DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
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BIOFIRE DIAGNOSTICS, LLC
KRISTEN KANACK, PHD
VICE PRESIDENT OF REGULATED PRODUCTS
390 WAKARA WAY
SALT LAKE CITY UT 84108

February 19, 2015

Re: K143005
Trade/Device Name: FilmArray Gastrointestinal (GI) Panel for use with the FilmArray 2.0
Regulation Number: 21 CFR 866.3990
Regulation Name: Gastrointestinal microorganism multiplex nucleic acid-based assay
Regulatory Class: II
Product Code: PCH, OOI
Dated: January 15, 2015
Received: January 20, 2015

Dear Dr. Kanack:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Uwe Scherf -S for

Sally Hojvat, M. Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K143005

Device Name
FilmArray Gastrointestinal (GI) Panel

Indications for Use *(Describe)*
The FilmArray Gastrointestinal (GI) Panel is a qualitative multiplexed nucleic acid-based in vitro diagnostic test intended for use with FilmArray systems. The FilmArray GI Panel is capable of the simultaneous detection and identification of nucleic acids from multiple bacteria, viruses, and parasites directly from stool samples in Cary Blair transport media obtained from individuals with signs and/or symptoms of gastrointestinal infection. The following bacteria (including several diarrheagenic E. coli/Shigella pathotypes), parasites, and viruses are identified using the FilmArray GI Panel:

- Campylobacter (C. jejuni/C. coli/C. upsaliensis)
- Clostridium difficile (C. difficile) toxin A/B
- Plesiomonas shigelloides
- Salmonella
- Vibrio (V. parahaemolyticus/V. vulnificus/V. cholerae) including specific identification of Vibrio cholerae
- Yersinia enterocolitica
- Enteroaggregative Escherichia coli (EAEC)
- Enteropathogenic Escherichia coli (EPEC)
- Enterotoxigenic Escherichia coli (ETEC) lt/st
- Shiga-like toxin-producing Escherichia coli (STEC) stx1/stx2 (including specific identification of the E. coli O157 serogroup within STEC)
- Shigella/Enteroinvasive Escherichia coli (EIEC)
- Cryptosporidium
- Cyclospora cayetanensis
- Entamoeba histolytica
- Giardia lamblia (also known as G. intestinalis and G. duodenalis)
- Adenovirus F 40/41
- Astrovirus
- Norovirus GI/GII
- Rotavirus A
- Sapovirus (Genogroups I, II, IV, and V)

The FilmArray GI Panel is indicated as an aid in the diagnosis of specific agents of gastrointestinal illness and results are meant to be used in conjunction with other clinical, laboratory, and epidemiological data. Positive results do not rule out co-infection with organisms not included in the FilmArray GI Panel. The agent detected may not be the definite cause of the disease.
Concomitant culture is necessary for organism recovery and further typing of bacterial agents.
This device is not intended to monitor or guide treatment for C. difficile infection.
Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for E. coli O157, Plesiomonas shigelloides, Yersinia enterocolitica, Astrovirus, and Rotavirus A were established primarily with retrospective clinical specimens.
Performance characteristics for Entamoeba histolytica, and Vibrio (V. parahaemolyticus, V. vulnificus, and Vibrio cholerae) were established primarily using contrived clinical specimens.
Negative FilmArray GI Panel results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.
A gastrointestinal microorganism multiplex nucleic acid-based assay also aids in the detection and identification of acute

gastroenteritis in the context of outbreaks.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

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510(k) Summary
BioFire Diagnostics, LLC

FilmArray Gastrointestinal (GI) Panel for use with FilmArray 2.0

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitted by:

BioFire Diagnostics, LLC
390 Wakara Way
Salt Lake City, UT 84108
USA

Telephone: 801-736-6354
Facsimile: 801-588-0507

Contact: Kristen Kanack, ext. 330

Date Submitted: October 17, 2014

Device Name and Classification:

Trade Name: FilmArray Gastrointestinal (GI) Panel

Regulation Number: 21 CFR 866.3990

Classification Name: Gastrointestinal microorganism multiplex nucleic acid-based assay

Predicate Device:

K140407 – FilmArray GI Panel

Intended Use:

The FilmArray Gastrointestinal (GI) Panel is a qualitative multiplexed nucleic acid-based *in vitro* diagnostic test intended for use with FilmArray systems. The FilmArray GI Panel is capable of the simultaneous detection and identification of nucleic acids from multiple bacteria, viruses, and parasites directly from stool samples in Cary Blair transport media obtained from individuals with signs and/or symptoms of gastrointestinal infection. The following bacteria (including several diarrheagenic *E. coli/Shigella* pathotypes), parasites, and viruses are identified using the FilmArray GI Panel:

