

SUPPLEMENTAL - TABLE S1 Comparator PCR assays and FilmArray ME Panel Limits of Detection (LoD)

Analyte	Assay Target	Analytical Validation			Comparator Assay Enrolled CSF Samples		
		Comparator LoD (TCID ₅₀ /mL or CFU/mL) ^a	FilmArray LoD (TCID ₅₀ /mL or CFU/mL) ^a	Median Comparator Assay Cq of Samples at LoD	Median of Cq Values	Range of Cq Values	Number of Detections
Viruses							
CMV	UL123	100	100	17.5	20.2	16.3 - 24.0	3
	UL54	100		17.1	19.7	15.5 - 23.1	3
EV	5utr1	1 - 89 ^b	5 - 50 ^a	15.4 - 22.0 ^b	17.4	7.1 - 26.7	46
	5utr2	1 - 100 ^b		19.5 - 26.5 ^b	18.8	5.0 - 30.9	45
HSV-1	UL30	100	250	29.2	20.9	19.6 - 22.1	2
	UL42	1,000		26.4	16.5	16.3- 16.8	2
HSV-2	UL30	66	50	28.3	29.9	24.1 - 33.1	10
	UL42	66		19.8	21.6	15.0 - 25.8	10
HHV-6	DR2	1,000 ^c	10,000	19.1	19.5	14.4 - 25.1	21
	U31	1,000 ^c		20.2	20.8	16.4 - 25.5	18
HPeV	5utr1	10	500	15.8	23.6	18.8 - 29.2	7
	5utr2	10		19.8	18.1	7.7 - 23.9	9
VZV	ORF62	0.10	0.10	20.3	19.9	12.2 - 25.8	4
	ORF63	0.10		18.7	13.3	12.3 - 14.2	2
Yeast							
<i>Cryptococcus</i>	cCryp-ATP6	175 - 1,000 ^d	100	24.4 - 24.5 ^d	27.7	-	1
	cCryp-COX2	175 - 1,000 ^d		19.0 - 23.5 ^d	23.9	-	1

^a TCID₅₀/mL were for viral targets and CFU/mL were for *Cryptococcus* target.

^b Four Enterovirus groups (A, B, C, and D) were evaluated separately; the range of results is shown.

^c Units are in copies/mL.

^d Two *Cryptococcus* species (*C. neoformans* and *C. gattii*) were evaluated separately; the range of results is shown.

Abbreviations: TCID₅₀/mL, tissue culture infective dose 50 percent/ mL; CFU/mL, colony forming units/mL; Cq, Quantification Cycle (analogous to Ct, Cycle Threshold)

SUPPLEMENTAL- TABLE S2 Discrepant Investigation for Samples with Discordant Results [FilmArray ME Panel (FA) versus Comparator Methods]

Patient No.	Target	Demographic Information:		CSF Parameters						Discrepancy Investigation			Final Resolution of FA Result ^d
		Age, Sex	Immune Status ^e	Glucose (mg/dL)	Protein (mg/dL)	CSF Appearance	RBC (cells/ μ L)	WBC (cells/ μ l)	Gram Stain	AAC given before LP ^b	Additional Analysis or Supplemental Testing ^a	Summary of Clinical Diagnosis from Medical Records (final diagnosis) ^c :	
	False Positive												
1	<i>E. coli</i> K1	35-64 yr, F	0	51	28	Clear	4	3	NOS	none	2 nd target PCR (neuC) = negative	Non-infectious, CNS disease (Hyperviscosity syndrome, no infection)	FP
2	<i>H. influenzae</i>	2-23 mo, M	0	5	175	Cloudy	19	1255	GND C	none	2 nd target PCR (OMP P6) = positive	Infectious, CNS disease (Meningitis, presumed Gram Negative)	TP
3	<i>S. agalactiae</i>	+65 yr, M	0	72	21	Clear	81	1	NOS	VAN, TZP	2 nd target PCR (cfb) = negative	Infectious, non-CNS (Sepsis)	FP

											HSV-2 also detected by FA(TP) and SOC testing	secondary to prostatitis, negative blood cultures)	
4	<i>S. pneumoniae</i>	2-23 mo, M	0	32	157	Clear	0	101	NOS	none	2 nd target PCR (α -fucosidase) = positive, FA retest = positive Blood and joint fluid culture positive for <i>S. pneumoniae</i> , CSF PCR positive for <i>S. pneumoniae</i> by LDT PCR	Infectious, CNS disease (Bacteremia, septic joint and ME with <i>S pneumoniae</i>)	TP
5	<i>S. pneumoniae</i>	18-34 yr, M	4	9	204	Xanthochromic	2000	3968	NOS	CRO, AZM, AMB, 5FC, FLC	2 nd target PCR (α -fucosidase) = positive, FA retest = positive	Infectious, non-CNS (Cryptococcal sepsis, HIV)	TP
6	<i>S. pneumoniae</i>	35-64 yr, M	0	62	277	Xanthochromic	190	1450	NOS	CRO, VAN, ACV	2 nd target PCR (α -fucosidase) = positive, FA retest = positive	Unknown, not definitive (Heavy WBC, concern of falsely negative CSF culture)	TP

