QUIDEL

Sofia 2 Campylobacter FIA

For use with Sofia 2

For *in vitro* diagnostic use.

℞ ONLY

A symbols glossary can be found at quidel.com/glossary.

INTENDED USE

Sofia 2 Campylobacter FIA employs immunofluorescence for the rapid qualitative detection of a *Campylobacter*-specific antigen in human fecal specimens. Sofia 2 Campylobacter FIA is designed to detect *C. jejuni, C. coli, C. lari* and *C. upsaliensis* from patients with signs and symptoms of gastroenteritis. The test is intended for use with preserved fecal specimens in transport media and unpreserved fecal specimens. Test results should be considered in conjunction with clinical findings and patient history.

SUMMARY AND EXPLANATION

In the United States, *Campylobacter* spp. are now the number one cause of bacterial diarrheal illness, with an increasing incidence of infection per 100,000 population of 19.5 and causing over 1.3 million cases of diarrhea each year.[1,2] Rates in developing countries are much higher, with children under the age of 5 most at risk.[3] Most people with *Campylobacter* infections have only mild illness and recover with no medical intervention. Those with more serious symptoms may seek diagnosis and treatment, typically with oral rehydration therapy or antibiotics.[4] The uncomfortable symptoms of *Campylobacter* gastroenteritis (e.g., diarrhea, nausea, vomiting, fever, abdominal pain) cannot be distinguished from those of other intestinal illnesses. In addition, *Campylobacter* infection carries a risk of more serious complications, such as Guillain-Barre Syndrome, an acute auto-immune paralysis, or reactive arthritis.[5] Complicating this picture, *Campylobacter* spp. are showing increasing resistance to antibiotics commonly used for treatment.[6] This makes accurate diagnosis important for selecting appropriate therapy for *Campylobacter* and avoiding ineffective treatment if another bacterial or viral pathogen is causing the illness.

Bacterial culture has long been the standard method for identification of *Campylobacter* in patient stool specimens. However, culture has drawbacks that result in inaccuracies and time-consuming testing.[7,8] Specimen collection, transport and storage expose these microaerophilic organisms to air, causing random decreases in the viability that is needed for culture. Once plated, *Campylobacter* grow slowly, taking up to 72 hours for reportable negative results. Additionally, the culture plates used by many laboratories contain antibiotics to which *C. jejuni* and *C. coli* are resistant, but which inhibit the growth of other pathogenic species like *C. lari* and *C. upsaliensis* making identification of these less-common species difficult.[9,10]

The Sofia 2 Campylobacter FIA detects four of the most prevalent *Campylobacter* species, *C. jejuni, C. coli, C. lari* and *C. upsaliensis*. Air exposure of collected specimens does not impact test performance. The entire test can be performed in 17 minutes.

PRINCIPLE OF THE TEST

The Sofia 2 Campylobacter FIA employs immunofluorescence technology that is used with Sofia 2 for the rapid qualitative detection of *Campylobacter jejuni, Campylobacter coli, Campylobacter lari,* and *Campylobacter upsaliensis* specific antigens in fecal samples.

The patient's sample is placed in the Specimen Diluent Tube containing the Specimen Diluent, making the antigenic components more accessible to the specific antibodies. An aliquot of the diluted sample is dispensed through a filter to remove particulates, making them more compatible for testing, into the Test Cassette sample well. From the sample well, the sample migrates through a test strip containing various unique chemical environments. If *Campylobacter jejuni, Campylobacter coli, Campylobacter lari,* or *Campylobacter upsaliensis* specific antigens are present, they will be bound by antibodies coupled to fluorescent microparticles that migrate through the test strip. The fluorescent microparticles containing bound proteins will be captured by antibodies at a defined location on the test strip where they are detected by Sofia 2. If *Campylobacter jejuni, Campylobacter coli, Campylobacter lari,* or *Campylobacter upsaliensis* specific antigens are not present, the fluorescent microparticles will not be trapped by the capture antibodies nor detected by Sofia 2.

The Test Cassette is placed inside of Sofia 2 for automatically timed development (WALK AWAY Mode), or pre-incubated on the bench top prior to loading into Sofia 2 (READ NOW Mode), where Sofia 2 will scan, measure, and interpret the immunofluorescent signal using method-specific algorithms. Sofia 2 will display the test results (Positive, Negative, or Invalid) on the screen.

The fluorescence signal obtained with this assay is invisible to the unaided eye. The test results can only be obtained with the proper use of Sofia 2.

REAGENTS AND MATERIALS SUPPLIED

25-Test Kit:

- Individually Packaged Test Cassettes (25)
- 100 µm Top Filters (Green) (Dropper Tips) (25)
- Specimen Diluent Tubes (25) containing 0.05% ProClin®
- Graduated Pipettes (25)
- Positive Control (1) containing 0.05% ProClin
- Negative Control (1) containing 0.05% ProClin
- Package Insert (1)
- Quick Reference Instructions (1)
- QC Card (located on kit box)

MATERIALS NOT SUPPLIED IN KIT

- Timer or watch for use in READ NOW Mode
- Sofia 2
- Calibration Cassette (supplied with Sofia 2)
- Clean, dry container for specimen collection

WARNINGS AND PRECAUTIONS

- For *in vitro* diagnostic use.
- Rx Only
- Do not use the kit contents beyond the expiration date printed on the outside of the box.
- Use appropriate precautions in the collection, handling, storage, and disposal of patient samples and used kit contents.[9]

