Adventist HealthCare

TRAINING UPDATE

Lab Location:	SGMC, WOMC	**Date Distributed:**	11/18/24
Department:	Core Lab, Microbiology	**Due Date:**	12/3/24
		Implementation:	**12/3/24**

DESCRIPTION OF PROCEDURE REVISION

Name of procedure:
AHC.M 1025 BioFire ® Filmarray ® Gastrointestinal (GI) Panel
Description of change(s):
New PCR Test. Live date is December 3, 2024. Read the attached SOP and take the quiz.

Document your compliance with this training update by taking the quiz in the MTS system.

AHC.M 1025 BioFire ® Filmarray ® Gastrointestinal (GI) Panel

Copy of version 1.0 (approved, not yet effective)

Last Approval or Periodic Review Completed	11/15/2024
Next Periodic Review Needed On or Before	11/15/2026
Effective Date	12/3/2024

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Organization	Adventist HealthCare

Approval and Periodic Review Signatures

Type	Description	Date	Version	Performed By	Notes
Approval	Lab Director	11/15/2024	1.0	Nicolas Cacciabeve MD Nicolas Cacciabeve	
Approval	Laboratory Operations Director	11/15/2024	1.0	Robert SanLuis Robert SanLuis	
Approval	Microbiology Director	11/13/2024	1.0	Vittal Ponraj	

Version History

Version	Status	Type	Date Added	Date Effective	Date Retired
1.0	Approved, Not Yet Effective	Initial version	10/7/2024	12/3/2024	Indefinite

Technical SOP

Title	**BioFire ® Filmarray ® Gastrointestinal (GI) Panel**	
Prepared by	Dr. Vittal Prakash Ponraj, Ph.D., SM(ASCP)^{CM}	Date: 9/20/24
Owner	Dr. Vittal Prakash Ponraj, Ph.D., SM(ASCP)^{CM}	Date: 9/20/24

Laboratory Approval	**Local Effective Date:**	
Print Name and Title	**Signature**	**Date**
Refer to the electronic signature page for approval and approval dates.		

TABLE OF CONTENTS

1. TEST INFORMATION

Assay	Method/Instrument	Test Code
BioFire ® Filmarray ® Gastrointestinal (GI) Panel	Reverse transcription, polymerase chain reaction (PCR)/ BioFire Torch	BFGI

Synonyms/Abbreviations
GI PCR panel

Department
Microbiology laboratory

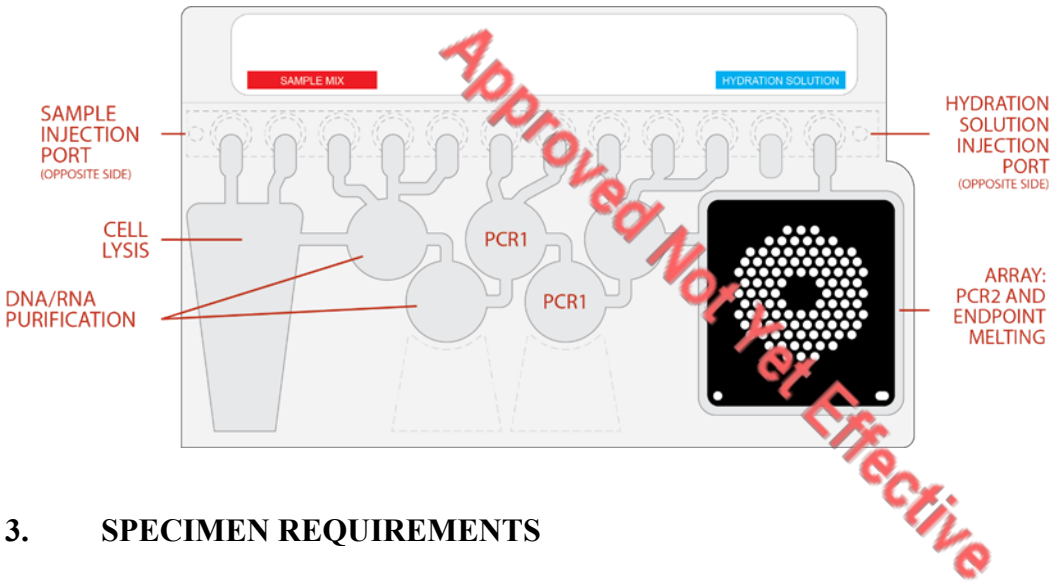
2. ANALYTICAL PRINCIPLE

The BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel is a qualitative multiplexed nucleic acid-based in vitro diagnostic test intended for use with BIOFIRE® FILMARRAY® Systems. The BIOFIRE 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 BIOFIRE GI Panel

- *Campylobacter* (*C. jejuni*/*C. coli*/*C. upsaliensis*)
- *Clostridium difficile* (*C. difficile*) toxin A/B (*C. diff* target not reported in our lab)
- *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 col*i (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)

During a run, the BIOFIRE System:

- **Lyses** the sample by agitation (bead beating).
- **Extracts** and **purifies** all **nucleic acids** from the sample using magnetic bead technology.
- **Performs nested multiplex PCR** by:
  - First performing reverse transcription and a single, large volume, massively multiplexed reaction (PCR1), and
  - Then performing multiple singleplex second-stage PCR reactions (PCR2) to amplify sequences within the PCR1 products.
- **Uses endpoint melting curve data to detect and generate a result for each target** on the BIOFIRE GI Panel array.



3. SPECIMEN REQUIREMENTS

3.1 Patient Preparation

Component	Special Notations
Fasting/Special Diets	N/A
Specimen Collection and/or Timing	See Special Collection Procedures

Component	Special Notations
Special Collection Procedures	• Collect stool preserved in Cary-Blair medium by using the medium manufacturer's recommended collection procedure or collect unpreserved and unformed (liquid or soft) stool specimens and place as soon as possible into the Cary-Blair medium by using the medium manufacturer's recommended collection procedure. • It is recommended that Cary-Blair preserved specimens be stored refrigerated at 2-8°C until GI testing is completed (for up to 4 days after collection). For repeat testing, prepare the specimen in a new Stool Prep Buffer as described in the Specimen Processing section (see Section 8.2). • Patient should not use antacids, barium, bismuth, antibiotics, anti-malarial agents, antidiarrheal medication or oily laxatives prior to specimen collection. After administration of any of these compounds, specimen collection should be delayed for 5 to 10 days, or at least two weeks after barium or antibiotics. Avoid contamination of stool specimen with urine or water. Specimens are best collected in a bedpan or a clean dry container. A suitable area (i.e. bloody, slimy, watery) from the sides, ends and middle of the stool should be selected using the collection spoon provided. Fill with sufficient stool to bring the liquid level up to the "Fill" line. This will result in approximately 5 mL of sample. Stir each specimen with the spoon provided, tighten the cap and shake firmly until the specimen is adequately mixed. When mixing is complete the specimen should appear uniform. Complete the label on the vial and replace the vial in the plastic bag. Transport the specimen to the laboratory.
Other	

