Changi General Hospital
SingHealth

Tel: (65) 6788 8833
Fax: (65) 6788 0933
Changi General Hospital
2 Simei Street 3
Singapore 529889
www.cgh.com.sg
Reg No 198904226R

Test Name	**Meningitis / encephalitis PCR (Biofire FilmArray)**
Specimen Type	**Cerebrospinal fluid, collected by lumbar puncture.** **PLEASE NOTE:** Special attention should be paid to careful aseptic technique during specimen collection, with consideration of the use of surgical masks or N95 masks during collection to reduce the rate of specimen contamination with oral flora.
Special Instructions For Laboratory	**Special notes for CSF testing from patients with suspected CJD disease** Although CSF is a relatively low risk body fluid for CJD prion infectivity, decontamination methods for prion spillage require very harsh chemical or physical methods. Occasional pouch failure may occur for the FilmArray PCR system, resulting in potential fluid leakage. Such pouch failures occurring in a sample potentially containing CJD would result in the disposal of the entire PCR system, incurring very high costs, as the PCR system would be irreparably damaged by the decontamination methods. CSF samples from patients with possible CJD infection should therefore only be tested by the FilmArray system when there is reasonable clinical probability of acute microbial infection. The FilmArray test should not be used as a screening test in such patients. A suggested approach to assessing the need for FilmArray testing in such patients includes: 1) Assess clinical probability, based on clinical assessment, of the likelihood of ACUTE viral/bacterial/fungal infection 2) Review point 1 in light of biochemical parameters of CSF e.g. white cell count, protein, glucose levels 3) Consider standard HSV/VZV PCR as an initial first line of assessment, as working practices for standard PCR may allow for easier biocontainment of CSF sample For non-SingHealth laboratories, in patients with suspected CJD, we would suggest documenting the clinical indications for testing together with the FEME and chemical parameters of the CSF sample sent for testing. This reduce the chance of subsequent delay in testing, as absence of this information would require discussion between the requesting doctor and a microbiologist at CGH.
Specimen Storage And Transport	**Minimum sample volume required: 0.5 ml** **Transport to laboratory as quickly as possible. Samples should be refrigerated, if delay in specimen transport is anticipated. Refrigerated samples may be stored and tested for up to approximately 7 days.**
Specimen Minimum Volume	**0.5 ml**
Test Method	PCR
Expected Result	-
Reference Ranges	n/a
Turn Around Time	1 day
Days Of Testing	Daily
Hospital	CGH

Changi General Hospital
SingHealth

Tel: (65) 6788 8833
Fax: (65) 6788 0933
Changi General Hospital
2 Simei Street 3
Singapore 529889
www.cgh.com.sg
Reg No 198904226R

Laboratory	Microbiology Lab
Discipline	Microbiology
Contact Details	68504935
Clinical Information	The FilmArray ME Panel is an FDA-approved PCR test validated for testing of cerebrospinal fluid obtained via lumbar puncture from individuals with signs and/or symptoms of meningitis and/or encephalitis. The following organisms are detected by FilmArray: **Bacteria:** -Escherichia coli (K1 antigen positive) -Haemophilus influenzae -Listeria monocytogenes -Neisseria meningitidis (encapsulated) -Streptococcus agalactiae -Streptococcus pneumoniae **Viruses:** -Cytomegalovirus -Enterovirus group -Herpes simplex virus 1 -Herpes simplex virus 2 -Human herpesvirus 6 -Human parechovirus -Varicella zoster virus **Fungi:** -Cryptococcus neoformans / gattii The FilmArray ME Panel is NOT INTENDED for testing of specimens collected from indwelling central nervous system (CNS) medical devices. For patients suspected to have hospital-onset meningitis (e.g. post-surgical), please consider standard CSF culture. For a selected sub-group of patients with HO-meningitis (e.g. those who have received antimicrobial therapy prior to CSF collection), testing with the Bacteria / Candida Multiplex PCR MAY be considered, although CSF is an unvalidated sample type for the Bacteria / Candida PCR.
Link Out For Additional Information	A systematic review and diagnostic test accuracy meta-analysis https://www.sciencedirect.com/science/article/pii/S2589537022000050

Tel: (65) 6788 8833
Fax: (65) 6788 0933
Changi General Hospital
2 Simei Street 3
Singapore 529889
www.cgh.com.sg
Reg No 198904226R