- Use of Nitrile or Latex (or equivalent) gloves is recommended when handling patient samples.[9]
- Do not reuse any used Test Cassettes, Specimen Diluent Tubes, Dropper Tips, or Pipettes. These items are for single use only.
- The Calibration Cassette must be kept in the provided storage pouch between uses.
- To obtain accurate results, the Package Insert instructions must be followed.
- Inadequate or inappropriate sample collection, storage, and transport may yield false test results.
- Sample collection and handling procedures require specific training and guidance.
- Use the Graduated Pipette, provided with this assay, to collect samples.
- The user should never open the foil pouch of the Test Cassette exposing it to the ambient environment until the Test Cassette is ready for immediate use.
- Discard and do not use any damaged Test Cassette or material.
- Do not pour samples from the Specimen Diluent Tube into the Test Cassette sample well. Use the provided Dropper Tip when adding the sample to the Test Cassette.
- Do not write on the barcode or top of the Test Cassette. This is used by Sofia 2 to identify the type of test being run.
- Do not attempt to scan a Test Cassette more than one time. The barcode on the Test Cassette contains a unique identifier that will prevent Sofia 2 from performing a second read on a previously scanned Test Cassette. An error message will be displayed if a Test Cassette is scanned more than once on the same Sofia 2.
- As the detection reagent is a fluorescent compound, no visible results will form on the test strip. Sofia 2 must be used for result interpretation.
- Testing should be performed in an area with adequate ventilation.
- Dispose of containers and unused contents in accordance with Federal, State and Local requirements.
- Wear suitable protective clothing, gloves, and eye/face protection when handling the contents of this kit.
- Wash hands thoroughly after handling.
- For additional information on hazard symbols, safety, handling and disposal of the components within this kit, please refer to the Safety Data Sheet (SDS) located at quidel.com.

KIT STORAGE AND STABILITY

Store the kit at room temperature, 59°F to 86°F (15°C to 30°C), out of direct sunlight. Kit contents are stable until the expiration date printed on the outer box. Do not freeze.

QUALITY CONTROL

There are three types of Quality Control for Sofia 2 and the Test Cassette: Sofia 2 Calibration Check Procedure, Built-in Procedural Control features, and External Controls.

Sofia 2 Calibration Check Procedure

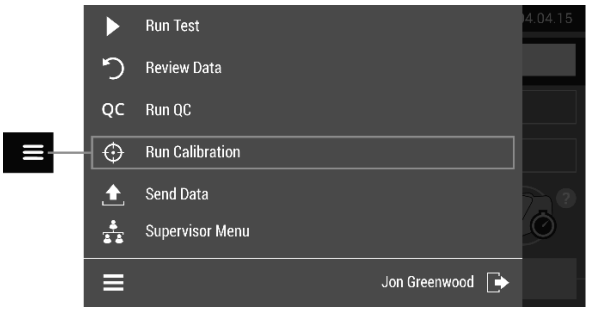
Note: This is a "Calibration Check" procedure.

The Calibration Check Procedure should be performed every 30 days. Sofia 2 will remind the user to complete the Calibration Check Procedure by on-screen notification 1 day prior to expiration.

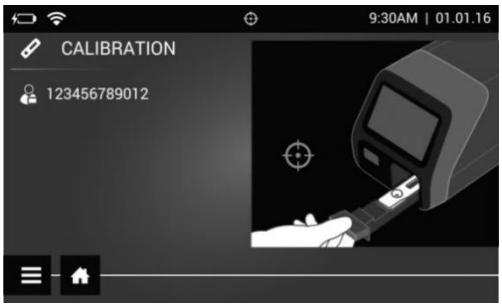
The Calibration Check is a required function that checks Sofia 2 optics and calculation systems using a specific Calibration Cassette. This Calibration Cassette is supplied with Sofia 2. Refer to the Sofia 2 User Manual for details regarding the Calibration Check Procedure.

Important: Ensure that the Calibration Cassette is stored in the provided storage pouch between uses to protect from exposure to light.

1. To check the calibration of Sofia 2, select “Run Calibration” from the Main Menu.



2. Following the prompts, insert the Calibration Cassette into Sofia 2 and close the drawer. Sofia 2 performs the Calibration Check automatically within one minute with no user input required.



Sofia 2 indicates when the Calibration Check is completed, ✓ or ✗. Select ⌂ to return to the Run Test screen.

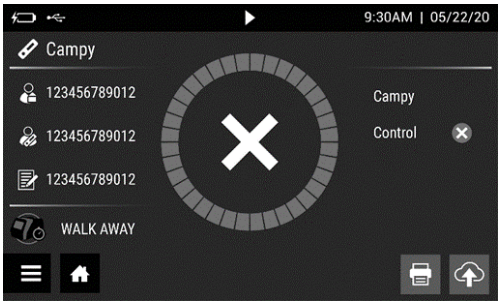
NOTE: If the Calibration Check does not pass, notify the on-site Supervisor or contact Quidel Technical Support for assistance Monday through Friday from 7:00 a.m. to 5:00 p.m. Pacific Time at 800.874.1517 (in the U.S.); 858.552.1100 (outside the U.S.); Fax: 858.455.4960; customerservice@quidel.com (Customer Service); technicalsupport@quidel.com (Technical Support); or contact your local distributor.

Built-in Procedural Controls

The Sofia 2 Campylobacter FIA contains a built-in procedural control feature. Each time a test is run, the procedural control area is scanned by Sofia 2 and the result is displayed on the Sofia 2 screen.

The manufacturer's recommendation for daily control is to document the results of these built-in procedural controls for the first sample tested each day. This documentation is automatically logged in Sofia 2 with each test result.

A ✓ result obtained from the procedural control demonstrates that the test flowed correctly and the functional integrity of the Test Cassette was maintained. **The procedural control is interpreted by Sofia 2 after the Test Cassette has developed for 15 minutes. If the test does not flow correctly, Sofia 2 will indicate that the result is ✗.** Should this occur, review the procedure and repeat the test with a new aliquot of the same sample.