3.2 Specimen Type & Handling

Criteria	
Type -Preferred	Liquid or soft stool specimen collected in Cary-Blair (Para-Pak C&S transport media) Medium
-Other Acceptable	Fresh raw stool (<1 hour old). Must be transferred to Cary-Blair (Para-Pak C&S transport media) immediately upon receipt in laboratory.
Collection Container	Liquid or soft stool preserved in Para-Pak C&S transport Cary-Blair medium

Criteria	
Volume - Optimum - Minimum	0.2 mL 0.2 mL
Transport Container and Temperature	Specimen collected in Para-Pak C&S transport Cary-Blair medium per manufacturer's instructions at room temperature.
Stability & Storage Requirements	Room Temperature: Up to 4 days in Cary-Blair medium
	Refrigerated: 4 days
	Frozen: Unacceptable
Timing Considerations	Specimen must be transported to lab immediately and tested ASAP. If unable to test immediately, sample should be stored at 2-8°C and brought to room temperature before testing.
Unacceptable Specimens & Actions to Take	• Raw stool > 1 hours old. • Stool in Cary-Blair Medium not filled to the pre-marked "Fill" line.
Compromising Physical Characteristics	N/A
Other Considerations	N/A

NOTE: Labeling requirements for all reagents, calibrators and controls include: (1) Open date, (2) Substance name, (3) Lot number, (4) Date of preparation, (5) Expiration date, (6) Initials of tech, and (7) Any special storage instructions. Check all for visible signs of degradation.

4. REAGENTS

The package insert for a new lot of kits must be reviewed for any changes before the kit is used. A current Package Insert is included as a Related Document.

4.1 Reagent Summary

Reagents / Kits	Supplier & Catalog Number
BioFire GI Panel Reagent Pouch Kit	BIOMÉRIEUX Catalog # RFIT-ASY-0116 30 test kit

4.2 Reagent Preparation and Storage

Assay Kit	
Kit Contents	Each kit contains sufficient reagents to test 30 specimens Individually packaged BioFire GI Panel Pouches • Sample Buffer Ampoule • Hydration injection vial (blue cap) • Sample injection vial (red cap) • Individually- packaged Transfer Pipettes All Kit components should be stored and used together. Do not use components from one kit with those of another kit.
Storage	15-25°C
Stability	Until expiration date on box.
Preparation	Ready to use.

Reagent	10 % Bleach
Container	1 bottle
Storage	Room temperature (15°C to 30°C)
Stability	Stable for 24 hours after preparation.
Preparation	Add 10 ml concentrated bleach to a 100 ml graduated cylinder then dilute with distilled water to 100 ml.

Reagent	70% Ethanol
Container	4 L bottle
Storage	Room temperature (15°C to 30°C)
Stability	Stable until manufacturer expiration date.
Preparation	Ready to use.

5. CALIBRATORS/STANDARDS

N/A

6. QUALITY CONTROL

6.1 Controls Used

Controls	Supplier and Catalog Number
Internal RNA Process Control	Included in each pouch
Internal PCR2 Process Control	Included in each pouch
NATrol GI Control, pool 1 & 2	ZeptoMetrix Cat. # NATGIC-BIO

6.2 Control Preparation and Storage

Control	Internal RNA Process Control
Preparation	Ready to use.
Storage/Stability	Stable until date on box when stored at 15 - 25 °C

Control	Internal PCR2 Process Control
Preparation	Ready to use.
Storage/Stability	Stable until date on box when stored at 15 - 25 °C

Control	NATrol GI Control (ZeptroMetrix)
Preparation	Mix Vigorously for at least 5 seconds. Process according to BioFire instructions for samples results assays.
Storage/Stability	2-8°C in the original packaging until expiration date on box.

6.3 Frequency

Internal Controls: Process controls are run with each test.

External control: (NATrol GI control (Zeptrometrix) Is run once per day (until the IQCP is completed). These serve as positive and negative controls.

Document which module is used to run the QC material to ensure they are rotated periodically. Controls are to be treated in the same manner as a patient sample. QC must be performed on each system which is defined as a computer or reader, and the associated sample processing modules.

6.4 Tolerance Limits and Criteria for Acceptable QC

A. Tolerance Limits

Tolerance Limits	
External Positive	*Detected*
External Negative	*Not Detected*
Internal Controls	
RNA process Control	*Passes if it meet assigned acceptance criteria*
PCR2 process control	*Passes if it meet assigned acceptance criteria*

Control Component	Strain	GI Control 1	GI Control 2
C. difficile	NAP1	Positive	Negative
P. shigelloides	Z130	Positive	Negative
V. cholera	Z133; non-toxigenic	Positive	Negative
Y. enterocolitica	clinical isolate	Positive	Negative
E. coli	92.0147; EAEC[1]	Positive	Negative
S. sonnei	Z004	Positive	Negative
E. coli	EDL933; O157	Positive	Negative
C. parvum	Iowa	Positive	Negative
Adenovirus Type 41	TAK	Positive	Negative
Sapovirus	Recombinant[2]	Positive	Negative
Rotavirus	Wa	Positive	Negative
C. coli	clinical isolate	Negative	Positive
C. jejuni	clinical isolate	Negative	Positive
S. enterica typhimurium	Z005	Negative	Positive
E. coli	7.1493; O84:H28; EPEC[1]	Negative	Positive
E. coli	ETEC; ST+, LT+	Negative	Positive
C. cayetanensis	Recombinant[2]	Negative	Positive
E. histolytica	DS4-868	Negative	Positive
G. lamblia	H3	Negative	Positive
Astrovirus	Recombinant[2]	Negative	Positive
Norovirus GI	Recombinant[2]	Negative	Positive
Norovirus GII	Recombinant[2]	Negative	Positive

- The RNA Process Control assay targets an RNA transcript from the yeast *Schizosaccharomyces pombe*. The yeast is present in the pouch in a freeze-dried form and becomes rehydrated when sample is loaded. The control material is carried through all stages of the test process, including lysis, nucleic acid purification, reverse transcription, 1st stage PCR, dilution, 2nd stage PCR
- The PCR2 Control assay detects a DNA target that is dried into wells of the array along with the corresponding primers. A positive result indicates that 2nd stage PCR was successful.
- Both control assays must be positive for the test run to pass. If either control fails, the Controls field of the test report (upper right-hand corner) will

display Failed, and all results will be listed as Invalid. If the controls fail, the sample should be retested using a new pouch.

