510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K260213

B Applicant

BD Diagnostic Systems

C Proprietary and Established Names

BD BACTEC FXI Culture System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MDB	Class I	21 CFR 866.2560, Microbial Growth Monitor	83, Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantially equivalent determination for a premarket notification for the BD BACTEC FXI Culture System for use with BD BACTEC Plus Aerobic/F Culture Vials, BD BACTEC Lytic/10 Anaerobic/F Culture Vials, and BD BACTEC Plus Anaerobic/F Culture Vials inoculated with human blood.

B Measurand:

Growth of aerobic, anaerobic and facultative microorganisms in BACTEC Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F Culture Vials from blood.

C Type of Test:

BACTEC FXI Culture System is a continuous monitoring blood culture system to be used in conjunction with BACTEC Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F Culture Vials. These blood culture vials contain liquid culture media for recovery of microorganisms from blood. The BACTEC FXI Culture System measures reflected light from colorimetric

sensors embedded in each vial to monitor the presence and production of carbon dioxide generated by the growing organism.

III Intended Use/Indications for Use:

A Intended Use(s):

The automated BD BACTEC FXI Culture System is designed for the qualitative detection of bacteria and fungi in blood. Samples are collected from patients and injected directly into BD BACTEC Culture Vials, which are placed into the instrument for incubation and testing.

B Indication(s) for Use:

Same as the intended use

C Special Conditions for Use Statement(s):

Prescription Use Only

BACTEC FXI Culture System is indicated for use only with BD BACTEC Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F Culture Vials.

D Special Instrument Requirements:

Not Applicable

IV Device/System Characteristics:

A Device Description:

The BD BACTEC FXI Culture System is an update to the originally cleared BD BACTEC 9050 blood culture fluorescent instruments and the later version named BACTEC FX. The BACTEC FXI Culture System automates the instrument's workflow while retaining the same fluorescence detection technology as the BD BACTEC fluorescent series instruments. The BACTEC FXI is intended for use by trained laboratory personnel.

The device consists of two modules: the Workflow Module and the Analyzer Module. The Workflow Module is responsible for the automated loading of BD BACTEC culture vials into the Analyzer Module. The Analyzer Module is responsible for incubation and agitation of the culture vials, acquiring vial measurement readings on a regular interval via a fly-by measurement system, and allows for the manual loading and unloading of culture vials. The BACTEC FXI may consist of either one (total capacity of 480 vials) or two (total capacity of 960 vials) Analyzer Modules connected to a single Workflow Module.

B Principle of Operation:

When microorganisms are present in blood culture vials during incubation in the BD BACTEC FXI Culture System, they metabolize nutrients in the culture medium, releasing carbon dioxide (CO_2). A dye in the sensor at the bottom of the BD BACTEC culture vial reacts with CO_2. This modulates the amount of light that is absorbed by fluorescent material in the sensor. A photo

detector within the BD BACTEC FXI Culture System measures the level of fluorescence from each vial, which corresponds to the amount of CO_2 released by organisms. Vial measurements are acquired at two separate excitation wavelengths at regular intervals and continuously assessed by the BD BACTEC FXI Culture System. Multiple algorithms are used to test for vial positivity. Some algorithms are media specific for greater sensitivity. If a culture vial has not triggered a positivity algorithm by the end of the defined protocol length and there are no instrument error conditions that would prevent accurate detection of positives, the vial is declared a negative vial. However, the positivity algorithms continue to run until the vial is removed from the instrument. After the results, positive and negative vials are processed per laboratory protocol.

C Instrument Description Information:

1. Instrument Name:

   BD BACTEC FXI Culture System

2. Specimen Identification:

   Specimen identification is performed using barcode labels on the BD BACTEC culture vials (both testing site and vial-specific barcodes) or vial and patient identification information can be entered manually.

3. Specimen Sampling and Handling:

   The FXI Culture System provides automated loading and unloading of culture vials.

   A maximum of 30 culture vials can be loaded at any time into each shelf, allowing for up to 60 culture vials to be placed at one time. Vials can be loaded individually or by loading culture vials into racks. Once loaded, they are recognized by the Workflow Module and robotic loading is initiated. Each vial is scanned and imaged for barcode information, weighed for an individual blood volume measurement, and robotically loaded into the Analyzer Module.