For example: This display shows an invalid result.

External Quality Control

External Controls are used to demonstrate that the reagents and assay procedure are performed properly.

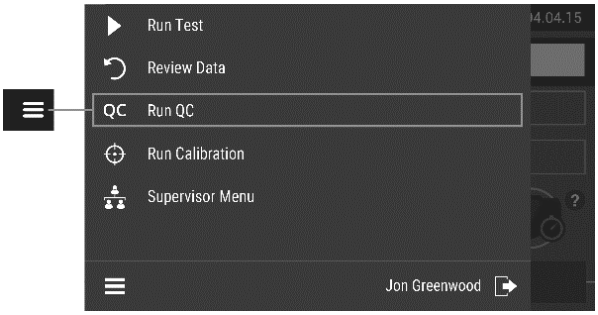
Quidel recommends that Positive and Negative External Controls be run:

- Once for each untrained operator.
- Once for each new shipment of kits – provided that each different lot received in the shipment is tested.
- As deemed additionally necessary by your internal quality control procedures, and in accordance with Local, State and Federal regulations or accreditation requirements.

To test External Controls, follow the instructions below.

External Quality Control Test Procedure

1. From the main menu. Select Run QC



2. Follow the prompts on the screen. Scan the QC Card (located on the kit box).

3. Sofia 2 prompts the user to select the desired mode (WALK AWAY or READ NOW) and then to run the External Controls.

4. Use the following procedure to test each of the control solutions. **The Positive Control must be run first, followed by the Negative Control.**

    a. Prepare a **Positive Control Cassette** by adding **5 drops** of the Positive Control solution (red cap) to the round Test Cassette sample well. Then follow the Sofia 2 screen instructions for developing and analyzing the Positive Control Cassette.

    b. Prepare a **Negative Control Cassette** by adding **5 drops** of the Negative Control solution (blue cap) to the round Test Cassette sample well. Then follow the Sofia 2 screen instructions for developing and analyzing the Negative Control Cassette.

5. After both the Positive and Negative External Controls have been run, the results will be displayed as ✓ or ✗.

If both the Positive and Negative Controls fail ⊗, repeat testing with new Positive and Negative Controls a second time. If only a single Control fails, the user has the option of repeating both the Positive and Negative Controls OR to repeat only the Control that failed. The user may select » on the Sofia 2 display to skip the Control test that previously passed. The QC Results will show a skipped Control test as » on Sofia 2.

Do not perform patient tests or report patient test results if either of the QC test results are ⊗.

SPECIMEN COLLECTION AND HANDLING

Collect fecal specimen in a clean, dry specimen collection container per standard procedures. Neat, unpreserved fecal specimens may be stored refrigerated (2°C to 8°C) or at room temperature (15°C to 30°C) for up to 4 days or frozen (≤ –10°C) for up to 13 days prior to use in the Sofia 2 Campylobacter FIA. Fecal specimens that are frozen may be thawed up to 4 times. Alternatively, specimens may be stored in Thermo Scientific Protocol® Cary Blair or Thermo Scientific Protocol C&S transport media for up to 4 days prior to use when refrigerated (2°C to 8°C) or at room temperature (15°C to 30°C).

TEST PROCEDURE

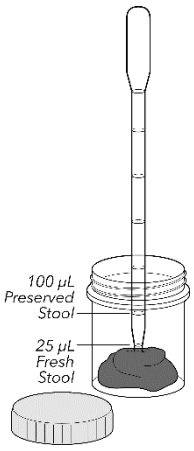
Important:

- DO NOT open the foil pouch containing the Test Cassette until ready to test the sample. Place the Test Cassette on a clean and level surface.
- **All clinical samples and test materials must be at room temperature before beginning the test.**
- **All stool samples must be mixed prior to testing.**
- **Expiration Date:** Check expiration date on each individual test package or outer box before using. Do not use any test past the expiration date on the label.

1. Verify that Sofia 2 is set to the desired mode: **WALK AWAY** or **READ NOW**.
   See the "Using Sofia 2" section for more information.

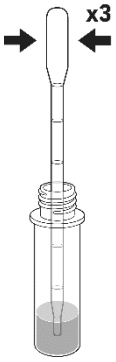
2. Collect 25 µL (1st Graduation) of Specimen using the Graduated Pipette provided in the kit.

   Note: For Specimens in Transport Media (preserved), collect 100 µL (2nd Graduation) using the Graduated Pipette provided in the kit.



3. Transfer the Specimen to the Specimen Diluent Tube and mix the solution by squeezing and releasing the top bulb of the Graduated Pipette 3 times.

   Remove the Graduated Pipette from the Specimen Diluent Tube.



4. Screw the green Dropper Tip to Specimen Diluent Tube and mix well.

5. Remove the small clear cap, hold the Specimen Diluent Tube in a vertical position and dispense **5 drops** into the Test Cassette sample well.

6. Proceed to the "Using Sofia 2" section to complete the test.

USING SOFIA 2

WALK AWAY/READ NOW Modes

Refer to the Sofia 2 User Manual for operating instructions.

Sofia 2 may be set to two different modes (WALK AWAY and READ NOW). The procedures for each mode are described below. The Supervisor has the option to set the Sofia 2 to "Locked Walk Away Mode" which will prevent an operator from selecting any other mode than Walk Away for running a test.

WALK AWAY MODE

In WALK AWAY Mode, the user **immediately** inserts the Test Cassette into Sofia 2. Sofia 2 will automatically time the test development, and the results will be displayed in 15 minutes.

READ NOW MODE

Critically important: Allow the test to develop for the FULL 15 minutes BEFORE placing it into Sofia 2.