- *Campylobacter* (*C. jejuni/C. coli/C. upsaliensis*)
- *Clostridium difficile* (*C. difficile*) toxin A/B
- *Plesiomonas shigelloides*

- *Salmonella*
- *Vibrio* (*V. parahaemolyticus/V. vulnificus/V. cholerae*) including specific identification of *Vibrio cholerae*
- *Yersinia enterocolitica*
- Enteroaggregative *Escherichia coli* (EAEC)
- Enteropathogenic *Escherichia coli* (EPEC)
- Enterotoxigenic *Escherichia coli* (ETEC) *lt/st*
- Shiga-like toxin-producing *Escherichia coli* (STEC) *stx1/stx2* (including specific identification of the *E. coli* O157 serogroup within STEC)
- *Shigella/*Enteroinvasive *Escherichia coli* (EIEC)
- *Cryptosporidium*
- *Cyclospora cayetanensis*
- *Entamoeba histolytica*
- *Giardia lamblia* (also known as *G. intestinalis* and *G. duodenalis*)
- Adenovirus F 40/41
- Astrovirus
- Norovirus GI/GII
- Rotavirus A
- Sapovirus (Genogroups I, II, IV, and V)

The FilmArray GI Panel is indicated as an aid in the diagnosis of specific agents of gastrointestinal illness and results are meant to be used in conjunction with other clinical, laboratory, and epidemiological data. Positive results do not rule out co-infection with organisms not included in the FilmArray GI Panel. The agent detected may not be the definite cause of the disease.

Concomitant culture is necessary for organism recovery and further typing of bacterial agents.

This device is not intended to monitor or guide treatment for *C. difficile* infection.

Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *E. coli* O157, *Plesiomonas shigelloides, Yersinia enterocolitica,* Astrovirus, and Rotavirus A were established primarily with retrospective clinical specimens.

Performance characteristics for *Entamoeba histolytica,* and *Vibrio (V. parahaemolyticus, V. vulnificus,* and *Vibrio cholerae)* were established primarily using contrived clinical specimens.

Negative FilmArray GI Panel results in the setting of clinical illness compatible with gastroenteritis may be due to infection by pathogens that are not detected by this test or non-infectious causes such as ulcerative colitis, irritable bowel syndrome, or Crohn's disease.

A gastrointestinal microorganism multiplex nucleic acid-based assay also aids in the detection and identification of acute gastroenteritis in the context of outbreaks.

Device Description:

The FilmArray Gastrointestinal (GI) Panel is a multiplex nucleic acid test designed to be used with FilmArray systems. The FilmArray GI pouch contains freeze-dried reagents to perform nucleic acid purification and nested, multiplex PCR with DNA melt analysis. The FilmArray Gastrointestinal (GI) Panel simultaneously conducts 22 tests for the identification of GI pathogens from stool specimens collected in Cary Blair transport medium (Table 1). Results from the FilmArray GI Panel test are available within about one hour.

Table 1. Bacteria, Viruses, Diarrheagenic *E. coli/Shigella*, and Parasites Detected by the FilmArray GI Panel

Bacteria	**Viruses**
Campylobacter (*C. jejuni/C. coli/C. upsaliensis*) *Clostridium difficile* (toxin A/B) *Plesiomonas shigelloides* *Salmonella* *Vibrio(V. parahaemolyticus/V. vulnificus/V. cholerae)* *Vibrio cholerae* *Yersinia enterocolitica*	Adenovirus F 40/41 Astrovirus Norovirus GI/GII Rotavirus A Sapovirus (Genogroups I, II, IV, and V)
Diarrheagenic *E. coli/Shigella*	**Parasites**
Enteroaggregative *E. coli* (EAEC) Enteropathogenic *E. coli* (EPEC) Enterotoxigenic *E. coli* (ETEC) *lt/st* Shiga toxin-producing *E. coli* (STEC) *stx1/stx2* *E. coli* O157 *Shigella*/Enteroinvasive *E. coli* (EIEC)	*Cryptosporidium* *Cyclospora cayetanensis* *Entamoeba histolytica* *Giardia lamblia*

A test is initiated by loading Hydration Solution into one port of the FilmArray pouch and a stool sample (in Cary Blair transport medium) mixed with the provided Sample Buffer into the other port of the FilmArray GI pouch and placing it in the FilmArray Instrument. The pouch contains all of the reagents required for specimen testing and analysis in a freeze-dried format; the addition of Hydration Solution and sample/Sample Buffer Mix rehydrates the reagents. After the pouch is prepared, the FilmArray Software guides the user though the steps of placing the pouch into the instrument, scanning the pouch barcode, entering the sample identification, and initiating the run.