   Upon user request or if configured for automatic removal, the Workflow Module removes positive vials from the Analyzer Module. Any vials that are determined to be negative are automatically moved to the waste container at the bottom of the Workflow Module; users can change this default setting to not automatically output to waste. Users can also access the drums to manually load or unload vials if needed. Positive vials are processed according to laboratory workflow.

4. Calibration:

   Calibration of the BACTEC FXI Culture System Workflow and Analyzer Modules are performed at the time of manufacture. The end user does not conduct calibration during use of the device.

   In summary, the load cell contained within the BACTEC FXI Culture System Workflow Module, which is used in the blood volume measurement process, has a zero-offset calculated and a sensitivity set at the time of instrument manufacture. Both the offset and sensitivity are determined using a vial that is designed to mimic a BACTEC culture vial with

a known weight. The load cell accuracy is verified using this vial by BD service at the required preventative maintenance interval.

Calibration of the BACTEC FXI Culture System Analyzer Module is performed using standard vials that mimic the form of the BACTEC culture vials. These standard vials are formulated to have consistent fluorescence. Calibration is defined here as adjusting LED brightness to ensure consistent response to standard vial fluorescence. To calibrate the LED brightness, the Analyzer Module is brought to incubation temperature and multiple fluorescence measurements from the standard vial in each row are collected. The measurement data is used to adjust the current applied to the LED for each row of vial stations such that the fluorescence of the standard vial for that row is a specific value. These current settings for the vial stations are stored in the instrument.

5. Quality Control:

   See Section VII.A.5.(a) below.

V Substantial Equivalence Information:

A Predicate Device Name(s):

BD BACTEC 9050 System

B Predicate 510(k) Number(s):

K962210

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device: K260213 BD BACTEC FXI System	Predicate: K962210 BD BACTEC 9050 System
Device Trade Name	BD BACTEC FXI Culture System	BACTEC 9050 SYSTEM
General Device Characteristic Similarities		
Intended Use/Indications for Use	The automated BD BACTEC FXI Culture System is designed for the qualitative detection of bacteria and fungi in blood. Samples are collected from patients and injected directly into BD BACTEC culture vials, which are placed into the instrument for incubation and testing.	The BACTEC 9050 system is a non-radiometric automated blood culturing system which is designed for the monitoring and detection of clinical cultures of blood for the presence of microorganisms.
Detection Technology	A dye in the sensor at the bottom of the vial reacts with CO_2. This modulates the	Same

Device & Predicate Device(s):	Device: K260213 BD BACTEC FXI System	Predicate: K962210 BD BACTEC 9050 System
	amount of light that is absorbed by fluorescent material in the sensor. A photo detector in a fly-by measurement system at each layer of the drum measures the level of fluorescence.	
Data Analysis	Utilizes embedded software	Same
Incubation Temperature	35.0 to 36.5°C	Same
General Device Characteristic Differences		
Specimen Types	Blood only	Blood/ Blood Products/ Sterile Body Fluids (BD BACTEC Myco/F Lytic only)
Vial Types	BD BACTEC Plus Aerobic/F BD BACTEC Lytic /10 Anaerobic/F BD BACTEC Plus Anaerobic/F	BD BACTEC Plus Aerobic/F BD BACTEC Lytic/10 Anaerobic/F BD BACTEC Plus Anaerobic/F BD BACTEC Peds Plus BD BACTEC Standard/10 Aerobic/F BD BACTEC Standard Anaerobic/F BD BACTEC Myco/F Lytic
Photo Detector	Dual excitation channels	Single excitation channel
Agitation/Incubation Assembly	Rack assembly	Drum assembly
Algorithms	Minor changes to the existing algorithms to adjust for instrument changes as well as two additional new algorithms.	Multiple algorithms are used to test for vial positivity, including some media specific algorithms for greater sensitivity.
Capacity	480/960 vials	50 vials
Vial Loading	User places vials individually or in batches on the input/output (I/O) shelves on the Workflow Module. Vials are then automatically scanned, imaged, weighed and placed into the Analyzer	User scans vials one at a time and manually loads into the designated space in the drum.