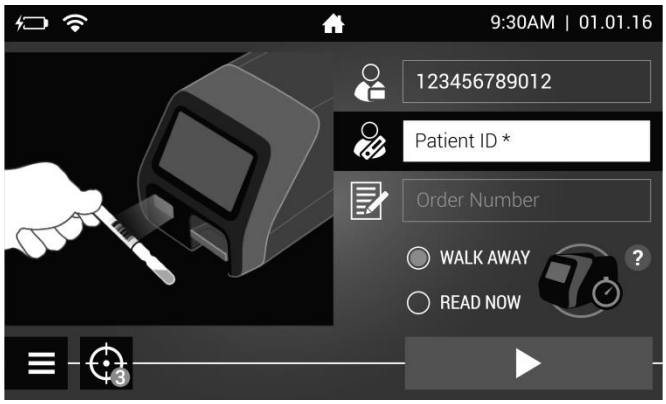
The user must first place the Test Cassette onto the counter or bench top for 15 minutes (outside of Sofia 2) and manually time this development step. Then, the user inserts the Test Cassette into Sofia 2. In READ NOW Mode, Sofia 2 will scan and display the test result within 1 minute. **Warning: Results must not be interpreted past 30 minutes after inoculation. Using the Sofia 2 past this time may result in false results.**

Run Test

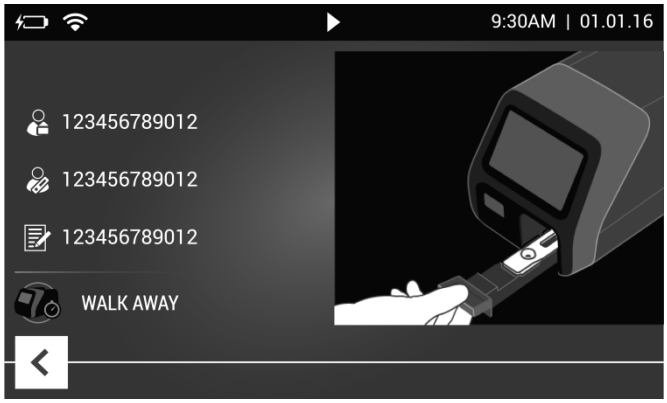
1. Input the User ID using the barcode scanner or manually enter the data using the touchscreen.

   NOTE: *If you mistakenly scan the incorrect barcode, select the field again to re-highlight it. Then simply rescan using the correct barcode, and the previous one will be overwritten with the correct barcode.*

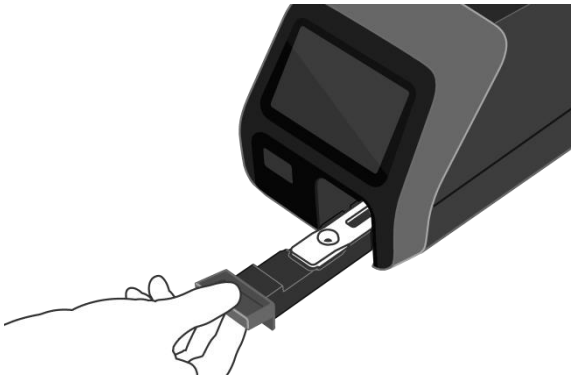
2. Input the Patient ID and Order #, if applicable, using the barcode scanner or manually enter the data using the touchscreen.



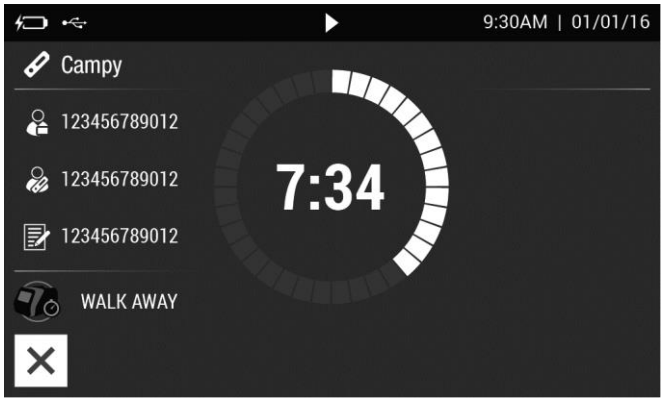
3. Verify that the correct development mode, WALK AWAY or READ NOW, has been selected. Press ▶ and open the Sofia 2 drawer.



4. Insert the prepared patient Test Cassette into the drawer of Sofia 2 and gently close the drawer.



5. Sofia 2 will start automatically and display the progress as shown in the example below. In WALK AWAY Mode, Sofia 2 will automatically time the test development and the result will be displayed in 15 minutes. In READ NOW Mode, the test results will be displayed on the screen within 1 minute. See Interpretation of Results section.



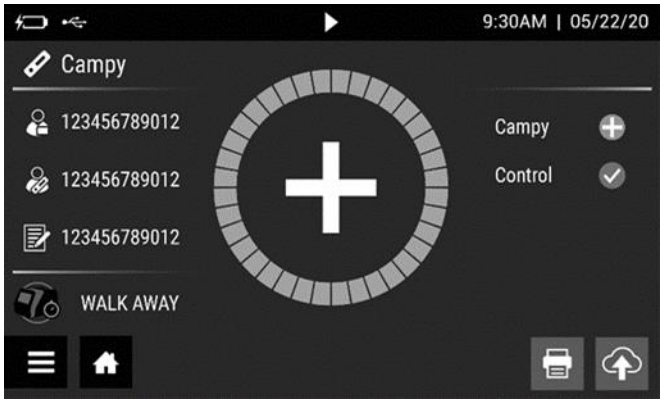
For example: This display shows that the test has 7 minutes, 34 seconds remaining.