- The BIOFIRE Software will automatically fail the run if the melting temperature (Tm) for either the RNA Process Control or the PCR2 Control is outside an acceptable range (80.2-84.2 for the RNA Process Control and 74.1-78.1 for the PCR2 Control). If required by local, state, or accrediting organization quality control requirements, users can monitor the system by trending Tm values for the control assays and maintain records according to standard laboratory quality control practices. The PCR2 Control is used in all pouch types and can therefore be used to monitor the system when multiple pouch types are used on the same BIOFIRE System.
- All analytes in the positive NATrol GI Control must be Detected. All analytes in the negative NATro GI control must be Negative.

B. Criteria for Acceptable QC

- All controls must yield acceptable results
- Controls and patient data must be reviewed for acceptability and for atypical or unexpected results or trends prior to reporting patient results.
- DO NOT release results from runs with unacceptable controls or with unusual patterns, trends or distribution in patient values.

C. Corrective Action

- All rejected runs must be effectively addressed and include the following documentation:
  - Control(s) that failed (e.g., 2-2S QC rule violated, positive control with negative result) and/or atypical or unexpected patient results
  - Actions taken
  - Statement of what was done with the patient samples from the affected run/batch,
  - Date and initials of the person recording the information.
- Patient samples in failed analytical runs must be reanalyzed.

NOTE: The laboratory director or designee may override rejection of partial or complete runs. Justification for the override must be documented in detail.

6.5 Documentation

- Record all Quality Control results (failed and successful) manually or electronically.
- QC data must be documented, including any QC failure and corrective action on the QC form.
- Refer to Quest Diagnostics Records Management Program for Quality Control record retention requirements.

6.6 Quality Assurance Program

The laboratory participates in CAP proficiency testing.

7. EQUIPMENT and SUPPLIES

7.1 Assay Platform

- BioFire ®FilmArray ®Torch Systems
- BioFire FilmArray Software

7.2 Equipment

- BIOFIRE ®Torch System
- BIOFIRE Pouch Loading Station
- Vortex
- Biological Safety Cabinet (BSC)

7.3 Supplies

- Individually packaged Transfer Pipettes
- 10% bleach solution
- 70% ethanol
- Distilled water
- Gauze squares 4” x 4”
- Sharps container
- Gloves

8. PROCEDURE

NOTE: For all procedures involving specimens, buttoned lab coats, gloves, and face protection are required minimum personal protective equipment. Report all accidents to your supervisor.

Refer to BioFire® FilmArray® Torch Systems Maintenance procedure for required maintenance.

8.1	Instrument Set-up Protocol
1.	**Only one BIOFIRE GI Panel pouch should be prepared at a time. Once sample is added to the pouch, it should be promptly transferred to the module to start the run. After the run is complete, the pouch should be discarded in a biohazard container.**

8.1	Instrument Set-up Protocol
2.	Thoroughly clean the work area and the Pouch Loading Station with freshly prepared 10% bleach followed by a water rinse. The water rinse is then followed by wiping with 70% ethanol. Obtain the following required materials and place in the clean hood: • BIOFIRE GI Panel pouch • Sample Buffer ampoule • Hydration Injection Vial (blue cap) • Sample Injection Vial (red cap) • Transfer Pipette
3.	Place a blue-capped Hydration Injection Vial in the blue well of the Pouch Loading Station.
4.	Place a red-capped Sample Injection Vial in the red well of the Pouch Loading Station.
5.	Obtain patient sample and place into hood.
6.	Remove the BIOFIRE GI Panel pouch from its vacuum-sealed package by tearing or cutting the notched outer packaging and opening the protective canister**. NOTE: If the vacuum seal of the pouch is not intact, the pouch may still be used. Attempt to hydrate the pouch using the steps in the Hydrate Pouch section. If hydration is successful, continue with the run. If hydration fails, discard the pouch, and use a new pouch to test the sample.**
7.	Slide the pouch into the Pouch Loading Station so that the red and blue labels on the pouch align with the red and blue arrows on the Pouch Loading Station.

8.2	Hydrate Pouch
1.	Twist the Hydration Injection Vial (blue cap), leaving cap in Pouch Loading Station, and insert the tip of the cannula into the hydration port of the pouch located directly below the blue arrow of the Pouch Loading Station. Push down forcefully in a firm and quick motion until you hear a faint “pop” and feel an ease in resistance. The correct volume of liquid will be pulled into the pouch by vacuum.
2.	Verify that the pouch has been hydrated. Flip the barcode label down and check to see that fluid has entered the reagent wells (located at the base of the rigid plastic part of the pouch). Small air bubbles may be seen. If the pouch fails to hydrate (dry reagents appear as white pellets), verify that the seal of the port was broken by ensuring the vial cannula was fully inserted into the hydration port. If the pouch fails to hydrate, retrieve a new pouch, and repeat from Step 2 of the Prepare Pouch section.

8.3	Prepare Sample Mix
1.	Hold the Sample Buffer ampoule so that the tip is facing up. **NOTE: Use care to avoid touching the tip during handling, as this may introduce contamination.**
2.	To open the Sample Buffer ampoule: • If the ampoule has a plastic tab on the tip: Gently twist and remove tab at the tip of the Sample Buffer ampoule. If the ampoule does not have a plastic tab on the tip: Firmly pinch the textured plastic tab on side of ampoule until the seal snaps.

8.3	Prepare Sample Mix
3.	Re-position thumb and forefinger to grip between the textured plastic tab and the bottom of the ampoule, then invert over the red Sample Injection Vial and dispense Sample Buffer using a slow, forceful squeeze, followed by a second squeeze. Avoid generating excessive bubbles.
4.	Thoroughly mix the patient specimen.
5.	Using the Transfer Pipette provided in the test kit, draw sample to the second line (approximately 0.2 mL). Add sample to the red Sample Injection Vial. **NOTE: DO NOT use the transfer pipette to mix the sample once it is loaded into the Sample Injection Vial.**
6.	Tightly close the lid of the Sample Injection Vial and mix by gently inverting at least 3 times.
7.	Return the Sample Injection Vial to the Pouch Loading Station.