The FilmArray instrument contains a coordinated system of inflatable bladders and seal points, which act on the pouch to control the movement of liquid between the pouch blisters. When a bladder is inflated over a reagent blister, it forces liquid from the blister into connecting channels. Alternatively, when a seal is placed over a connecting channel it acts as a valve to open or close a channel. In addition, electronically controlled pneumatic pistons are positioned over multiple plungers in order to deliver the rehydrated reagents into the blisters at the appropriate

times. Two Peltier devices control heating and cooling of the pouch to drive the PCR reactions and the melt curve analysis.

Nucleic acid extraction occurs within the FilmArray pouch using mechanical and chemical lysis followed by purification using standard magnetic bead technology. After extracting and purifying nucleic acids from the unprocessed sample, a nested multiplex PCR is executed in two stages. During the first stage, a single, large volume, highly multiplexed reverse transcription PCR (rt-PCR) reaction is performed. The products from first stage PCR are then diluted and combined with a fresh, primer-free master mix and a fluorescent double stranded DNA binding dye (LC Green® Plus, BioFire Defense, LLC). The solution is then distributed to each well of the array. Array wells contain sets of primers designed specifically to amplify sequences internal to the PCR products generated during the first stage PCR reaction. The 2nd stage PCR, or nested PCR, is performed in each well of the array. At the conclusion of the 2nd stage PCR, the array is interrogated by melt curve analysis for the detection of signature amplicons denoting the presence of specific targets. A digital camera placed in front of the array captures fluorescent images of the PCR2 reactions and software interprets the data.

The FilmArray software automatically interprets the results of each DNA melt curve analysis and combines the data with the results of the internal pouch controls to provide a test result for each organism on the panel.

Substantial Equivalence:

The FilmArray GI Panel for use with FilmArray 2.0 is substantially equivalent to the FilmArray GI Panel (K140407), which was cleared for use with the FilmArray on May 2, 2014 and determined to be a Class II device.

The following table compares the FilmArray GI Panel for use with FilmArray 2.0 to the previously cleared FilmArray GI Panel (K140407). The table outlines the similarities and differences for the GI Panel tested on the two devices.

Table 2. Comparison of the FilmArray GI Panel on FilmArray 2.0 to the FilmArray GI Panel on the FilmArray(Predicate).

Element	Predicate: FilmArray Gastrointestinal Panel (K140407)	New Device: FilmArray Gastrointestinal Panel for use with FilmArray 2.0
Organisms Detected	*Campylobacter (C. jejuni/C. coli/C. upsaliensis), Clostridium difficile (C. difficile) toxin A/B, Plesiomonas shigelloides, Salmonella, Vibrio (V. parahaemolyticus/V. vulnificus/V. cholerae)* including specific identification of *Vibrio cholera, Yersinia enterocolitica, Enteroaggregative Escherichia coli* (EAEC), *Enteropathogenic Escherichia coli* (EPEC), *Enterotoxigenic Escherichia coli* (ETEC) *lt/st, Shiga-like toxin-producing Escherichia coli* (STEC) *stx1/stx2* (including specific identification of the *E. coli O157* serogroup within STEC), *Shigella/Enteroinvasive Escherichia coli* (EIEC),*Cryptosporidium, Cyclospora cayetanensis, Entamoeba histolytica, Giardia lamblia* (also known as *G. intestinalis* and *G. duodenalis*), Adenovirus F 40/41, Astrovirus, Norovirus GI/GII, Rotavirus A, and Sapovirus (Genogroups I, II, IV, and V).	Same
Analyte	RNA/DNA	Same
Specimen Types	Human stool in Cary Blair transport medium	Same
Technological Principles	Nested multiplex RT-PCR followed by high resolution melting analysis to confirm identity of amplified product.	Same
Instrumentation	FilmArray	FilmArray or FilmArray 2.0
Time to result	About 1 hour	Same
Test Interpretation	Automated test interpretation and report generation. User cannot access raw data.	Same
Sample Preparation Method	Sample Processing is automated in the FilmArray GI pouch.	Same
Reagent Storage	Reagents are stored at room temperature.	Same
Controls	Two controls are included in each reagent pouch to control for sample processing and both stages of PCR and melt analysis.	Same
User Complexity	Moderate/Low	Same

Summary of Performance Data

Clinical Performance

The original FilmArray GI Panel was developed for use with the current, single instrument FilmArray. A clinical study was conducted to compare the performance observed when testing clinical specimens using the GI Panel on the current system to results obtained when testing with the modified system (FilmArray 2.0).