Remarks

Clinical validation was done by manufacturer through evaluation of prospective specimens or archived specimens when some analytes* had a low prevalence in the prospective study.
Based on recently published meta-analysis [1], the following performance data is available for each of the analytes, as follows:

E. coli K1: 76.3 (47.9-91.9) / 99.6 (98.7-99.9)
H. influenzae: 81.1 (55.6-93.6) / 99.8 (99.5-99.9)
L. monocytogenes: 80.4 (40.4-96.1) / 99.5 (97.8-99.9)
N. meningitidis: 84.4 (53.9-96.2) / 99.1 (98.8-99.9)
S. agalactiae: 81.4 (52.3-94.6) / 99.4 (97.7-99.9)
S. pneumoniae: 93 (83.3-97.2) / 99.4 (98.2-99.8)
CMV**: 100 (n/a) / 99.8 (n/a)
EV (Species A-D): 99.8 (86.1-97.4) / 99.9 (99.7-100)
HSV-1: 78.2 (58.1-90.3) / 99.9 (99.8-100)
HSV-2: 94.5 (84.2-98.2) / 99.9 (99.8-100)
HHV-6**: 85.7 (n/a) / 99.7 (n/a)
HPeV**: 100 (n/a) / 99.8 (n/a)
VZV: 93.3 (83.6-97.4) / 99.9 (99.6-100)
C. neoformans/gattii**: 100 (n/a) / 99.7 (n/a)

[1] eClinicalMedicine 2022;44: 101275: adjusted rates following discrepant analysis
[**] manufacturer data

CLINICAL CONSIDERATIONS
A listing of the most significant clinical considerations is given below:

a) False negative results may occur when the microbial load in the specimen is very low (below the test limit of detection). In particular, failure of the FA ME panel to detect low viral loads of HSV1 have been reported [2], such as may occur in early or late disease. For patients with high index of suspicion of HSV encephalitis, additional testing using standalone HSV PCR should be considered.
b) The risk of false positive results with *Streptococcus pneumoniae* and *Streptococccus agalactiae* targets is reported to be higher [1]. Positive PCR results should be interpreted in conjunction with clinical and microbiological data.
c) Test performance has not been established for CSF specimens from patients without signs and/or symptoms of meningitis and/or encephalitis. As with any laboratory test, testing patients with a low pre-test probability of disease increases the risk of false-positive results.
d) The effect of antibiotic treatment on test performance has not been evaluated.
e) HHV-6 or CMV can exist in latent form that is reactivated during infection due to other pathogens (e.g., *Mycobacterium tuberculosis* or HIV). HHV-6 or CMV should be considered as the likely cause of meningitis/encephalitis only in appropriate clinical settings (usually patients with significant underlying immunosuppression).
f) *S. pneumoniae* and *H. influenzae* can be shed from the respiratory tract of healthy individuals. HSV-1 may also be shed from individuals with active or recurrent cold sores. Strict precautions should be exercised during specimen collection to prevent contamination leading to false positive results.
g) Only E. coli strains possessing the K1 capsular antigen will be detected. All other E. coli strains/serotypes will not be detected.
h) Only encapsulated strains of *N. meningitidis* will be detected. Unencapsulated *N. meningitidis* will not be detected.

[2] Clinical Microbiology and Infection 28 (2022); 79-84

TECHNICAL INFORMATION
The Limit of Detection (LOD) was determined by manufacturer through testing dilutions of contrived samples.
In CGH lab settings, LOD was verified by testing spiked-in CSF sample containing the next lowest concentration

Tel: (65) 6788 8833
Fax: (65) 6788 0933
Changi General Hospital
2 Simei Street 3
Singapore 529889
www.cgh.com.sg
Reg No 198904226R

near the defined LOD of the organism for bacteria and spiked-in CSF sample containing low viral load for viruses.

LOD for each organism is as below.
E. coli K1: 1000 CFU/mL
H. influenzae: 1000 CFU/mL
L. monocytogenes: 1000 CFU/mL
N. meningitidis: 100 CFU/mL
S. agalactiae: 1000 CFU/mL
S. pneumoniae: 100 cells/mL
CMV: 4300 copies/mL
EV(Species A-D): 5-50 TCID50/mL
HSV-1: 1510 copies/mL
HSV-2: 1290 copies/mL
HHV-6: 10000 copies/mL
HPeV: 500 TCID50/mL
VZV: 1660 copies/mL
C. neoformans/gattii: 100 CFU/mL