8.4	Load Sample Mix
1.	Slowly unscrew the Sample Injection Vial from the cap and pause for 3-5 seconds. **NOTE: It is important to pause after unscrewing the Sample Injection Vial to avoid sample leakage and contamination of the work area.**
2.	Remove Sample Injection Vial leaving cap in Pouch Loading Station and insert the cannula tip into the port in the pouch fitment located directly below the red arrow of the Pouch Loading Station. Push down forcefully in a firm and quick motion until you hear a faint “pop” and feel an ease in resistance. The correct volume of liquid will be pulled into the pouch by vacuum.
3.	Verify that the sample has been loaded. Flip the barcode label down and check to see that fluid has entered the reagent well next to the sample loading port. If the pouch fails to pull sample from the Sample Injection Vial, the pouch should be discarded. Retrieve a new pouch and repeat from Step 2 of the Prepare Pouch section.
4.	Discard the Hydration Injection Vial and Sample Injection Vial in an appropriate biohazard sharps container.
5.	Record the Sample ID in the provided area on the pouch label (or affix a barcoded Sample ID) and remove the pouch from the Pouch Loading Station.

8.5	RUN POUCH
1.	Ensure that the BIOFIRE Torch system is on.
2.	Select an available Module on the touch screen.

8.5	RUN POUCH
3.	Scan the barcode on the BIOFIRE pouch using the barcode scanner. Pouch identification (Lot Number and Serial Number), Pouch Type and Protocol are preprogrammed in the rectangular barcode located on the BIOFIRE pouch. The information will be automatically entered when the barcode is scanned. If it is not possible to scan the barcode, the pouch Lot Number, Serial Number, Pouch Type and Protocol can be manually entered from the information provided on the pouch label into the appropriate fields. To reduce data entry errors, it is strongly recommended that the pouch information be entered by scanning the barcode.
4.	Enter the Sample ID. The Sample ID can be entered manually or scanned in by using the barcode scanner when a barcoded Sample ID is used.
5.	Insert the pouch into the Module. Ensure that the pouch fitment label is lying flat on top of pouch and not folded over. As the pouch is inserted, the Module will grab onto the pouch and pull it into the chamber.
6.	If necessary, select and/or confirm a protocol from the protocol drop down list.
7.	Enter operator username and password, then select Next. **NOTE: The font color of the username is red until the username is recognized by the software.**
8.	Review the entered run information on the screen. If correct, select Start Run. Once the run has started, the screen displays a list of the steps being performed by the instrument and the number of minutes remaining in the run. **NOTE: The bead-beater apparatus can be heard as a high-pitched noise (whine) during the first minute of operation.**
9.	At the end of the run, the status of the Module changes to Finished and the pouch is partially ejected.
10.	Select the Finished Module on the Dashboard to view the report. Select Print to print the report or save to save the report as a file.
11.	Remove the pouch from the Module and immediately discard the pouch in a biohazard container**.** **NOTE: Once the pouch has been removed, the report can only be viewed through the Browse Runs feature.**

NOTE: In the event that the test system becomes inoperable, notify supervision or designee for further direction. Patient specimens must be stored in a manner that maintains the integrity of the specimen.

9. CALCULATIONS

N/A

10. REPORTING RESULTS AND REPEAT CRITERIA

10.1 Interpretation of Data

The BIOFIRE Software automatically analyzes and interprets assay results and displays the results in a test report.

For many organisms detected by the BIOFIRE GI Panel, the organism is reported as Detected if a single corresponding assay is positive. For example, *Plesiomonas shigelloides* will have a result of *Plesiomonas shigelloides* Detected if at least two of the three replicates of the one *Plesiomonas shigelloides* assay have similar positive melt peaks with Tm values that are within the assay-specific Tm range.

The following organisms are detected using a single assay: toxigenic *C. difficile* (*C. diff* target not reported in our lab), *P. shigelloides*, *Salmonella*, *Vibrio cholerae*, *Y. enterocolitica*, EAEC, Shigella/EIEC, Adenovirus F 40/41, Astrovirus, Sapovirus (Genogroups I, II, IV, and V), *C. cayetanensis*, *E. histolytica* and *G. lamblia*.

Test results for several other organisms rely on the combination of multiple assays. These include *Campylobacter* (*C. jejuni/C. coli/C. upsaliensis*), *Vibrio* (*V. parahaemolyticus/ V. vulnificus/V. cholerae*), *Cryptosporidium*, Norovirus GI/GII, and Rotavirus A. The test results for several Diarrheagenic *E. coli*(s) include multiple assays for genetic markers to identify various classic pathotypes of *E. coli* including EPEC, ETEC, and STEC (including O157), (as well EAEC and Shigella/EIEC included above).

Table 1: Reporting of Results and Required Actions

Results	Explanation	Actions
DETECTED	The run was successfully completed, AND The pouch controls were successful (Passed), AND The assay(s) associated with the interpretation were positive based on the following requirements for at least 2 of the 3 assay replicates: -a positive melt curve, and -the Tm for the melt data were within the assay specific limits, and -the Tm for the melt data were within 1°C of each other.	Report and Call results

Results	Explanation	Actions
Not Detected	The run was successfully completed, AND The pouch controls were successful (Passed), AND The assay(s) associated with the interpretation were negative (did not meet the requirements for a positive assay described in Detected)	None. Report results.
N/A (applies to *E. coli* O157 and EPEC only)	The run was successfully completed, AND The pouch controls were successful (Passed), AND For *E. coli* O157: Shiga-like toxin-producing *E. coli* was Not Detected. For EPEC: Shiga-like toxin-producing *E. coli* was Detected.	None. Report results.
Invalid	The run did not complete successfully (Aborted, Incomplete, Instrument Communication Error, Instrument Error, or Software Error) OR The pouch controls were not successful (Failed)	See Table 2, Interpretation of Controls Field on BIOFIRE Report, for instruction.

10.2 Rounding

N/A

10.3 Units of Measure

N/A

10.4 Clinically Reportable Range (CRR)

N/A

10.5 Review Patient Data

- Review patient results for unusual patterns, trends or distribution.
- Report atypical or unexpected results or trends for this test to appropriate supervisory personnel, prior to releasing results.

10.6 Repeat Criteria and Resulting

IF the result is …	THEN…
If four or more distinct organisms are detected in a specimen	Retesting is recommended to confirm the polymicrobial result.

