen cerebrospinal fluid that was negative for at least one of the laboratory-developed PCRs and with negative Gram stain and bacterial culture (n = 66) was studied; the laboratory-developed tests and the multiplex panel had 100% negative agreement.			Cerebrospinal fluid was prospectively collected. The cryptococcal antigen lateral flow assay (IMMY) and quantitative fungal cultures were used as the Gold standard.

NA = Not applicable

References :

1. **Leber AL, Everhart K, Balada-Llasat JM, Cullison J, Daly J, Holt S, Lephart P, Salimnia H, Schreckenberger PC, DesJarlais S, Reed SL, Chapin KC, LeBlanc L, Johnson JK, Soliven NL, Carroll KC, Miller JA, Dien Bard J, Mestas J, Bankowski M, Enomoto T, Hemmert AC, Bourzac KM.** 2016. Multicenter evaluation of BioFire FilmArray meningitis/encephalitis panel for detection of bacteria, viruses, and yeast in cerebrospinal fluid specimens. J Clin Microbiol **54:**2251-2261.
2. **Messacar K, Breazeale G, Robinson CC, Dominguez SR.** 2016. Potential clinical impact of the film array meningitis encephalitis panel in children with suspected central nervous system infections. Diagn Microbiol Infect Dis **86:**118-120.
3. **Hanson KE, Slechta ES, Killpack JA, Heyrend C, Lunt T, Daly JA, Hemmert AC, Blaschke AJ.** 2016. Preclinical assessment of a fully automated multiplex PCR panel for detection of central nervous system pathogens. J Clin Microbiol **54:**785-787.
4. **Graf EH, Farquharson MV, Cardenas AM.** 2017. Comparative evaluation of the FilmArray meningitis/encephalitis molecular panel in a pediatric population. Diagn Microbiol Infect Dis **87:**92-94.
5. **Rhein J, Bahr NC, Hemmert AC, Cloud JL, Bellamkonda S, Oswald C, Lo E, Nabeta H, Kiggundu R, Akampurira A, Musubire A, Williams DA, Meya DB, Boulware DR, Team A-C.** 2016. Diagnostic performance of a multiplex PCR assay for meningitis in an HIV-infected population in Uganda. Diagn Microbiol Infect Dis **84:**268-273.