7	<i>S. pneumoniae</i>	>65 yr, F	0	10	998	Xanthochromic	11	5740	GPC	Broad Cvg.	2 nd target PCR (α -fucosidase) = positive, FA retest = positive	Infectious, non-CNS (<i>S. pneumoniae</i> sepsis)	TP
8	<i>S. pneumoniae</i>	>65 yr, M	0	10	858	Xanthochromic	386	2720	GPC	none	2 nd target PCR (α -fucosidase) = positive	Non-infectious, non-CNS (Broken arm, delirium)	TP
9	<i>S. pneumoniae</i>	<2 mo, M	8	46	71	Clear	560	3	NOS	none	2 nd target PCR (α -fucosidase) = negative, FA retest =negative	Infectious, non-CNS (<i>S. agalactiae</i> in urine)	FP
10	<i>S. pneumoniae</i>	<2 mo, M	0	65	5	Clear	7	3	NOS	none	2 nd target PCR (α -fucosidase) = negative, FA retest =negative	Infectious, non-CNS (Parainfluenza)	FP
11	<i>S. pneumoniae</i>	2-17 yr, M	0	53	5	Clear	0	0	NOS	CRO	2 nd target PCR (α -fucosidase) = negative, FA retest =negative	Infectious, non-CNS (Folliculitis)	FP
12	<i>S. pneumoniae</i>	18-34 yr, F	0	56	49	Clear	0	1	NOS	none	2 nd target PCR (α -fucosidase) = negative, FA retest =negative	Non-infectious, CNS disease (Epilepsy)	FP
13	<i>S. pneumoniae</i>	18-34 yr, F	0	58	19	Clear	0	1	NOS	none	2 nd target PCR (α -fucosidase) = negative,	Infectious, non-CNS (Bell's	FP

											FA retest =negative	palsy)	
14	<i>S. pneumoniae</i>	35-64 yr, M	0	101	35	Clear	0	1	NOS	SXT, FLC, ACV	2 nd target PCR (α -fucosidase) = negative, FA retest =negative	Infectious, non-CNS (Hepatitis B, Multiple Myeloma)	FP
15	<i>S. pneumoniae</i>	>65 yr, M	0	60	45	Clear	186	2	NOS	none	2 nd target PCR (α -fucosidase) = negative	Unable to obtain	FP
16	CMV	2-17 yr, F	0	0	192	Cloudy	255	615	GPD C	none	2 nd target PCR (UL38) = positive CSF positive for <i>S pneumoniae</i> by FA (TP)	Infectious, CNS disease (Bacterial ME, <i>S. pneumoniae</i>)	TP
17	CMV	<2 mo, F	0	50	67	Clear	0	2	NOS	none	2 nd target PCR (UL38) = negative	Unknown, not definitive (Febrile illness, pyelonephritis)	FP
18	CMV	<2 mo, M	8	49	79	Xanthochromic	2480	9	NOS	ERY, ACV	2 nd target PCR (UL38) = negative	Non-infectious, non CNS (hyperbilirubinemia)	FP
19	EV	<2 mo, F	0	38	38	Clear	3	2	NOS	none	2 nd target PCR (5'UTR) = positive	Infectious, non-CNS (sepsis, unspecified)	TP
20	EV	<2	0	52	166	Bloody	21000	9	NOS	none	2 nd target PCR	Unknown/n	TP

		mo, M									(5' UTR) = positive CSF also positive for HPeV by FA (TP)	ot definitive (Fever, at risk for sepsis, not meningitis due to normal LP and labs)	
21	EV	<2 mo, M	0	43	639	Bloody	5730	149	NOS	Broad AM and AV	CSF positive for Enterovirus by LDT PCR	Unknown/n ot definitive (Neonate, lethargic and sleepy)	TP
22	EV	2-23 mo, F	0	74	5	Clear	0	3	NOS	none	2 nd target PCR (5' UTR) = positive, CSF negative for Enterovirus by LDT PCR	Infectious, non-CNS (Rhinovirus /Enteroviru s)	TP
23	EV	2-17 yr, F	0	58	50	Clear	20	6	NOS	none	2 nd target PCR (5' UTR) = positive	Non- infectious, CNS (Status-post brain tumor resection, fever, malaise, and nausea/vom iting)	TP
24	EV	2-17 yr, F	0	61	31	Clear	2	1	NOS	none	2 nd target PCR (5' UTR) =	Unknown/n ot	FP