INTERPRETATION OF RESULTS

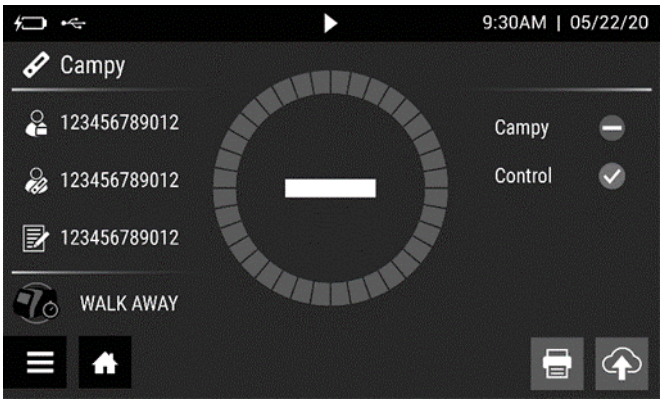
When the test is complete, the results will be displayed on the Sofia 2 screen. Test Lines, which are fluorescent, cannot be seen with the naked eye.

The Sofia 2 screen will display results for the procedural control as being ✓ or ✗, and will provide a ⊕ or ⊖ result for *Campylobacter* specific antigen. If the procedural control is ✗, a repeat test should be performed with a new aliquot of the same sample.

Valid Results:

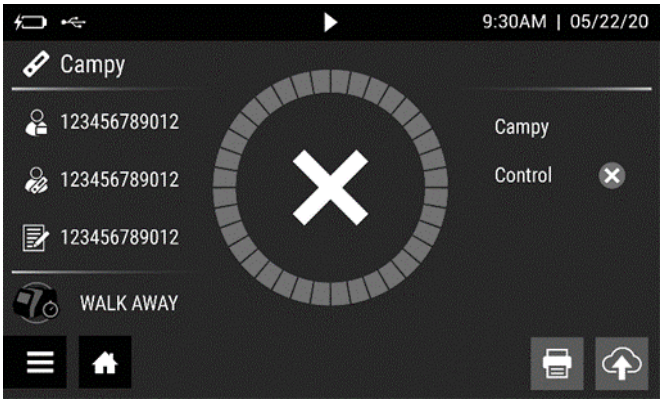


This display shows a valid positive result for Campylobacter specific antigen.



This display shows a valid negative result for Campylobacter specific antigen.

Invalid Result:



This result shows an invalid result.

Invalid Result: If the test is invalid, a repeat test should be performed with a new aliquot of the same sample.

LIMITATIONS

- The Sofia 2 Campylobacter FIA is for the qualitative detection of *Campylobacter*-specific antigens from fecal specimens.
- The Sofia 2 Campylobacter FIA detects both viable and nonviable *Campylobacter* bacteria and may yield a positive result in the absence of living organisms.
- A negative test result does not definitively rule-out the presence of *Campylobacter* species in suspected patients. Levels of organism may be present in feces beneath the limit of detection for the Sofia 2 Campylobacter FIA, and therefore, if *Campylobacter* is suspected, alternative testing should be conducted.
- A negative result may occur if the sample was collected, transported, or stored improperly.
- Failure to follow the Test Procedure may adversely affect test performance and/or invalidate the test result.

- Test results must be evaluated in conjunction with other clinical data available to the physician.
- Negative test results do not rule-out other possible infections.
- Positive test results do not rule-out co-infections with other pathogens.
- The Sofia 2 Campylobacter FIA was evaluated using only fresh fecal samples and fecal samples stored in Cary Blair media or C&S media. The performance of fecal samples stored in other transport media (e.g., formalin, polyvinyl alcohol) has not been evaluated and therefore, should not be used.
- No data exists on the effects of colonic washes, barium enemas, laxatives, or bowel preparations on the performance of the Sofia 2 Campylobacter FIA. All of these procedures can result in extensive dilution or the presence of additives that may affect test performance.
- Transferring too little specimen, or failure to mix and completely suspend the specimen in the specimen diluent, may result in a false-negative test result.
- The performance of this test has not been evaluated for use in patients without signs and symptoms of gastroenteritis.
- *Campylobacter helveticus* at levels greater than 1.98 x 10^5 CFU/mL may cross-react or interfere with the performance of the test.

EXPECTED VALUES

In the United States, >1% of the population acquires *Campylobacter* spp. infection each year. Rates in developing countries are much higher, with children under the age of 5 most at risk.[3] Age-specific rates of *Campylobacter jejuni* isolation in patients with diarrhea differ among countries. In industrialized countries, *C. jejuni* is isolated from 5%–16% of children with diarrhea, with a prevalence of infection in healthy children of 0%–1.5%.[2]

PERFORMANCE CHARACTERISTICS

The following studies were performed with Sofia 2 Campylobacter FIA and Sofia 2.

Limit of Detection

The limit of detection (LoD) for Sofia 2 Campylobacter FIA was determined for four *Campylobacter* species in fecal matrix and in Cary Blair and C&S transport media. The LoD ranged from 9.82 x 10^4 to 5.21 x 10^6 colony forming units (cfu)/mL in fecal matrix, 1.57 x 10^5 to 5.21 x 10^6 cfu/mL in Cary Blair medium, and 1.50 x 10^5 to 2.71 x 10^6 cfu/mL in C&S medium (Table 1).