- As rates of asymptomatic carriage of *C. difficile* can be high in very young children and hospitalized patients, the *C. difficile* target results are HIDDEN, or NOT REPORTED for this GI panel.
- When suspected of *C. difficile* infection (CDI), a separate *C. difficile* test should be ordered as per local hospital guidelines using appropriate test codes

Table 2. Interpretation of Controls Field on the BioFire GI Test Report

Control result	Explanation	Action required	Outcome
Passed	The run was successfully completed, AND Both pouch controls were successful.	None	Report the results provided on the test report**.**
Failed	The run was successfully completed, BUT At least one of the pouch controls (RNA Process Control and/or PCR2 Control) failed.	Repeat the test using a new pouch.	Accept the results of the repeat testing. If the error persists, contact Customer Technical Support for further instruction**.**

Control result	Explanation	Action required	Outcome
Invalid	The controls are invalid because the run did not complete. (Typically, this indicates a software or hardware error).	Note any error codes displayed during the run and the Run Status field in the Run Details section of the report. Refer to the appropriate BIOFIRE Operator's Manual or contact Technical Support for further instruction. Once the error is resolved, repeat the test, or repeat the test using another module**.**	Accept the valid results of the repeat testing. If the error persists, contact Customer Technical Support for further instruction.

Message Code	Message
D	Detected
ND	Not Detected

11. EXPECTED VALUES

11.1 Reference Ranges

Not Detected

11.2 Critical Values

None

11.3 Standard Required Messages

None

12. CLINICAL SIGNIFICANCE

Despite advances in food safety, sanitation, and medical treatment, infectious gastroenteritis remains a significant problem in industrialized countries among all age groups. In the United States, around 76 million cases of foodborne disease, resulting in 325,000 hospitalizations and 5,000 deaths, are estimated to occur each year. Additionally, there are over 300,000 *C. difficile* diagnoses per year in the US4 resulting in estimated costs of at least $1 billion. Globally, infectious diarrheal illness is a significant cause of mortality in young children resulting in an estimated 800,000 deaths per year in children under the age of 5. In addition to this significant morbidity and mortality, diarrhea in children contributes to malnutrition, increased susceptibility to other infections, and may lead to delays in growth and intellectual development.

- ***Campylobacter* (*C. jejuni/C. coli/C. upsaliensis*)**. Campylobacters are gram-negative, non-spore forming, s-shaped or spiral bacteria that are usually motile. Most sporadic infections are acquired through ingestion of undercooked poultry or from cross-contamination of other foods. Outbreaks have been associated with unpasteurized dairy, contaminated water, poultry, and produce. Transmission from the stool of household pets has also been documented. *C. jejuni* and *C. coli* are the species most associated with diarrheal illness, followed distantly by *C. upsaliensis*. Other species such as *C. lari* and *C. fetus* are more uncommon. Infection with Campylobacter species is common throughout the world, representing a large and perhaps under-recognized health burden. Campylobacters are a leading cause of bacterial enteritis in the US (est. 845,000 infections annually with almost 8,500 hospitalizations12) and the most common cause of foodborne illness in the EU (over 220,000 confirmed cases reported by EU member states in 2011. Enteric Campylobacter infections range from asymptomatic to severe infections characterized by bloody or non-bloody diarrhea, fever, and abdominal cramping. Infections may also lead to long-term health issues such as Guillain-Barré syndrome (GBS) and reactive arthritis. Campylobacter infections are a notifiable disease in the US and are tracked by the European Surveillance System (TESSy)

  ***Clostridium difficile* (re-classified as *Clostridioides difficile*)** are obligately anaerobic, gram-positive rods capable of forming hardy spores and are widespread in nature. These bacteria are acquired from the environment or transmitted via the fecal-oral route. Some *C. difficile* strains produce two enterotoxins, toxin A and toxin B, which damage the large intestine of the infected individual. *C. difficile* infection (CDI) is the major cause of hospital-acquired diarrhea and is responsible for more than 300,000 cases of diarrheal disease and 14,000 deaths annually in the US, resulting in over a billion dollars in health care costs. CDI presents a similar healthcare burden in the EU. Antibiotic treatment, which severely disrupts the normal gastrointestinal flora, is a major risk factor for the development of CDI. Community-acquired CDI, which has a somewhat lower association with antibiotic exposure, has also been emerging in the last few years. Clinical manifestations of *C. difficile* infection range from asymptomatic carriage (estimated to occur in 3-5% of healthy adults and up to 30% of healthy neonates) to pseudomembranous colitis, involving bloody diarrhea, severe abdominal pain, and fever. Due to the high asymptomatic carriage rates, especially in young children, the clinical relevance of the detection of toxigenic *C. difficile* from stool should be considered in the context of other clinical findings, patient age, and risk factors including hospitalization and antibiotic exposure. **(*C. diff* target not reported in our lab)**

- ***Plesiomonas shigelloides*. Plesiomonas shigelloides**, gram-negative rod-shaped bacteria and members of the Enterobacteriaceae family, are isolated from a wide range of environmental sources including freshwater and many animals, both wild and domestic. *P. shigelloides* gastroenteritis often follows consumption of seafood, as well as contaminated water used for drinking or used in preparing uncooked foods. Symptoms generally include watery diarrhea, though dysenteric diarrhea can occur, and infections may be prolonged (>2 weeks duration) but are generally self-limiting. Most cases reported in the US are from individuals with pre-existing health problems leading to a more severe disease outcome. The incidence of *Plesiomonas* infection in the US, EU, or other regions is largely unknown.

- ***Salmonella***. *Salmonella enterica* and *S. bongori* are the sole members of the Salmonella genus. Greater than 2,500 different serotypes of Salmonella have been recognized, with most pathogenic serotypes being within the *S. enterica* species. These motile, rod-shaped, gram-negative, facultative bacteria are commonly recognized as a food contaminant associated with meat, poultry, produce, and manufactured products. Salmonella may be classified as typhoidal and non-typhoidal based on the disease that they cause. The non-typhoidal Salmonella are associated with intestinal illness resulting in acute, watery diarrhea, often with fever, and are a common cause of foodborne illness in the US and EU. Typhoidal Salmonella cause a severe, systemic disease (typhoid fever) that includes GI illness. Though rare in developed countries, it is common in the developing world (>70% of US cases are related to foreign travel). In contrast, infection with non-typhoidal Salmonella is one of the most common causes of foodborne illness in the US and EU with greater than one million cases per year. While large outbreaks do occur, most cases are sporadic with peak in incidence in late summer/early fall. The highest incidence is seen in children aged <5 years. In general Salmonella-related gastroenteritis is self-limiting except in cases of severe or typhoidal illness. Salmonellosis is a notifiable disease in the US and is tracked by TESSy in the EU.

- ***Vibrio* (*V. parahaemolyticus/V. vulnificus/V. cholerae*).** Vibrios are motile, gram-negative, comma-shaped bacteria typically found in marine environments. Several species are capable of causing illness in humans, both extraintestinal (soft tissue infection, septicemia, eye and ear infections) and intestinal. Gastrointestinal illness is most commonly associated with *V. cholerae, V. parahaemolyticus, V. vulnificus, V. fluvialis, V.mimicus* or *V. alginolyticus* and infections are associated with consumption of contaminated food, particularly in coastal regions.