											negative	definitive (Convulsions, fever)	
25	EV	18-34 yr, F	3	54	110	Clear	19	136	NOS	Broad AM and AV	2 nd target PCR (5' UTR) = negative, CSF negative for Enterovirus by LDT PCR	Unknown/not definitive (Kidney Transplant, extremity weakness and facial droop)	FP
26	HSV-1	2-23 mo, M	0	132	12	Clear	0	1	NOS	CRO	2 nd target PCR (US7) = negative, Enhanced comparator = negative, CSF negative for HSV by LDT PCR	Non-infectious, CNS (Complex Febrile Seizures, Rhinovirus)	FP
27	HSV-1	2-23 mo, F	0	63	11	Clear	94	3	NOS	CRO	2 nd target PCR (US7) = negative, CSF positive for HHV-6 by FA (TP)	Infectious, not definitive (Fever of unknown origin, neck pain, bulging fontanel)	FP
28	HSV-2	35-64 yr, M	0	58	256	Clear	9	367	NOS	CRO	CSF positive for HSV by LDT PCR	Infectious, CNS (Viral meningitis, HSV)	TP
29	HSV-2	35-64 yr, F	0	92	28	Clear	19	2	NOS	none	2 nd target PCR (US2) =	Unknown, not	FP

											negative	definitive	
30	HHV-6	18-34 yr, F	2	66	35	Clear	1540	2	NOS	none	2 nd target PCR (pol) = positive	Non-infectious, non-CNS (Acute myeloblastic leukemia)	TP
31	HHV-6	2-23 mo, M	0	59	22	Clear	2	79	NOS	none	2 nd target PCR (pol) = negative	Unknown, not definitive (Fever)	FP
32	HHV-6	2-17 yr, M	0	57	56	Clear	16	79	NOS	none	2 nd target PCR (pol) = negative	Non-infectious, CNS disease (Transverse myelitis)	FP
33	HHV-6	2-17 yr, M	0	53	42	Clear	9	134	NOS	none	2 nd target PCR (pol) = negative	Infectious, CNS disease (Viral/aseptic ME, unspecified)	FP
34	HPeV	<2 mo, M	8	49	42	Clear	0	2	NOS	none	2 nd target PCR (5'UTR) = negative CSF negative and Blood positive for HPeV by LDT PCR	Infectious, non-CNS (HPeV in blood)	TP
35	HPeV	<2 mo, F	0	55	45	Clear	10	7	NOS	GEN	2 nd target PCR (5'UTR) = negative	Infectious, non-CNS (HPeV in	TP

											CSF negative and Blood/throat positive for HPeV by LDT PCR	blood)	
36	HPeV	<2 mo, F	8	40	44	Clear	2	14	NOS	none	2 nd target PCR (5'UTR) = negative CSF positive for HPeV by LDT PCR	Infectious, CNS (Viral/aseptic ME, HPeV)	TP
37	VZV	35-64 yr, F	0	64	58	Clear	2	422	NOS	ACV	2 nd target PCR (ORF17) = negative CSF negative for VZV by LDT	Infectious, non-CNS (Herpes zoster oticus)	TP
38	VZV	>65 yr, F	0	51	62	Clear	74	20	NOS	none	2 nd target PCR (ORF17) = negative Serum positive for HSV IgM	Infectious, non-CNS (VZV/Herpes zoster)	TP
39	VZV	18-34 yr, M	4	9	204	Xanthochromic	2000	3968	NOS	CRO, AZM, AMB, 5FC, FLC	2 nd target PCR (ORF17) = negative	Infectious, non-CNS (cryptococcal sepsis, HIV)	FP
40	<i>C. neoformans/gattii</i>	35-64 yr, M	0	27	90	Clear	21	18	Yeast	none	CSF positive for Cryptococcal Ag Repeat comparator ^e =	Infectious, CNS (Fungal/cryptococcal ME)	TP

											negative		
41	<i>C. neoformans/gattii</i>	35-64 yr, M	4	11	162	Clear	1	37	NOS	HAAR T, VRC	CSF positive for Cryptococcal Ag	Infectious, CNS (Fungal/cryptococcal ME)	TP
42	<i>C. neoformans/gattii</i>	<2 mo, F	8	110	62	Clear	1	7	NOS	none	CSF negative for Cryptococcal Ag	Infectious, non-CNS (<i>E. coli</i> UTI, rhinovirus NPS)	FP
43	<i>C. neoformans/gattii</i>	16-34 yr, M	0	62	56	Clear	0	1	NOS	none	CSF negative for Cryptococcal Ag	Unknown/n of definitive (EBV serology high)	FP
	<i>False Negative</i>												
44	<i>S. agalactiae</i>	+65 yr, M	0	81	32	Clear	8	1	NOS	none	2 nd target PCR (cfb) = negative FA retest = negative	Infectious, CNS disease (Soft tissue infection with Gp B Strep. related to spinal implant)	FN
45	EV	<2 mo, F	0	51	50	Clear	1	9	NOS	none	2 nd target PCR (5' UTR) = positive, FA retest = positive	Infectious, non-CNS (Enterovirus hand-foot-mouth disease)	FN