Specimens previously obtained during the FilmArray GI prospective clinical evaluation comprised the base of the specimen set used for testing. This set was supplemented with other archived specimens collected from external medical facilities and reference laboratories to increase the number of specimens being tested for low prevalence analytes. Contrived clinical specimens were also used for GI analytes which are rare (*Entamoeba histolytica, Vibrio* spp., and *V. cholerae*). A total of 104 specimens were selected such that each analyte was represented 3-5 times.

System performance for testing these 104 specimens on each platform was calculated. For the current system, a total of 105 runs were attempted, 104 of which were completed (99.0%; 104/105). One run was aborted by the user (0.9%). No control failures were observed.

For the modified system, a total of 104 runs were attempted, all of which were completed (100%; 104/104). There was one control failure. One norovirus specimen was excluded following the control failure due to insufficient specimen volume for retesting.

As shown in Table 3, 100% concordance was observed for most analytes (14/22) between the current and modified system. For PPA, 19/22 analytes were 100% concordant, and for NPA, 15/22 analytes were 100% concordant. Occasional discrepant results were observed where an analyte was detected by one out of two pouches; in many cases this was attributed to analyte levels below the limit of detection (LoD) in specimens that had previously been characterized as positive for the discrepant analyte. Overall PPA was 96.4% with the lower bound of the two-sided 95% confidence interval (95% CI) at 91.0%. Overall NPA was 99.4% with the lower bound of the two-sided 95% CI at 98.9 %.

Table 3. Analyte Detections for Modified vs. Current System, where results from the Current System are shown as the denominator. Comparisons demonstrating performance less than 100% but are shaded in yellow. CS = Current System, MS = Modified System

Analyte	MS vs CS			
	PPA	%	NPA	%
Bacteria				
Campylobacter	5/5	100%	96/97[a]	99.0%
Clostridium difficile toxin A/B	5/5	100%	95/97[b]	97.9%
Plesiomonas shigelloides	3/3	100%	99/99	100%
Salmonella	5/5	100%	97/97	100%
Vibrio	6/7[c]	85.7%	94/95[c]	98.9%
Vibrio cholerae	3/3	100%	98/99[c]	99.0%
Yersinia enterocolitica	4/4	100%	98/98	100%
Diarrheagenic *E. coli* / *Shigella*				
Enteroaggregative *E. coli* (EAEC)	8/8	100%	94/94	100%

Analyte	MS vs CS			
	PPA	%	NPA	%
Enteropathogenic *E. coli* (EPEC)	11/12[d]	91.7%	84/84	100%
Enterotoxigenic *E. coli* (ETEC)	5/5	100%	96/97[e]	99.0%
Shiga-like toxin-producing *E. coli* (STEC)	6/6	100%	96/96	100%
Escherichia coli O157	3/3	100%	3/3	100%
Shigella/Enteroinvasive *E. coli* (EIEC)	6/6	100%	96/96	100%
Parasites				
Cryptosporidium	6/6	100%	96/96	100%
Cyclospora cayetanensis	4/4	100%	98/98	100%
Entamoeba histolytica	5/5	100%	97/97	100%
Giardia lamblia	6/6	100%	96/96	100%
Viruses				
Adenovirus F 40/41	7/9[f]	77.8%	90/93[f]	96.8%
Astrovirus	5/5	100%	97/97	100%
Norovirus GI/GII	4/4	100%	96/98[g]	98.0%
Rotavirus A	4/4	100%	98/98	100%
Sapovirus	5/5	100%	97/97	100%
Overall agreement/	**116/120**	**96.7%**	**2011/2022**	**99.5%**
95% CI	**91.7-99.1%**		**99.0-99.7%**	

[a] *Campylobacter* was detected in specimen 014111-GI-0028 when tested on the Modified System but was not detected when tested on the Current System. This specimen was originally characterized as positive for *Campylobacter*.
[b] Specimens 014111-GI-0039 and 014111-GI-0060 were positive for *C. difficile* when tested with the Modified System but were not detected on the Current System. Both specimens were originally characterized as positive for *C. difficile*.
[c] *Vibrio* was detected in specimen 014111-GI-0106 when tested on the Current System but was not detected when tested on the Modified System. *V. cholerae* was detected with the Vchol assay in specimen 014111-GI-0108 when tested with the Modified System but not the Current System; a positive result of with the Vchol assay also resulted in a metacall for *Vibrio*. Both of these specimens were contrived specimens that had been spiked with *Vibrio* organism.
[d] EPEC was detected in specimen 014111-GI-0007 when tested on the Current System but was not detected when tested on the Modified System. EPEC had not been reported in this specimen by the source laboratory.
[e] ETEC was detected by one of three ETEC assays in specimen 014111-GI-0015 when tested on the Modified System but not on the Current System. ETEC had not been reported in this specimen by the source laboratory.
[f] Adenovirus F 40/41 was alternately detected in five specimens (014111-GI-0080, 014111-GI-0084, 014111-GI-0085, 014111-GI-0088, and 14111-GI-0094) by the Current and Modified systems. Adenovirus F 40/41 had not been reported in any of these specimens by the source laboratory.
[g] Specimens 014111-GI-0022 and 014111-GI-0086 were positive for Norovirus GI/GII when tested with the Modified System but were not detected on the Current System. Specimen 014111-GI-0022 was originally characterized as positive for Norovirus GI/GII, but specimen 014111-GI-0086 was not.