- ***V. cholerae*** is the only Vibrio species that causes endemic, epidemic, and pandemic cholera. There are three major subgroups of *V. cholerae*: *V. cholerae* O1, *V. cholerae* O139, and *V. cholerae* non-O1/non-O139. Classic cholera is characterized by passing copious amounts of watery diarrhea leading to extreme dehydration and death. Severe disease is mediated by the presence of cholera toxin (CTX). Cholera is endemic in many parts of the world and new outbreaks often follow natural disasters or social upheaval. As such, cholera remains a significant cause of morbidity and mortality in much of the world. In the US and EU, occasional cases of cholera are seen in travelers returning from overseas.

- **Vibriosis and cholera** are notifiable diseases in the US and are tracked by the Cholera and Other Vibrio Illness Surveillance Network (COVIS). While *V. cholerae* infections are exceedingly rare in the US, other Vibrio species are estimated to cause approximately 50,000 food-borne infections per year though only ~400 isolates recovered from stool were reported to COVIS in 2009 (the majority of which were *V. parahaemolyticus*). This discrepancy between estimated prevalence and actual detections is due to specialized testing required to recover Vibrio organisms from stool, leaving most cases undiagnosed. The risk of Vibrio infection in Europe is thought to be very low and is not tracked by TESSy.
- ***Yersinia enterocolitica*** are small, gram-negative bacilli, which generally appear as single cells or short chains. *Y. enterocolitica* is transmitted through ingestion of contaminated food or water, often raw undercooked meats (especially pork), and is estimated to cause almost 100,000 foodborne illnesses in the US annually (though only about 1,000 cases are laboratory-

confirmed; possibly because *Y. enterocolitica* are not identified by routine enteric pathogen testing). A higher incidence of Yersiniosis is observed in European countries, particularly in continental Europe with nearly 7,000 confirmed cases reported in 2011. The severity of the illness is based on the serotype of the infecting strain and ranges from self-limiting gastroenteritis to terminal ileitis and mesenteric lymphadenitis. Symptoms of illness mimic appendicitis and may lead to unnecessary surgery, highlighting the importance of properly identifying this organism when it is present in stool specimens. Yersiniosis is a notifiable disease in the US and is tracked by TESSy in the EU.

- **Pathogenic *E. coli/Shigella*** are a significant cause of diarrheal illness worldwide. There are several pathotypes of Diarrheagenic *E. coli/Shigella* that differ in the mechanisms and location of colonization as well as the clinical manifestations, progression, and severity of the diseases they cause. Some of these differences are attributable to the production of specific virulence factors including adhesins, invasins, and toxins. Genes encoding these virulence factors or their regulators are targeted as genetic markers by molecular assays to detect and differentiate these pathogens. The five major Diarrheagenic *E. coli/Shigella* pathotypes are Enteroaggregative *E. coli* (EAEC), Enteropathogenic *E. coli* (EPEC), Enterotoxigenic *E. coli* (ETEC), Shiga-like toxin-producing *E. coli* (STEC), and Shigella/Enteroinvasive *E. coli* (EIEC). Each pathotype and their characteristic genetic markers are discussed below. It should be noted that these genetic markers have been shown to be horizontally transferred between strains during the evolution of these pathotypes, and more recently during the emergence of new pathotypes containing several of these genetic markers (e.g., the 2011 epidemic *E. coli* O104:H4 which contained genetic markers characteristic of both STEC and EAEC)

- **Enteroaggregative *E. coli* (EAEC**) is defined by their "stacked brick" aggregative adherence pattern when observed on cultured cells. This phenotypic description of the pathotype results in a heterogeneous and highly divergent group of *E. coli*. Although they display a wide variety of virulence factors which are not conserved across all strains, most EAEC carry the aggregative adherence (pAA) plasmid (although genetic composition of this plasmid is variable). Strains that contain aggR on the pAA plasmid (encoding a regulator of several virulence factors) have been classified as typical EAEC, while those that do not contain this marker are considered atypical EAEC. The aatA marker (an outer membrane protein) is also carried on the pAA plasmid of many EAEC strains, both typical and atypical. Transmission of EAEC is generally by the fecal-oral route via contaminated food and water. EAEC cause an inflammatory diarrheal illness characterized by watery and sometimes bloody stool, accompanied by low grade fever, vomiting, and abdominal pain. EAEC infections may also be asymptomatic. Data regarding the incidence of EAEC are limited due to the lack of widespread testing; however, based upon various studies, EAEC are suggested to be one of the most common causes of diarrheal illness in the US and EU across all age groups, a cause of persistent diarrhea in children and HIV-infected individuals, the second most common cause of travelers' diarrhea, and has been identified as the cause of large outbreaks worldwide.

- **Enteropathogenic *E. coli* (EPEC**) does not produce enterotoxins or Shiga-like toxins. Rather, EPEC contain additional virulence factors including those encoded by the chromosomal locus of enterocyte effacement (LEE) pathogenicity island. The adhesion protein, intimin, is encoded by the gene eae within the LEE pathogenicity island and is considered a definitive marker for

EPEC. Strains may be further categorized as typical or atypical depending on the presence of a plasmid encoding bundle-forming pili (bfpA; found in typical EPEC). Globally, EPEC are estimated to have a prevalence of 8.8%. community setting, 9.1% in the outpatient setting, and 15.6% in the inpatient setting. While typical EPEC remains a significant pathogen of young children in the developing world, atypical EPEC is more prevalent in both developing and developed countries. Typical EPEC, however, has been associated with several deadly outbreaks at hospital nurseries in developed countries in the past. Outbreaks appear to peak in the warmer months of summer and early fall. Illness caused by typical EPEC is associated with acute diarrhea whereas atypical EPEC cause a prolonged, non-bloody diarrhea, and vomiting with fever. When untreated in children, EPEC illness can lead to malnutrition and associated growth defects. Asymptomatic carriage of EPEC has also been documented with some studies reporting similar rates to symptomatic individuals.