46	EV	2-23 mo, M	0	58	32	Clear	0	3	NOS	none	FA retest = negative, CSF positive for Enterovirus by LDT PCR	Infectious, CNS (Enterovirus ME)	FN
47	HHV-6	2-23 mo, F	0	50	27	Clear	1300	2	NOS	CRO, ACV	2 nd target PCR (pol) = negative	Infectious, non-CNS (<i>E. coli</i> UTI)	FN
48	HHV-6	2-17 yr, M	0	46	93	Clear	2	255	NOS	none	Comparator retest = positive CSF positive for EV by FA (TP)	Infectious, CNS disease (Viral/aseptic ME, unspecified)	FN
49	HHV-6	<2 mo, M	0	52	96	Clear	254	324	NOS	none	2 nd target PCR (pol) = negative CSF positive for EV by FA (TP)	Infectious, CNS disease (Viral/aseptic ME, unspecified)	TN

^a Additional analyses may have included a 2nd commercially available PCR assay performed at BioFire (target gene), repeat testing with FA or comparator testing, or results of testing done at trial sites as standard of care. Investigational testing was limited by specimen volumes.

^b Antimicrobial or other chemotherapeutics (antivirals) given within 24 hours prior to collection of CSF by spinal tap.

^c Information collected for discrepancy investigation from additional review of the medical record by each trial site to determine the final clinical diagnosis.

^d Final resolution determined as agreement with 2 of 3 results: 1) FA testing, 2) comparator testing, and 3) composite findings from Gram stain, additional analysis/supplemental testing, and final clinical diagnosis.

^e Immune status was determined and categorized as follows according to 2013 Infectious Diseases Society of America Guidelines.¹³

0. Immunocompetent
1. Combined primary immunodeficiency disorder (e.g., severe combined immunodeficiency)
2. Receiving cancer chemotherapy
3. Within two months after solid organ transplantation or receiving augmented immunosuppression for rejection
4. With Human Immunodeficiency Virus (HIV) infection with a CD4 T-lymphocyte count <200 cells/mm³ for adults and adolescents and percentage <15 for infants and children
5. Receiving daily corticosteroid therapy with a dose ≥ 20 mg (or >2 mg/kg/day for patients who weigh <10 kg) of prednisone or equivalent for ≥ 14 days
6. Receiving certain biologic immune modulators, that is, a tumor necrosis factor-alpha (TNF- α) blocker or rituximab
7. Premature birth with a corrected gestational age <40 weeks
8. Infants <30 days who are full term

Abbreviations: 5 FC, 5-flucytosine; AAC, antimicrobial agents and chemotherapy; ACV, acyclovir; AM, antimicrobial; AMB, amphotericin B; AV, antiviral; AZM, azithromycin; Broad Cvg, broad coverage, not otherwise specified; CNS, central nervous system; CSF, cerebral spinal fluid; CRO, ceftriaxone; ERY, erythromycin; F, female; FLC, fluconazole; FP, false positive; GEN, gentamicin; GNDC, Gram negative diplococci; GPC, Gram positive cocci; GPDC, gram positive diplococci; HAART, highly active antiretroviral therapy; LDT, laboratory-developed test; LP, lumbar puncture; M, male; ME, meningitis/encephalitis; NOS, no organisms seen in smear; TZP, piperacillin/tazobactam; SXT, trimethoprim-sulfamethoxazole; TN, true negative; TP, true positive; UTI, urinary tract infection; VAN, vancomycin; WBC, white blood cells.