Table 1
Limits of Detection

Campylobacter Species	Minimum Detectable Limit*		
	Fecal Matrix	Cary Blair	C&S
	cfu/mL	cfu/mL	cfu/mL
C. jejuni	9.82 x 10^4	1.57 x 10^5	1.50 x 10^5
C. coli	1.15 x 10^6	1.59 x 10^6	9.02 x 10^5
C. lari	2.00 x 10^6	1.75 x 10^6	2.25 x 10^6
C. upsaliensis	5.21 x 10^6	5.21 x 10^6	2.71 x 10^6

cfu/mL = colony forming units per milliliter

*The levels of bacteria were determined by limiting dilution, bacterial culture, and colony counting to give cfu/mL.

Analytical Reactivity

Analytical reactivity for Sofia 2 Campylobacter FIA was demonstrated using 17 additional strains of *Campylobacter* tested at approximately 2.95 x 10^5 to 1.44 x 10^7 colony forming units (cfu)/mL (Table 2).

Table 2
Analytical Reactivity

***Campylobacter* species**	**Strain**	**Level Detected***
Campylobacter jejuni	CCUG 6951	2.95 x 10^5 cfu/mL
	CCUG 12081	2.95 x 10^5 cfu/mL
	CCUG 29411	2.95 x 10^5 cfu/mL
	CCUG 38106	2.95 x 10^5 cfu/mL
Campylobacter jejuni subspecies *doylei*	CCUG 24567	2.95 x 10^5 cfu/mL
Campylobacter coli	CCUG 10956	3.45 x 10^6 cfu/mL
	CCUG 17755	3.45 x 10^6 cfu/mL
	CCUG 36994	3.45 x 10^6 cfu/mL
	CCUG 53138	3.45 x 10^6 cfu/mL
Campylobacter lari	2015/2189	6.00 x 10^6 cfu/mL
	2015/1657	6.00 x 10^6 cfu/mL
	2015/2983	6.00 x 10^6 cfu/mL
	2016/1130H	6.00 x 10^6 cfu/mL
Campylobacter upsaliensis	2016/1950	1.44 x 10^7 cfu/mL
	2016/2826	1.44 x 10^7 cfu/mL
	2017/0349	1.44 x 10^7 cfu/mL
	2018/1669	1.44 x 10^7 cfu/mL

cfu/mL = colony forming units per milliliter

*The levels of bacteria were determined by limiting dilution, bacterial culture, and colony counting to give cfu/mL.

Analytical Specificity

The cross reactivity of the Sofia 2 Campylobacter FIA was evaluated with a total of 48 bacterial and fungal microorganisms and 24 viral isolates. None of the bacteria, fungi, or viruses below in Table 3 showed cross reactivity in the assay at the concentrations listed. For microbial interference testing, the same microorganisms and viruses in Table 3 were pre-mixed with *C. jejuni* at 2-3x LoD and tested in the assay. None showed any signs of microbial interference in the assay.

Table 3
Cross Reactivity / Microbial Interference Testing

Organism/Virus	**Test Concentration***
Bacteria/Fungus	
Acinetobacter baumannii	≥10^7 cells/mL
Aeromonas hydrophila	≥10^7 cells/mL
Bacillus cereus	≥10^7 cells/mL
Bacillus subtilis	≥10^7 cells/mL
Bacteroides fragilis	≥10^7 cells/mL
Campylobacter concisus	≥10^7 cells/mL
Campylobacter fetus	7.8 x 10^6 CFU/mL
Campylobacter helveticus	1.98 x 10^5 CFU/mL **
Campylobacter hyointestinalis	8.9 x 10^7 CFU/mL
Candida albicans	≥10^7 cells/mL
Citrobacter freundii	≥10^7 cells/mL
Clostridium bifermentans	≥10^7 cells/mL
Clostridiodes difficile	≥10^7 cells/mL
Clostridium perfringens	≥10^7 cells/mL

Organism/Virus	Test Concentration*
Edwardsiella tarda	≥10^7 cells/mL
Enterobacter cloacae	≥10^7 cells/mL
Enterococcus faecalis	≥10^7 cells/mL
Escherichia coli	≥10^7 cells/mL
Escherichia coli EIEC	≥10^7 cells/mL
Escherichia coli EPEC	≥10^7 cells/mL
Escherichia coli ETEC	≥10^7 cells/mL
Escherichia coli O157:H7 (non-toxigenic)	≥10^7 cells/mL
Escherichia coli O157:H7 (toxigenic)	≥10^7 cells/mL
Escherichia fergusonii	≥10^7 cells/mL
Escherichia hermannii	≥10^7 cells/mL
Helicobacter pylori	≥10^7 cells/mL
Klebsiella pneumoniae	≥10^7 cells/mL
Lactobacillus acidophilus	≥10^7 cells/mL
Lactococcus lactis	≥10^7 cells/mL
Listeria monocytogenes	≥10^7 cells/mL
Peptostreptococcus anaerobius	≥10^7 cells/mL
Plesiomonas shigelloides	≥10^7 cells/mL
Porphyromonas asaccharolytica	≥10^7 cells/mL
Prevotella melaninogenica	≥10^7 cells/mL
Proteus vulgaris	≥10^7 cells/mL
Pseudomonas aeruginosa	≥10^7 cells/mL
Pseudomonas fluorescens	≥10^7 cells/mL
Salmonella enterica typhimurium	≥10^7 cells/mL
Serratia marcescens	≥10^7 cells/mL
Shigella dysenteriae	≥10^7 cells/mL
Shigella flexneri	≥10^7 cells/mL
Shigella sonnei	≥10^7 cells/mL
Staphylococcus aureus	≥10^7 cells/mL
Staphylococcus aureus subsp. *aureus* Rosenbach *[formerly Cowan's]*	≥10^7 cells/mL
Staphylococcus epidermidis	≥10^7 cells/mL
Streptococcus agalactiae	≥10^7 cells/mL
Vibrio parahaemolyticus	≥10^7 cells/mL
Yersinia enterocolitica	≥10^7 cells/mL
Viruses	
Adenovirus Type 1	2.2 x 10^6 $TCID_{50}$/mL
Adenovirus Type 2	5.0 x $10^{5.5}$ $TCID_{50}$/mL
Adenovirus Type 3	5.0 x $10^{6.5}$ $TCID_{50}$/mL
Adenovirus Type 5	1.6 x $10^{8.0}$ $TCID_{50}$/mL
Human mastadenovirus F [formerly Adenovirus Type 40]	1.6 x $10^{4.0}$ $TCID_{50}$/mL
Adenovirus Type 41	1.6 x $10^{7.00}$ $TCID_{50}$/mL
Coxsackie virus B2	5.0 x $10^{6.75}$ $TCID_{50}$/mL
Coxsackie virus B3	2.8 x $10^{5.00}$ $TCID_{50}$/mL
Coxsackie virus B4	1.6 x $10^{6.0}$ $TCID_{50}$/mL
Coxsackie virus B5	5.0 x $10^{7.0}$ $TCID_{50}$/mL
Echovirus 9	1.6 x $10^{7.00}$ $TCID_{50}$/mL
Echovirus 11	5.0 x $10^{5.25}$ $TCID_{50}$/mL