- **Shiga-like toxin-producing *E. coli* (STEC),** including *E. coli* O157. There are two main types of Shiga-like toxins, Shiga-like toxin 1 (Stx1) and Shiga-like toxin 2 (Stx2) (also known as verotoxins). Shiga-like toxin-producing *E. coli* (STEC) may contain either one or both stx genes. STEC are a primary cause of bloody diarrhea and can progress to a potentially fatal condition known as hemolytic uremic syndrome (HUS; caused by Shiga-like toxin destruction of red blood cells that leads to renal failure), especially in the very young and very old. STEC are important foodborne pathogens. Infections may also be waterborne, transmitted person-to-person, or via contact with animals (especially cattle, which are a reservoir for STEC). Antimicrobial therapy for STEC may lead to an increased risk for HUS, especially in antibiotic-resistant strains, potentially by up-regulating production and thus increasing the amount of Shiga-like toxin available for absorption. Therefore, identification of Shiga-like toxin genes in a patient with gastrointestinal illness can aid in the decision of whether to prescribe antibiotics for patient care.
- A subset of STEC contain the O157 antigen (and flagellar H7 antigen). *E. coli* O157:H7 is currently the most frequently identified diarrheagenic *E. coli* in North America. There are over 170,000 STEC infections in the US each year, of which an estimated 73,000 illnesses and 60 deaths per year are attributable specifically to *E. coli O157*. Similar infection rates are observed in the EU. Disease presentation ranges from mild, non-bloody diarrhea to hemorrhagic colitis and HUS. An estimated 4% of O157:H7 infections lead to HUS and this serotype of *E. coli* is responsible for up to 80% of all HUS illness. The infectious dose is low, facilitating person-to-person transmission but most illness is caused by ingestion of contaminated ground beef, as dairy and beef cattle are often colonized with this bacterium. Although *STEC O157:H7* remains the most identified serotype of STEC associated with human illness worldwide, non-O157 STEC are increasing in importance in both sporadic diarrhea and outbreaks. Non-O157 STEC are likely underdiagnosed as testing methods are generally focused on detection of *E. coli* O157. STEC infections (including *E. coli* O157) are notifiable diseases in the US and are tracked by TESSy in the EU.

- **Shigella/Enteroinvasive *E. coli* (EIEC**). There are four subgroups of *Shigella* species: subgroup A (*S. dysenteriae*), subgroup B (*S. flexneri*), subgroup C (*S. boydii*), and subgroup D (*S. sonnei*). All Shigella are non-motile, gram-negative rods which are typically transferred through person-to-person contact or ingestion of contaminated food or water (humans and other primates are the only known animal reservoirs). Infections are most common where

hygiene is compromised, for example institutional settings (day care, nursing homes) and may become endemic in developing societies without running water and indoor plumbing. Shigella are responsible for multiple illnesses including shigellosis and bacillary dysentery which can result in bloody or non-bloody diarrhea.

- **Enteroinvasive *E. coli* (EIEC**), unlike most *E. coli* do not decarboxylate lysine, and do not ferment lactose. EIEC strains contain a plasmid encoding virulence factors (such as invasion plasmid antigen ipaH) that allow the bacteria to invade the colon and produce a watery diarrhea syndrome that is identical to that caused by Shigella. EIEC is rare in the US and EU and is also less common worldwide than ETEC and EPEC. Shigella and EIEC infections are generally treated in the same manner.
- Multiple copies of the ipaH gene are present in all four *Shigella* species (*S. dysenteriae, S. flexneri, S. boydii,* and *S. sonnei*) as well as in the virulence plasmid of Enteroinvasive *E. coli* (EIEC). IpaH, along with other factors encoded by the invasion plasmid, mediate entry of Shigella and EIEC into host cells. This is a common target for laboratory developed molecular tests.
- There are an estimated 130,000 Shigella infections associated with foodborne illness in the US each year12 however no data exists for EIEC. Shigellosis is a notifiable disease in the US and is tracked by TESSy in the EU.

- **Cryptosporidium** is a genus of protozoa capable of causing infections of the human stomach, intestine, and biliary ducts following ingestion of chlorine-tolerant oocysts which are shed in fecal material and can contaminate drinking water, recreational water, or food. Cryptosporidium is among the most common parasitic causes of diarrhea in developed nations. There are an estimated 60,000 illnesses every year in the US due to Cryptosporidium infection with rates being highest in summer months. At least 10 species infect humans though *C. hominis* and *C. parvum* are the most common.10 Illness is generally characterized by short-term gastroenteritis that resolves without treatment. However, severe illness is possible in immunocompromised individuals, particularly those with AIDS, where illness resolves slowly or not at all and can be fatal. Cryptosporidiosis is a notifiable disease in the US and is tracked by TESSy in the EU.

- ***Cyclospora cayetanensis*** are parasitic protozoa that cause gastroenteritis in humans, which are the only known hosts. Unpopulated oocysts are disseminated in feces. After a period of maturation (days to weeks), the oocysts become infectious and can cause illness if ingested through contaminated food or water. Infections are most common in tropical, subtropical, or warm temperate regions. In the US and EU, infections are associated with travelers' diarrhea in persons returning from endemic areas. Additionally, outbreaks have been associated with consumption of contaminated food from other countries. There are an estimated 11,000 foodborne illnesses due to *C. cayetanensis* infections annually in the US, but the true incidence may be underestimated due to the difficulty of diagnosing infection. Illness presents as non-bloody diarrhea that may be up to several months in duration. Cyclosporiasis is a notifiable disease in the US but is not tracked by TESSy in the EU.

- ***Entamoeba** histolytica* are pathogenic protozoa which are found worldwide with a particularly high prevalence in tropical and subtropical regions. *E. histolytica* cysts are generally ingested

from materials contaminated with feces, such as food and water, but infection may also be transmitted sexually. Humans are the primary reservoir. Most infections from *E. histolytica* appear to be asymptomatic but some infections cause invasive amebiasis which results in Ftis or dysentery-like illness that can be severe and include amebic liver abscess. The epidemiology of *E. histolytica* is uncertain because it is indistinguishable from non-pathogenic *E. dispar* using the current clinical reference standard (microscopy). In endemic regions, the prevalence of Entamoeba in stool can be as high as 50% of the general population. An estimated 500 million people world-wide are infected every year with Entamoeba. As *E. dispar* is thought to be 10-fold more prevalent, this translates to an estimated 50 million *E. histolytica* infections, which result in more than 100,000 deaths. The BIOFIRE GI Panel *E. histolytica* assay demonstrates cross-reactivity with high levels of *E. dispar*.

- ***Giardia lamblia*** (also referred to as *G. duodenalis* and *G. intestinalis*) are intestinal flagellate parasites found world-wide. Giardia are the most common intestinal parasites isolated in the US and EU and are a leading cause of parasitosis worldwide. Populations with the highest risk of *G. lamblia* infection include children in day care centers, hikers, and the immunocompromised. *G. lamblia* prevalence is about 1-7% in developed countries and as high as 50% in developing countries. Transmission occurs through ingestion of contaminated food or water, with approximately 77,000 foodborne illnesses in the US annually. Infection rates are highest during summer months. Most *G. lamblia* infections are asymptomatic, but those who develop illness experience nausea, fever, and watery diarrhea. Infections are generally self-limiting; though symptoms are long-lasting, and some patients go on to develop chronic illness, which can lead to complications. Giardiasis is a notifiable disease in the US and is tracked by TESSy in the EU.