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

Positive FilmArray ME Target	Demographic Information:		CSF Parameters				AAC given before LP ^b	Summary of Clinical Diagnosis for Medical Records (Final Diagnosis) ^c
	Age, Sex	Immune Status ^a	Glucose (mg/dL)	Protein Conc. (mg/dL)	WBC Count (cells/ μ L)	Gram Stain		
<i>E.coli</i> K1	35-64 yr, M	0	60	70	2000	GNR	VAN, CAZ	Bacterial ME (<i>E. coli</i>); status post neurosurgery
<i>E.coli</i> K1	2-23 mo, F	0	72	152	11	NOS	<i>none</i>	Bacterial ME (<i>E. coli</i> and <i>S. viridans</i>); E coli sepsis and meningitis, venous sinus thrombosis, R femoral DVT, seizures.
<i>H. influenzae</i>	35-64 yr, F	9 ^a	42	109	1485	NOS	<i>none</i>	Bacterial ME (<i>H. influenzae</i>); Haemophilus meningitis
<i>S. pneumoniae</i>	35-64 yr, M	0	2	468	7250	NOS	VAN, CAZ	Bacterial ME (<i>S. pneumoniae</i>); <i>S. pneumoniae</i> sepsis and meningitis
<i>S. pneumoniae</i>	2-17 yr, F	0	0	192	615	GPDC	<i>none</i>	Bacterial ME (<i>S. pneumoniae</i>); <i>S. pneumoniae</i> meningitis
<i>S. pneumoniae</i>	2-23 mo, M	0	84	136	528	GPDC	VAN, CRO, ACV	Bacterial ME (<i>S. pneumoniae</i>); <i>S. pneumoniae</i> meningitis, complex febrile seizure, pos for <i>S. pneumoniae</i> and Rhino/EV from NP

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

<i>S. pneumoniae</i>	35-64 yr, M	2	48	298	1518	GPC	Broad CVG	Infectious, non-CNS; advanced oropharyngeal squamous cell carcinoma. Presenting with pneumonia, sepsis and altered mental status. (pneumonia, unspecified sepsis)
CMV	18-34 yr, M	4	52	28	2	NOS	TZP, SXT, AZM, GCV, FOS	Viral/aseptic ME (CMV); HIV/AIDs with a CD4 of <20. CNS lymphoma, CMV encephalitis, and being treated empirically for possibility of CNS toxoplasmosis.
CMV	<2 mo, F	0	62	115	5	NOS	<i>none</i>	Unknown/not definitive; fever
CMV	<2 mo, F	1	25	86	73	NOS	FEP, ACV, FLC	Infectious, non-CNS (CMV); jaundice and hyperbilirubinemia. CMV pos
EV	2-17 yr, M	0	46	93	255	NOS	<i>none</i>	Viral/aseptic ME (unspecified); viral meningitis
EV	<2 mo, M	8	33	71	163	NOS	<i>none</i>	Viral/aseptic ME (EV); enterovirus meningitis
EV	2-23 mo, M	0	48	130	47	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus meningoencephalitis and viremia
EV	<2 mo, F	8	44	79	23	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus meningitis
EV	2-17 yr, M	0	69	24	2	NOS	<i>none</i>	Non-infectious, CNS disease; Migraine
EV	2-17 yr, F	0	50	27	79	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus meningitis

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

EV	<2 mo, M	8	22	185	4	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus meningitis
EV	<2 mo, M	0	49	24	1	NOS	<i>none</i>	Unknown/not definitive; Fever of the newborn
EV	<2 mo, M	8	43	95	1	NOS	AMP, GEN	Viral/aseptic ME (EV); meconium aspiration/pneumonia, sepsis, enterovirus meningitis
EV	<2 mo, F	8	40	43	77	NOS	AMP, ACV	Viral/aseptic ME (EV); enterovirus meningitis (fever, macular rash, EV pos in CSF, blood and swab.)
EV	<2 mo, F	8	35	80	550	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus aseptic meningitis (Present with fever, poor PO intake, aseptic meningitis. EV pos in CSF, blood, and pooled specimens)
EV	<2 mo, F	0	36	50	82	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus Infectious (Fever, EV pos in CSF and blood, EV/Rhino pos respiratory specimen)
EV	<2 mo, F	0	41	39	325	NOS	<i>none</i>	Viral/aseptic ME (EV); Neonatal sepsis (Fever, EV pos CSF and pooled specimen, pos EV/Rhinovirus respiratory specimen)
EV	2-17 yr, M	0	47	84	715	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus meningitis (Present fever, rash, myalgia, EV pos in CSF)

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

EV	<2 mo, M	0	36	96	299	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus meningitis (Present fever, EV pos CSF and pooled specimens)
EV	<2 mo, F	8	60	52	0	NOS	<i>none</i>	Infectious, non-CNS (EV in blood); Fever secondary to viral infection (Fever, EV pos in blood and pooled specimen)
EV	<2 mo, M	8	40	74	5	NOS	<i>none</i>	Viral/aseptic ME (EV); Fever secondary to viral infection (Fever, EV pos in blood and pooled specimen)
EV	<2 mo, F	0	39	280	760	NOS	AMP, GEN, ACV	Viral/aseptic ME (EV); Enterovirus meningitis, Cleft palate (developed tachypnea, pos for EV in CSF, some intraventricular hemorrhage, cerebral edema)
EV	<2 mo, F	8	57	50	29	NOS	<i>none</i>	Viral/aseptic ME (EV); Neonatal fever, Enterovirus, Anemia (Fever, EV positive in blood, CSF, pooled specimens, EV/RH pos respiratory specimen)
EV	<2 mo, M	0	62	110	25	NOS	<i>none</i>	Viral/aseptic ME (EV); Enterovirus meningitis (EV pos in blood & CSF)
EV	<2 mo, M	8	42	130	1779	NOS	<i>none</i>	Viral/aseptic ME (EV); Aseptic meningitis (Fever, EV pos in CSF and blood. RH/EV pos in respiratory specimen)