Organism/Virus	Test Concentration*
Echovirus 18 (ATCC® VR-1783)	$5 \times 10^{4.67}$ $TCID_{50}$/mL
Echovirus 18 (NCPV 0801131v)	$5.62 \times 10^{3.0}$ $TCID_{50}$/mL
Human parechovirus 1 [formerly Echovirus 22]	$5.0 \times 10^{4.75}$ $TCID_{50}$/mL
Echovirus 33	$10^{4.00}$ $TCID_{50}$/mL
Enterovirus 68	$2.3 \times 10^{5.00}$ $TCID_{50}$/mL
Enterovirus 69	$10^{6.0}$ $TCID_{50}$/mL
Enterovirus 70	$5.0 \times 10^{5.00}$ $TCID_{50}$/mL
Enterovirus 71	$8.9 \times 10^{5.00}$ $TCID_{50}$/mL
Human coronavirus	$8.9 \times 10^{5.00}$ $TCID_{50}$/mL
Human Rotavirus	$5.0 \times 10^{0.75}$ $TCID_{50}$/mL
Norovirus GI	***
Norovirus GII	***

cfu/mL = colony forming units per milliliter; $TCID_{50}$/mL = 50% tissue culture infectious dose per milliliter

*The levels of bacteria were either determined by limiting dilution, bacterial culture, and colony counting to give cfu/mL or were estimated using McFarland standards to give cells/mL.

***Campylobacter helveticus* tested positive in the Sofia 2 Campylobacter FIA assay at levels >1.98×10^5 CFU/mL.

*** Clinically positive Norovirus fecal specimens (genogroup I and II, determined by real-time reverse-transcriptase PCR) obtained from a clinical repository were used.

Interfering Substances

Several prescription and over-the-counter (OTC) products and endogenous substances were evaluated with the Sofia 2 Campylobacter FIA. Each substance was tested in the presence and absence of *C. jejuni* at 2-3x LoD. None of the substances listed in Table 4 interfered with the assay at the levels tested.

Table 4

Non-Interfering Substances

Substance	Concentration
Barium sulfate	5% w/v
Benzalkonium Chloride	1% w/v
Ciprofloxacin	0.25% w/v
Ethanol	1% w/v
Hog gastric mucin	3.5% w/v
Human blood	40% v/v
Hydrocortisone	1% w/v
Imodium®	5% v/v
Kaopectate®	5% v/v
Leukocytes	0.05% w/v
Maalox® Advanced	5% v/v
Mesalazine	10% w/v
Metronidazole	0.25% w/v
Mineral Oil	10% w/v
Mylanta®	4.2 mg/mL
Naproxen Sodium	0.05% w/v
Nonoxynol-9	1% w/v
Nystatin	1% w/v
Palmitic Acid/Fecal Fat	40% w/v
Pepto-Bismol®	5% v/v
Phenylephrine	1% w/v
MiraLax®	10% w/v
Prilosec OTC®	5 µg/mL

Substance	Concentration
Sennosides	1% w/v
Simethicone	10% w/v
Stearic Acid/Fecal Fat	40% w/v
TUMS®	50 µg/mL
Human Urine	5% v/v
Vancomycin	0.25% w/v

Hook Effect / High Analyte Concentration Testing

To ensure that a high concentration of Campylobacter antigen does not interfere with a positive reaction in the Sofia 2 Campylobacter FIA, high positive samples were prepared by spiking a negative fecal pool at a concentration possibly observed in clinical specimens. A total of 5 different dilutions of *C. jejuni, C. coli, C. lari,* and *C. upsaliensis* whole organism culture preparation, up to and including the clinically observed high concentration, were prepared and tested in triplicate. The results demonstrated that high analyte concentrations up to 5.0 x 10^7 for *C. jejuni* (CCUG 11284), up to 2.4 x 10^8 for *C. coli* (CCUG strain 11283), up to 1.6 x 10^8 for *C. lari* (strain 2015/1582), and up to 1.3 x 10^8 *C. upsaliensis* (strain 2018/0319H) did not affect the detection of the antigen.

Reproducibility

The reproducibility of the Sofia 2 Campylobacter FIA was evaluated at 3 different laboratories, one of which was internal, using two product lots. Two different operators at each site tested a series of coded, contrived samples, prepared in negative clinical matrix, ranging from negative (no bacteria) to moderate positive (2-3 x LOD) levels of *C. jejuni*. Testing was conducted over 5 consecutive days. The inter-laboratory agreement (Table 5) for negative samples was 100% and 100% for positive samples.