- **Adenovirus F 40/41**. Adenoviruses are double-stranded DNA viruses of the Adenoviridae family that cause a variety of diseases including respiratory illness and gastrointestinal illness. They are resistant to chemical and physical damage and are thus persistent in the environment, facilitating transmission. There are seven species of Adenoviruses (A-G) that are further categorized into approximately 57 serotypes; however, GI illness is primarily associated with species F (which is comprised of serotypes 40 and 41). Adenovirus F 40/41 is responsible for 5 to 15% of all acute diarrheal illness in children (especially in those under two years of age). Transmission is mostly through fecal-oral spread and outbreaks have been reported in hospitals and childcare centers. While Adenovirus infections mostly occur in children, adults may be affected as well. Illness is generally mild but of a relatively long duration (5-12 days). Immunocompromised patients may suffer chronic, prolonged diarrheal illness and other complications. Virus may be shed in stool for weeks to months following acute illness; therefore, identification of infected individuals may be important for patient isolation and control of disease spread.

- **Astrovirus**. Astroviruses (RNA viruses of the family Astroviridae) are named for their characteristic star-like structure and are found in a variety of animals, including birds and mammals. There are eight serotypes of human Astrovirus (HAstv 1-8) associated with gastroenteritis in both children and adults. The infection route is fecal-oral and at-risk populations include children, immunocompromised adults, caregivers of sick children, military troops, and those in nursing homes. It is estimated that there are over 15,000 foodborne

illnesses due to Astrovirus in the US each year, but diagnostic testing is limited, and the true incidence is not known. Symptoms are reported to be milder than other enteric viruses and include diarrhea, vomiting, abdominal pain, and fever lasting 72 hours. There is a 70-90% seroprevalence of antibodies to Astrovirus in school-aged children, indicating nearly universal exposure in childhood, but the presence of antibodies and their role in immunity is not well understood.

- **Norovirus GI/GII**. Noroviruses are highly contagious members of the Caliciviridae family of RNA viruses and can be divided into five genogroups (GI – GV). GI, GII, and GIV have been found most commonly in humans (though GIV is very rare) where they cause moderate to severe gastroenteritis consisting primarily of nausea, vomiting, and diarrhea accompanied by fever. Transmission occurs via the fecal-oral route or through aerosolized vomitus and the infectious dose may be as low as 18 particles. Symptoms of infection generally last 24-48 hours and the illness is self-limiting; though immunocompromised persons may suffer chronic diarrhea and some children have been reported to develop necrotizing colitis. Outbreaks are common in closed communities such as cruise ships, hospitals, nursing homes, schools, and military installations. Norovirus infections are the leading cause of foodborne gastroenteritis in the US, causing nearly 5.4 million illnesses (and over 14,000 hospitalizations) annually and are also a significant source of illness in the EU. Peak infection rates occur during winter months. Immunity following Norovirus illness is short lived as re-infection is possible within 6 months, even in the presence of high serum antibody titers.

- **Rotavirus A.** Rotaviruses are double stranded RNA viruses of the Reoviridae family and are the single most important etiologic agents of severe diarrheal illnesses in infants and young children worldwide. Of the seven groups of Rotaviruses (A through G), Rotavirus A, B, and C infect humans, with Rotavirus A being responsible for most infections. Symptoms of infection may be mild and last for a few days, but prolonged illness can lead to severe dehydration in children <2 years of age and Rotavirus A infections are a considerable cause of infant mortality in the developing world. Rotaviruses are shed before and after acute illness and are hardy to environmental factors, allowing them to survive on surfaces and resist inactivation. Disease rates peak during winter/spring in temperate climates and may account for up to a third of diarrheal diseases presenting to emergency rooms and outpatient clinics during this time in the US and EU. It is estimated that 2.7 million diarrheal illnesses per year in the US are caused by Rotavirus infection.56 Immunity is thought to be long-lasting following infection. There are two Rotavirus vaccines, Rotarix (RV1) and RotaTeq (RV5), which have been licensed worldwide and offer protection against Rotavirus A. RotaTeq was implemented in the US vaccination program in 200652 and has resulted in a decline in Rotavirus A infections.

- **Sapovirus (Genogroups I, II, IV, and V).** Sapovirus is a Calciviridae family member that is similar to Norovirus both genetically and in disease presentation. There are five genogroups (GI–GV); groups GI, GII, GIV, and GV are known to infect humans, whereas GIII causes diarrheal illness in pigs. Sapovirus causes disease mostly in children, though adults are susceptible as well, with outbreaks reported in long-term care facilities, prisons, cruise ships, and hospitals in the US and EU. Like Norovirus, Sapovirus is spread via the fecal-oral route and infections are highest during winter months. Symptoms primarily include vomiting and diarrhea with nausea and fever lasting 5 to 10 days. In general, illness is self-limiting with

treatment consisting of supportive care. Infections are attributed to an estimated 15,000 foodborne illnesses in the US annually, however the true incidence may be much higher as there is very limited testing available.

13. PROCEDURE NOTES

- **FDA Status: FDA Approved**
- **Validated Test Modifications: None**

14. LIMITATIONS OF METHOD

14.1 Analytical Measurement Range (AMR)

N/A

14.2 Precision

N/A

14.3 Interfering Substances

Accurate detection of analytes are impaired (false negative results) for samples prepared in media containing fixatives, particularly those containing formalin.

14.4 Clinical Sensitivity/Specificity/Predictive Values

Refer to BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel package insert.

15. SAFETY

Refer to the safety manuals and Safety Data Sheet (SDS) for detailed information on safety practices and procedures and a complete description of hazards.

16. RELATED DOCUMENTS

- Quality Control Program (AHC.QA 40)
- Biosafety (AHC.M38)
- BioFire FilmArray® Gastrointestinal (GI) Panel External QC Form (AG.F707)
- BioFire FilmArray® Gastrointestinal (GI) Panel Internal QC Log (AG.F708)
- Biological Safety cabinet (AHC.M 20)
- Biological Safety Cabinet Preventive Maintenance Chart (AG.F23)
- BioFire ®FilmArray® torch Maintenance Record (AG.F516)
- BioFire Failed Pouches for Credit Log (AG.F565)

17. REFERENCES

- BIOFIRE® FILMARRAY® Gastrointestinal (GI) Panel package insert. (08/2023)

18. REVISION HISTORY

Version	Date	Section	Reason	Reviser	Approval

19. ADDENDA

None