Selected Analytic Studies

Low Analyte

A comparison of performance at low analyte levels between the current FilmArray system (one instrument to one computer configuration) and the FilmArray 2.0 system (modified; up to eight instruments to one computer) was performed for the FilmArray Gastrointestinal (GI) Panel. The purpose of the testing was to determine whether detection of GI Panel analytes is equivalent between the systems.

Testing consisted of a titration of samples containing GI Panel analytes at concentrations above, at, and below (10×, 1×, 0.1× and 0.01×) LoD. Additional side-by-side testing at and near LoD (20 replicates on each system) was performed to further demonstrate consistency between the current and modified systems.

In the titration series testing, amplification, and detection of each analyte was found to be comparable between systems at all concentrations. Testing of additional replicates at LoD (Table 4) also revealed equivalent detection on both systems (≥95% agreement between current and modified and/or overlapping 2-sided 95% confidence intervals).

Table 4. Results of Replicate Testing at LoD for the Gastrointestinal (GI) Panel on Current and Modified FilmArray Systems

GI Panel Test Result	Species/Isolate	Current System	Modified System	Agreement Between Systems
		#Detected/Total (% Detected) [95% CI]	#Detected/Total (% Detected) [95% CI]	
Bacteria				
Campylobacter	*Campylobacter jejuni*	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Clostridium difficile toxin A/B	*Clostridium difficile*	20/20 (100%) [83.2% - 100%]	19/20 (95%) [75.1% - 99.9%]	**95%**
Plesiomonas shigelloides	*Plesiomonas shigelloides*	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Salmonella	*Salmonella enterica* subsp. *enterica*	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Vibrio/Vibrio cholerae	*Vibrio cholerae*	40/40[a] (100%) [91.2% - 100%]	37/40[a] (92.5%) [79.6% - 98.4%]	**96%**
Vibrio	*Vibrio parahaemolyticus*	40/40[a] (100%) [91.2% - 100%]	37/40[a] (92.5%) [79.6% - 98.4%]	**96%**
Yersinia enterocolitica	*Yersinia enterocolitica*	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Diarrheagenic *E. coli/Shigella*				
Enteroaggregative *E. coli* (EAEC)	*Escherichia coli* (EAEC)	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**

GI Panel Test Result	Species/Isolate	Current System	Modified System	Agreement Between Systems
		#Detected/Total (% Detected) [95% CI]	#Detected/Total (% Detected) [95% CI]	
Enteropathogenic *E. coli* (EPEC)	*Escherichia coli* (EPEC)	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Enterotoxigenic *E. coli* (ETEC) *It/st*	*Escherichia coli* (ETEC)	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*	*Escherichia coli* (STEC)	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Shiga-like toxin-producing *E. coli* (STEC) stx1/stx2 *E. coli* O157	*Escherichia coli* O157	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Shigella/Enteroinvasive *E. coli* (EIEC)	*Escherichia coli* (EIEC)	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
	Shigella sonnei	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Parasites				
Cryptosporidium	*Cryptosporidium parvum*	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Cyclospora cayetanensis	*Cyclospora cayetanensis*	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Entamoeba histolytica	*Entamoeba histolytica*	11/20[b] (55%) [31.5% - 77.0%]	15/20[b] (75%) [51.0% - 91.3%]	**80%**
Giardia lamblia	*Giardia intestinalis*	7/20[b] (35%) [15.4% - 59.2%]	10/20[b] (50%) [27.2% - 72.8%]	**85%**
Viruses				
Adenovirus F 40/41	Adenovirus F40	19/20 (95%) [75.1% - 99.9%]	20/20 (100%) [83.2% - 100%]	**95%**
	Adenovirus F41	20/20 (100%) [83.2% - 100%]	18/20[a] (90%) [68.3% - 98.8%]	**90%**
Astrovirus	Astrovirus	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Norovirus GI/GII	Norovirus GI	18/20[b] (90%) [68.3% - 98.8%]	19/20 (95%) [75.1% - 99.9%]	**95%**
Rotavirus A	Rotavirus A	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**
Sapovirus	Sapovirus	20/20 (100%) [83.2% - 100%]	20/20 (100%) [83.2% - 100%]	**100%**

[a] Initial testing of 20 replicates per system resulted in 20/20 Detected results on the current system and only 17/20 results on the modified system. Amplification data, which were comparable between the current and modified systems, indicated that the amount of analyte in the samples may have been below LoD, based on comparison to the original LoD study. Therefore, an additional 20 replicates were tested and the analyte was detected in 20/20 replicates (>95%) on both the current and modified systems. Data presented are the combination of the total number of replicates tested.
[b] Detection is lower than the expected 95% on the current and/or modified system(s) at LoD, though 95% confidence intervals are overlapping. Amplification data, which were comparable between the current and modified systems, indicated that the amount of analyte in the samples may have been below LoD, based on comparison to the original LoD study.