Table 5
Reproducibility Study Inter- Laboratory Agreement

Site	Negative* (C_0)		High Negative* (0.5-1X C_5)		Low Positive** (1-2X C_{95})		Moderate Positive** (2-3X C_{95})	
	Lot 1	Lot 2	Lot 1	Lot 2	Lot 1	Lot 2	Lot 1	Lot 2
1	30/30	30/30	30/30	30/30	30/30	30/30	30/30	30/30
2	30/30	30/30	30/30	30/30	30/30	30/30	30/30	30/30
3	30/30	30/30	30/30	30/30	30/30	30/30	30/30	30/30
Total	**180/180**		**180/180**		**180/180**		**180/180**	
% Overall Agreement (95% CI)	**100% (97.9% to 100%)**		**100% (97.9% to 100%)**		**100% (97.9% to 100%)**		**100% (97.9% to 100%)**	

*Bacteria not detected/total; **Bacteria detected/total

Clinical Performance

Prospective Clinical Study

The performance of the Sofia 2 Campylobacter FIA was compared to culture and identification in a multi-center prospective clinical study. One hundred ninety-one (191) fresh, neat specimens and six hundred twenty (620) fresh specimens in transport media were evaluated. Sixty-two percent (62%) of the subjects were female and thirty-eight percent (38%) were male. Subjects ranged in age between 2 years to over 60 years. The results of the prospective clinical study are shown in Table 6. The eight (8) consensus positive specimens (Sofia Positive/ Culture Positive) were identified as *Campylobacter jejuni* by species-specific RT-PCR and bi-directional sequence analysis. Of the six (6) discordant specimens (Sofia Positive / Culture Negative), three specimens were identified as positive for *C. jejuni*, two were *C. upsaliensis*, and one was *C. coli* by species-specific RT-PCR and bi-directional sequence analysis.

Table 6
Sofia 2 Campylobacter FIA Performance Compared to Culture with Fresh Specimens

	Culture		
	Pos	Neg	Total
Sofia Pos	8	6*	14
Sofia Neg	0	797	797
Total:	8	803	811

Sensitivity = 100% (8/8)
(95% CI=67.6% to 100%)

Specificity = 99.3% (797/803)
(95% CI=98.4% to 99.7%)

* Of the 6 culture negative – Sofia 2 Campylobacter FIA positive samples, all 6 were confirmed as positive by species-specific RT-PCR and bi-directional sequence analysis.

Archived Clinical Study

Seventy (70) frozen, characterized specimens were tested by the Sofia 2 Campylobacter FIA at a central laboratory including 35 culture-negative specimens preserved in transport media. Of the 35 positive specimens, there were a total of 11 specimens in transport media and 24 neat fecal specimens. The positive specimens were *Campylobacter* spp. culture-positive and were further characterized by species-specific RT-PCR and bi-directional sequencing to assess if weak positives were included in the archived study and determine performance of the Sofia 2 Campylobacter FIA with such specimens. All 35 specimens tested positive for Campylobacter spp. by all methods, yielding 100% correlation with all test methods. Thirty specimens were identified as positive for *C. jejuni* and five were *C. coli*. Additionally, all 35 negative specimens yielded 100% correlation with all test methods.

Rare Isolates Testing

A study was conducted to evaluate the performance of the Sofia 2 Campylobacter FIA with less common analytes not represented during the clinical studies. Five (5) strains of each species of *C. coli, C. lari,* and *C. upsaliensis* were prepared at concentrations of 1-2 times the limit of detection of the corresponding reference strains in neat fecal matrix, fecal matrix in Cary Blair transport medium, and fecal matrix in C&S transport medium and tested in the assay over a period of three days. Each strain was detected by the assay with >90% positivity (Table 7). Additionally, a negative sample was prepared in each matrix and tested in parallel, and the expected negative results were obtained each day.

Table 7
Sofia 2 Campylobacter FIA Performance With Rare Isolates

Sample	Concentration Tested (CFU/mL)	n	Number of Negatives and Positives						% Positivity			
			Day 1		Day 2		Day 3		Day 1	Day 2	Day 3	Total
			# Neg	# Pos	# Neg	# Pos	# Neg	# Pos				
Fecal Matrix												
Negative	N/A	30	30	0	30	0	30	0	0	0	0	0
C. coli	2.30 x 10^6	30	0	30	0	30	0	30	100	100	100	100
C. lari	4.00 x 10^6	30	0	30	0	30	0	30	100	100	100	100
C. upsaliensis	9.58 x 10^6	30	0	30	0	30	0	30	100	100	100	100
Cary Blair												
Negative	N/A	30	30	0	30	0	30	0	0	0	0	0
C. coli	3.06 x 10^6	30	0	30	0	30	0	30	100	100	100	100

Sample	Concentration Tested (CFU/mL)	n	Number of Negatives and Positives						% Positivity			
			Day 1		Day 2		Day 3		Day 1	Day 2	Day 3	Total
			# Neg	# Pos	# Neg	# Pos	# Neg	# Pos				
C. lari	3.50 x 10^6	30	1	29	0	30	0	30	97	100	100	99
C. upsaliensis	5.20 x 10^6	30	0	30	0	30	0	30	100	100	100	100
C&S												
Negative	N/A	30	30	0	30	0	30	0	0	0	0	0
C. coli	1.80 x 10^6	30	0	30	0	30	0	30	100	100	100	100
C. lari	2.50 X 10^6	30	0	30	0	30	0	30	100	100	100	100
C. upsaliensis	4.66 x 10^6	30	0	30	0	30	0	30	100	100	100	100

ASSISTANCE

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Positive control	Negative control