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

EV	<2 mo, M	0	52	525	70	NOS	<i>none</i>	Viral/aseptic ME (EV); Fever in newborn, r/o sepsis (Fever, congestion, EV pos in CSF, blood & rectal. EV/RH pos in respiratory specimen)
EV	<2 mo, M	0	39	212	226	NOS	<i>none</i>	Infectious, non-CNS (enterovirus/rhinovirus); Fever, diarrhea, EV/RH pos in respiratory specimen, EV pos in pooled specimen
EV	2-17 yr, M	0	58	43	28	NOS	<i>none</i>	Viral/aseptic ME (EV); Enteroviral meningitis (EV pos in CSF)
EV	<2 mo, F	8	49	80	0	NOS	<i>none</i>	Viral/aseptic ME (EV); fever in a neonate, Enterovirus infection (EV pos in CSF, blood and pooled specimen. EV/RH pos in respiratory specimen)
EV	<2 mo, M	0	48	19	4	NOS	<i>none</i>	Viral/aseptic ME (EV); Enteroviral meningitis (EV pos CSF and blood)
EV	<2 mo, F	0	43	83	594	NOS	<i>none</i>	Viral/aseptic ME (EV); Fever in newborn, Enterovirus meningitis (EV pos CSF and blood)
EV	18-34 yr, M	0	69	48	142	NOS	<i>none</i>	Viral/aseptic ME (EV); Aseptic meningitis, enterovirus (EV pos CSF)
EV	<2 mo, M	0	36	160	410	NOS	<i>none</i>	Viral/aseptic ME (EV)
EV	2-17 yr, M	9 ^b	95	89	943	NOS	<i>none</i>	Viral/aseptic ME (EV)

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

EV	<2 mo, M	0	40	90	117	NOS	<i>none</i>	Viral/aseptic ME (EV)
EV	2-23 mo, M	0	43	33	1	NOS	<i>none</i>	Infectious, non-CNS (viral syndrome); Likely viral syndrome, sepsis ruled out
EV	2-17 yr, M	0	52	10	34	NOS	<i>none</i>	Infectious, non-CNS (viral syndrome); Fever, viral syndrome, no signs of sepsis or meningitis
EV	2-17 yr, M	0	58	22	33	NOS	<i>none</i>	Viral/aseptic ME (EV)
EV	18-34 yr, F	9 ^c	58	46	46	NOS	<i>none</i>	Viral/aseptic ME (unspecified)
EV	18-34 yr, F	9 ^d	55	61	148	NOS	VAN, CRO, ACV	Viral/aseptic ME (unspecified)
EV	<2 mo, F	8	56	50	1	NOS	Amp, CTX	Infectious, non-CNS (rhinovirus); Upper respiratory infection – Rhino/Enterovirus
EV	<2 mo, F	0	51	50	2	NOS	amoxicillin	Viral/aseptic ME (EV)
EV	<2 mo, M	0	42	30	0	NOS	<i>none</i>	Unknown/not definitive; Fever, unspecified
EV	2-23 mo, F	0	55	47	29	NOS	<i>none</i>	Viral/aseptic ME (unspecified); acute upper respiratory infection, unspecified viral meningitis
EV	2-17 yr, M	0	53	27	16	NOS	<i>none</i>	Viral/aseptic ME (unspecified)
EV	2-23 mo, F	0	59	70	194	NOS	<i>none</i>	Viral/aseptic ME (unspecified)
EV	<2 mo, F	8	47	42	2	NOS	<i>none</i>	Viral/aseptic ME (unspecified)
EV	<2 mo, M	0	52	96	324	NOS	<i>none</i>	Viral/aseptic ME (unspecified)