Tm values from the LoD replicate samples were compared to assess whether Tm data are equivalent between the current and modified FilmArray systems. Normal Tm variation of the current FilmArray system is ±0.5˚C and it was observed that mean Tm values for all FilmArray GI Panel assays on the modified system were ± 0.4°C or less compared to the same samples tested on the current system (ΔTm in Table 5).

Table 5. Comparison of Mean Tm Values for FilmArray GI Panel Analytes on the Current and Modified Systems

GI Panel Test Result	Species/Isolate	Assay	Mean Tm Values		ΔTm [Current-Modified]
			Current System	Modified System	
Bacteria					
Campylobacter	*Campylobacter jejuni*	Campy1	77.8	77.9	**-0.1**
Clostridium difficile Toxin A/B	*Clostridium difficile*	Cdiff Tm1	75.7	75.6	**0.1**
		Cdiff Tm2	78.7	78.5	**0.2**
Plesiomonas shigelloides	*Plesiomonas shigelloides*	Pshig	90.7	90.4	**0.3**
Salmonella	*Salmonella enterica* subsp. *enterica*	Salm	82.2	82.0	**0.2**
Vibrio/Vibrio cholerae	*Vibrio cholerae*	Vchol	81.5	81.7	**-0.2**
Vibrio	*Vibrio parahaemolyticus*	Vibrio	82.2	81.9	**0.3**
Yersinia enterocolitica	*Yersinia enterocolitica*	Yent	85.6	85.4	**0.2**
Diarrheagenic *E. coli/Shigella*					
Enteroaggregative *E. coli* (EAEC)	*Escherichia coli* (EAEC)	EAEC	79.1	79.0	**0.1**
Enteropathogenic *E. coli* (EPEC)	*Escherichia coli* (EPEC)	Ec eae	80.6	80.4	**0.2**
Enterotoxigenic *E. coli* (ETEC) *It/st*	*Escherichia coli* (ETEC)	ETEC1	80.7	80.5	**0.2**
		ETEC2	78.8	78.7	**0.1**

GI Panel Test Result	Species/Isolate	Assay	Mean Tm Values		ΔTm [Current-Modified]
			Current System	Modified System	
		ETEC3	75.1	75.0	**0.1**
Shiga-like toxin-producing *E. coli* (STEC) *stx1/stx2*	*Escherichia coli* (STEC)	STEC1	82.8	82.6	**0.2**
		STEC2	84.9	84.7	**0.2**
Shiga-like toxin-producing E. coli (STEC) *stx1/stx2* E. coli O157	*Escherichia coli* (STEC) O157	EC O157	83.1	82.8	**0.3**
		STEC1	82.8	82.6	**0.2**
		STEC2	84.9	84.7	**0.2**
Shigella/Enteroinvasive *E. coli* (EIEC)	*Escherichia coli* (EIEC)	Shig	86.3	86.4	**-0.1**
	Shigella sonnei	Shig	86.5	86.2	**0.3**
Parasites					
Cryptosporidium	*Cryptosporidium parvum*	Crypt1	79.1	78.8	**0.3**
		Crypt2	71.8	71.7	**0.1**
Cyclospora cayetanensis	*Cyclospora cayetanensis*	Ccayet	86.6	86.3	**0.3**
Entamoeba histolytica	*Entamoeba histolytica*	Ehist	76.8	76.5	**0.3**
Giardia lamblia	*Giardia lamblia*	Glam	91.6	91.3	**0.3**
Viruses					
Adenovirus F 40/41	Adenovirus F40	AdenoF	84.6	84.5	**0.1**
	Adenovirus F41	AdenoF	86.8	86.5	**0.3**
Astrovirus	Astrovirus	Astro	85.5	85.3	**0.2**
Norovirus GI/GII	Norovirus GI	Noro1	83.6	83.8	**-0.2**
Rotavirus A	Rotavirus A	RotaA1 Tm1	78.3	77.9	**0.4**
		RotaA1 Tm2	81.2	80.8	**0.4**
		RotaA2	77.1	76.9	**0.2**
Sapovirus	Sapovius	Sapo	86.7	86.6	**0.1**

Reproducibility

A multicenter reproducibility study was performed to determine between-site/system and overall reproducibility of the FilmArray GI Panel on the multi-instrument FilmArray system.

Reproducibility testing occurred at three test sites using a panel of contrived stool samples, each spiked with various concentrations of five different GI Panel analytes. Each analyte was evaluated at three different concentrations (Negative, Low Positive and Moderate Positive).

The study incorporated a range of potential variation introduced by nine different operators, four different pouch lots, and nine different FilmArray 2.0instruments. A system consisted of three instruments connected to a single computer. Samples were stored refrigerated (4˚C) and tested on four different days at three testing sites (one system, A, B, or C per site) for 108 data points per sample.

A summary of results (percent (%) agreement with the expected result) for each analyte (by site/system and overall) is provided in Table 6 alongside the overall % Agreement with Expected Results originally obtained on the single-instrument system.

Table 6. Reproducibility of the FilmArray GI Panel Test Results

Organism Tested	Concentration Tested	Expected Result	% Agreement with Expected Result				
			Multi-instrument FilmArray System				Single-instrument FilmArray System
			Site/System A	Site/System B	Site/System C	All Sites/Systems (95% Confidence Interval)	All Sites (95% Confidence Interval)
Clostridium difficile **(toxinotype 0 A+B+) ATCC 9689**	**Moderate Positive 3× LoD $1.2x10^6$ CFU/mL**	**Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	108/108 100% (96.6 - 100%)
	Low Positive 1× LoD $4.0x10^5$ CFU/mL	**Detected**	35/36 97.2%	36/36 100%	36/36 100%	107/108 99.1% (95.0-100%)	108/108 100% (96.6 - 100%)
	Negative	**Not Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	360/360 100% (96.6 - 100%)
Shiga-toxin producing *Escherichia coli* (STEC O157) ATCC 43895	**Moderate Positive 3× LoD $3.0x10^4$ CFU/mL**	**Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	90/90 100% (96.0 - 100%)
	Low Positive 1× LoD $1.0x10^4$ CFU/mL	**Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	90/90 100% (96.0 - 100%)
	Negative	**Not Detected and N/A (O157)**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	576/576 100% (99.4 - 100%)

Organism Tested	Concentration Tested	Expected Result	% Agreement with Expected Result				
			Multi-instrument FilmArray System				Single-instrument FilmArray System
			Site/System A	Site/System B	Site/System C	All Sites/Systems (95% Confidence Interval)	All Sites (95% Confidence Interval)
***Cryptosporidium parvum* Waterborne P102C**	**Moderate Positive 3× LoD $1.5x10^4$ oocysts/mL**	**Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	90/90 100% (96.0 - 100%)
	Low Positive 1× LoD $5.0x10^3$ oocysts/mL	**Detected**	35/36 97.2%	36/36 100%	36/36 100%	107/108 99.1% (95.0-100%)	90/90 100% (96.0 - 100%)
	Negative	**Not Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	576/576 100% (99.4 - 100%)
Adenovirus F41 ATCC VR-930	**Moderate Positive 3× LoD 300 $TCID_{50}$/mL**	**Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	90/90 100% (96.0 - 100%)
	Low Positive 1× LoD 100 $TCID_{50}$/mL	**Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	90/90 100% (96.0 - 100%)
	Negative	**Not Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	576/576 100% (99.4 - 100%)
Astrovirus NCPV 10037071v	**Moderate Positive 3× LoD 150 FFU/mL**	**Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	90/90 100% (96.0 - 100%)
	Low Positive 1× LoD 50 FFU/mL	**Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	90/90 100% (96.0 - 100%)
	Negative	**Not Detected**	36/36 100%	36/36 100%	36/36 100%	108/108 100% (96.6-100%)	576/576 100% (99.4 - 100%)

[a] Summary of Reproducibility study results for select analytes taken from the original Reproducibility evaluation performed on the single-instrument FilmArray system (SDY-011541 "Evaluation of Reproducibility for the FilmArray Gastrointestinal (GI) Panel").

The test results obtained for the Gastrointestinal Panel on the FilmArray 2.0 were highly reproducible and are consistent with the data collected on the currentFilmArray in the original GI Panel Reproducibility evaluation.

The reproducibility of Tm for each positive assay was also evaluated by site/system and overall (all sites/systems) and a summary is provided in Table 7.