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

HSV-1	35-64 yr, F	0	68	130	137	NOS	Broad AM and AV	Unspecified ME; Multiple, focal neurologic deficits, including uncontrolled seizure and probably meningitis
HSV-1	35-64 yr, M	9°	117	260	878	NOS	CLI, ACV	Viral/aseptic ME (HSV); Herpes encephalitis, hypoxic brain injury, chronic kidney disease, peripheral nerve disorder, congenital spherocytosis, Type II diabetes
HSV-2	35-64 yr, M	4	49	690	240	NOS	none	Unknown/not definitive; HIV with CD4 >800 cells/mm ³
HSV-2	65+ yr, M	0	72	21	1	NOS	VAN, DAP, TZP	Infectious, non-CNS (unspecified sepsis); Sepsis secondary to prostatitis, negative blood cultures
HSV-2	35-64 yr, M	0	72	56	218	NOS	VAN, CRO, ACV	<i>Unable to obtain</i>
HSV-2	35-64 yr, F	2	28	70	124	NOS	<i>none</i>	Non-infectious/non-CNS; squamous cell lymphoma, metastatic endometrial CA and Hep C presenting with headaches, vomiting and abdominal pain

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

HSV-2	65+ yr, F	0	53	109	540	NOS	<i>none</i>	Non-infectious/non-CNS; Hypertension, diabetes type 2, hypothyroidism, Hyperlipidemia, esophagitis, presents to the ED with headache
HSV-2	35-64 yr, F	0	67	109	300	-	<i>none</i>	Unknown/not definitive; History of asthma; Migraines, and HTN. Presents with generalized body aches and constant headache for past 24 hrs.
HSV-2	35-64 yr, F	9 [†]	39	59	489	NOS	AMP, VAN, CRO, ACV	Viral/aseptic ME (HSV)
HSV-2	35-64 yr, M	0	73	64	312	NOS	ACV	Viral/aseptic ME (HSV); HSV meningoencephalitis based on HSV2 antibody in CSF
HSV-2	65+ yr, M	0	49	247	255	NOS	VAN, CRO, ACV	Viral/aseptic ME (HSV); recurrent HSV meningitis
HSV-2	18-34 yr, M	0	50	109	13	NOS	<i>none</i>	Viral/aseptic ME (unspecified)
HHV-6	18-34 yr, F	2	39	64	0	NOS	DAP, MEM, SXT, ACV	Unknown/not definitive; Acute lymphocytic leukemia
HHV-6	<2 mo, M	8	47	150	32	NOS	<i>none</i>	Infectious, non-CNS (<i>E. coli</i> UTI)
HHV-6	2-23 mo, F	0	149	71	1	NOS	<i>none</i>	Non-infectious/CNS disease; Cardiac arrest resulting in severe hypoxic ischemic encephalopathy
HHV-6	<2 mo, F	8	0	0	0	NOS	<i>none</i>	Infectious, non-CNS (herpetic whitlow)

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

HHV-6	<2 mo, F	0	47	64	11	NOS	<i>none</i>	Unknown/not definitive; Low-risk febrile illness
HHV-6	<2 mo, F	8	40	57	5	NOS	<i>none</i>	Infectious, non-CNS (herpetic whitlow)
HHV-6	<2 mo, F	8	41	122	3	NOS	AMP, CRO, ACV	Non-infectious/non-CNS; Severe mixed sleep apnea- acute life-threatening event
HHV-6	<2 mo, M	0	41	38	6	GNR	<i>none</i>	Bacterial ME (GNR meningitis)
HHV-6	2-23 mo, F	0	81	30	1	NOS	<i>none</i>	Unknown/not definitive; Fever, dehydration
HHV-6	<2 mo, M	0	49	44	2	NOS	AMP, GEN	Infectious, non-CNS (rhinovirus); Fever (Present with fever, cough, congestion, poor PO intake. Rhinovirus pos, loose stools)
HHV-6	2-23 mo, F	0	51	11	0	NOS	AMX	Infectious, non-CNS; Seizure-like activity, Acute Otitis Media, febrile, developed erythematous macular rash.
HHV-6	2-23 mo, F	0	63	11	3	NOS	CRO	Unknown/not definitive; Fever of Unknown origin ,Fever, neck pain, bulging fontanelle
HHV-6	2-23 mo, F	0	62	15	4	NOS	AMX	Infectious, non-CNS (rhinovirus); Fever, cough, congestion, poor PO intake. Rhinovirus pos, loose stools
HHV-6	2-23 mo, M	7	38	184	8	NOS	<i>none</i>	Infectious, non-CNS (pneumonia, UTI)
HHV-6	18-34 yr, M	0	63	15	1	NOS	TZP, GCV	Infectious, non-CNS (HHV-6)