Table 7. Reproducibility of Tm for Positive FilmArray GI Panel Assays on Multi-instrument FilmArray 2.0 Systems

Organism	Assay		Test Level	Test Site	Tm Reproducibility	
					Mean	StDev Tm
Bacteria and (Including Diarrheagenic *E. coli*)						
Clostridium difficile ATCC 9689	**Cdiff**[a]	**Tm 1**	**Moderate Positive 3× LoD 1.2x10^6 cells/mL**	**Site A**	75.5	± 0.2
				Site B	75.3	± 0.4
				Site C	75.0	± 0.4
				All Sites	**75.3**	± 0.4
			Low Positive 1× LoD 4x10^5 cells/mL	**Site A**	76.2	± 0.5
				Site B	76.0	± 0.5
				Site C	75.7	± 0.6
				All Sites	**76.0**	± 0.6
		Tm 2	**Moderate Positive 3× LoD 1.2x10^6 cells/mL**	**Site A**	78.7	± 0.2
				Site B	78.6	± 0.3
				Site C	78.3	± 0.3
				All Sites	78.5	± 0.4
			Low Positive 1× LoD 4x10^5 cells/mL	**Site A**	79.1	± 0.3
				Site B	78.9	± 0.4
				Site C	78.6	± 0.4
				All Sites	78.9	± 0.4
***Escherichia coli* (STEC) O157** ATCC 43895	**O157**		**Moderate Positive 3× LoD 3x10^4 CFU/mL**	**Site A**	83.6	±0.2
				Site B	83.4	±0.3
				Site C	83.1	±0.3
				All Sites	83.4	±0.3
			Low Positive 1× LoD 1x10^4 CFU/mL	**Site A**	83.5	±0.2
				Site B	83.4	±0.2
				Site C	83.0	±0.3
				All Sites	83.3	±0.3
	STEC 1		**Moderate Positive 3× LoD 3x10^4 CFU/mL**	**Site A**	83.2	±0.1
				Site B	83.0	±0.3
				Site C	82.7	±0.3
				All Sites	83.0	±0.3
			Low Positive 1× LoD 1x10^4 CFU/mL	**Site A**	83.1	±0.2
				Site B	83.0	±0.2
				Site C	82.7	±0.3
				All Sites	83.0	±0.3
	STEC 2		**Moderate Positive 3× LoD 3x10^4 CFU/mL**	**Site A**	85.4	±0.2
				Site B	85.2	±0.2
				Site C	84.9	±0.3
				All Sites	85.1	±0.3
			Low Positive 1× LoD 1x10^4 CFU/mL	**Site A**	85.3	±0.2
				Site B	85.2	±0.2
				Site C	84.9	±0.3
				All Sites	85.1	±0.3
Protozoa						
Cryptosporidium parvum Waterborne P102C	**Crypt 1**		**Moderate Positive 3x LoD 1.5x104 oocysts/mL**	**Site A**	79.5	±0.2
				Site B	79.4	±0.3
				Site C	79.0	±0.3
				All Sites	79.3	±0.3
			Low Positive 1× LoD	**Site A**	79.6	±0.2
				Site B	79.5	±0.3

Organism	Assay	Test Level	Test Site	Tm Reproducibility	
				Mean	StDev Tm
		$5x10^3$ oocysts/mL	**Site C**	79.2	±0.3
			All Sites	79.5	±0.3
	Crypt 2	**Moderate Positive 3× LoD 1.5x104 oocysts/mL**	**Site A**	71.8	±0.2
			Site B	71.7	±0.3
			Site C	71.4	±0.3
			All Sites	71.6	±0.3
		Low Positive 1× LoD $5x10^3$ oocysts/mL	**Site A**	72.2	±0.3
			Site B	72.1	±0.4
			Site C	72.0	±0.4
			All Sites	72.1	±0.4
Viruses					
Adenovirus F41 ATTC VR-930	**AdenoF**	**Moderate Positive 3× LoD 300 $TCID_{50}$/mL**	**Site A**	86.9	±0.2
			Site B	86.8	±0.3
			Site C	86.4	±0.3
			All Sites	86.7	±0.4
		Low Positive 1× LoD 100 $TCID_{50}$/mL	**Site A**	87.1	±0.2
			Site B	86.9	±0.3
			Site C	86.6	±0.3
			All Sites	86.8	±0.3
Astrovirus (Type 8) NCPV 1003071v	**Astro**	**Moderate Positive 3× LoD 150 FFU/mL**	**Site A**	85.9	±0.1
			Site B	85.8	±0.2
			Site C	85.4	±0.3
			All Sites	85.7	±0.3
		Low Positive 1× LoD 50 FFU/mL	**Site A**	86.0	±0.2
			Site B	85.8	±0.2
			Site C	85.5	±0.3
			All Sites	85.7	±0.3

[a] A characteristic double melt profile is observed when both *C. difficile* toxin genes (tcdA and tcdB) are present in a sample and two different Tm values are reported (Tm1 and Tm2).