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

HHV-6	35-64 yr, M	0	37	157	42	NOS	<i>none</i>	Infectious, CNS (MSSA pneumonia); Encephalopathy, unspecified, Pneumonia-MSSA
HHV-6	<2 mo, F	0	59	41	4	NOS	<i>none</i>	Infectious, non-CNS (unspecified bacteremia); fever
HHV-6	<2 mo, F	0	60	24	2	NOS	<i>none</i>	Viral/aseptic ME (unspecified)
HPeV	<2 mo, F	8	50	44	1	NOS	<i>none</i>	Infectious, non-CNS (unspecified viral); fever
HPeV	<2 mo, F	8	53	51	8	NOS	<i>none</i>	Infectious, non-CNS (unspecified viral sepsis); Culture negative septic shock- likely viral
HPeV	<2 mo, F	8	55	33	1	NOS	<i>none</i>	Unknown/not definitive; fever in infancy, heart murmur
HPeV	<2 mo, F	0	49	33	0	NOS	<i>none</i>	Infectious, non-CNS (HPeV in blood)
HPeV	<2 mo, F	0	56	47	0	NOS	<i>none</i>	Infectious, non-CNS (HPeV in blood, Rhino/EV NP)
HPeV	<2 mo, M	8	49	73	20	NOS	<i>none</i>	Viral/aseptic ME (HPeV); Rhino/Enterovirus respiratory illness (Parechovirus pos in CSF and blood, Rh/EV pos in respiratory specimen)
HPeV	<2 mo, F	0	58	28	1	NOS	<i>none</i>	Viral/aseptic ME (HPeV); Fever, parechovirus pos in CSF and blood
HPeV	<2 mo, M	0	55	33	8	NOS	<i>none</i>	Viral/aseptic ME (HPeV); HPeV meningitis, Rh/EV respiratory illness HPeV pos in CSF and blood, Rh/EV pos in respiratory specimen)

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

HPeV	<2 mo, M	0	52	166	9	NOS	<i>none</i>	Unknown/not definitive; Fever, at risk for sepsis. Not meningitis due to normal LP and labs.
VZV	35-64 yr, F	0	0	0	0	NOS	<i>none</i>	Non-infectious/non-CNS; Fever, at risk for sepsis. Not meningitis due to normal LP and labs
VZV	18-34 yr, M	0	57	88	426	NOS	Broad CVG	Unknown/not definitive; 36 hours of headache, neck pain, nausea, vomiting and one week of a rash
VZV	35-64 yr, M	2	36	116	62	NOS	VAN, ACV	Non-infectious/non-CNS; Diffuse Large B cell lymphoma
VZV	18-34 yr, F	0	55	83	300	NOS	<i>none</i>	Viral/aseptic ME (VZV); presumed acute VZV encephalitis, VZV rash
Cryptococcus	65+ yr, F	0	7	273	100	NOS	CRO	Fungal/cryptococcal ME; renal transplant with cryptococcal pulmonary and meningitis

^aImmune Status: Immune status was determined and categorized as follows according to 2013 Infectious Diseases Society of America Guidelines.(13)

1. Combined primary immunodeficiency disorder (e.g., severe combined immunodeficiency)
2. Receiving cancer chemotherapy
3. Within two months after solid organ transplantation or receiving augmented immunosuppression for rejection
4. With Human Immunodeficiency Virus (HIV) infection with a CD4 T-lymphocyte count <200 cells/mm³ for adults and adolescents and percentage <15 for infants and children
5. Receiving daily corticosteroid therapy with a dose ≥ 20 mg (or >2 mg/kg/day for patients who weigh <10 kg) of prednisone or equivalent for ≥ 14 days
6. Receiving certain biologic immune modulators, that is, a tumor necrosis factor-alpha (TNF- α) blocker or rituximab
7. Premature birth with a corrected gestational age <40 weeks
8. Infants <30 days who are full term
9. Other (with description)

^bAntimicrobial or other chemotherapeutics (antivirals) given within 24 hours prior to collection of CSF by spinal tap

SUPPLEMENTAL TABLE S3 Additional Information for CSF Specimens with Concordant Results [FilmArray ME Panel (FA) and Comparator Methods

^cInformation collected for final diagnosis by each trial site.

Abbreviations: AAC, antimicrobial agents and chemotherapy; ACV, acyclovir; AM, antimicrobial; AMP, ampicillin; AMX, amoxicillin; AV, antiviral ; AZM, azithromycin; Broad Cvg, broad coverage, not otherwise specified; CAZ, ceftazidime; CLI, clindamycin; CNS, central nervous system; CSF, cerebral spinal fluid; CRO, ceftriaxone; CTX, cefotaxime; DAP, daptomycin; DOX, doxycycline; F, female; FOS, foscarnet; FEP, cefipime; FLC, fluconazole; FP, false positive; GEN, gentamicin; GCV, ganciclovir; GPC, Gram positive cocci; GPDC, gram positive diplococci; LP, lumbar puncture; M, male; ME, meningitis/encephalitis; MEM, meropenem; NOS, no organisms seen in smear; TZP, piperacillin/tazobactam; pos, positive; SXT, trimethoprim–sulfamethoxazole; UTI, urinary tract infection; VAN, vancomycin; WBC, white blood cells.