Device & Predicate Device(s):	Device: K260213 BD BACTEC FXI System	Predicate: K962210 BD BACTEC 9050 System
	Module using robotics. Manual loading of vials is also available to users.	
Vial Unloading	Vials can be unloaded automatically based upon configuration, by user request, or manually. The instrument will output the vials to either the I/O shelves or chutes.	Positive and negative vials are manually scanned and unloaded.

VI Standards/Guidance Documents Referenced:

- CLSI M47-Ed2. Principles and procedures for blood cultures
- IEC 61010-1 Ed3.1 Safety requirements for electrical equipment for measurement, control, and laboratory use - Part 1: General requirements
- IEC 61326-1 Edition 3.0 Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 1: General requirements
- IEC 61326-2-6 Edition 4.0 Electrical equipment for measurement, control and laboratory use - EMC requirements - Part 2-6: Particular requirements - In vitro diagnostic (IVD) medical equipment
- IEC 62304 Edition 1.1 Medical device software - Software life cycle processes

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

After clearance of the BD BACTEC 9050 System (predicate device), the sponsor updated the device and named it as the BACTEC FX Culture System with appropriate labeling changes but no changes in scientific principle. The BACTEC FX System is a currently marketed device and thus is used as a comparator device in analytical and clinical performance studies.

1. Precision/Reproducibility:

(a) Reproducibility Study

The reproducibility of the FXI System was evaluated using six representative organisms of the most common pathogens associated with blood stream infections for Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F culture vials. The study was performed at three sites (1 internal and 2 external). For the Plus Anaerobic/F culture vial, the study was performed at one internal site only based upon the results from an acceptable media equivalency study. At the internal site, three separate operators using three separate instruments performed the testing. Please see VII. B. 2 for details. Three operators (at least one per site) performed four runs per day with four lots of culture vials over five days of testing for a total of 360 vials tested per vial type for a total of 1080 seeded vials.

Additionally, 180 negative control vials containing only blood were evaluated. For calculation of percent recovery, positive results reflect a positive flag by the instrument. One positive vial from each unique inoculum preparation (one culture vial type per organism inoculum) per testing day was subcultured to confirm purity and the presence of the appropriate organism. Vials flagged negative at the end of the 5-day protocol were subcultured to assess false negative rates.

The organisms evaluated and concentrations used for vial inoculation are shown in **Table 1**.

Table 1. Reproducibility Study Organisms

Microorganism	Inoculum Concentration	Vial Type		
		Plus Aerobic/F	Plus Anaerobic/F	Lytic/10 Anaerobic/F
Bacteroides fragilis	10 - 100 CFU/vial		X	X
Candida albicans		X		
Clostridium perfringens			X	X
Enterococcus faecalis			X	X
Escherichia coli		X	X	X
Haemophilus influenzae		X		
Pseudomonas aeruginosa		X		
Staphylococcus aureus		X	X	X
Streptococcus pneumoniae		X	X	X

The reproducibility study demonstrated that the FXI instrument generated 100% positive results for all seeded Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F culture vials evaluated. In addition, 100% of negative control vials were reported as negative by the instrument. Study results are shown in **Tables 2-4** for Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F culture vials, respectively.

Table 2. Reproducibility Study Results (Plus Aerobic/F)

Organism	% Recovery (# detected/# tested), [95% CI]				Time to Detection (hours)	
	Site 1	Site 2	Site 3	Overall	Mean	Range
Candida albicans	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	25.1	8.5 - 28.8
Escherichia coli	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	8.9	8.0 – 10.0
Haemophilus influenzae	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	16.4	13.7 – 19.2
Pseudomonas aeruginosa	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	14.7	13.2 – 17.1

Organism	% Recovery (# detected/# tested), [95% CI]				Time to Detection (hours)	
	Site 1	Site 2	Site 3	Overall	Mean	Range
Staphylococcus aureus	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	10.2	9.2 – 11.4
Streptococcus pneumoniae	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	13.0	11.4 – 14.9
Negative Controls	0% (0/20)	0% (0/20)	0% (0/20)	0% (0/60)	N/A	N/A

Table 3. Reproducibility Study Results (Lytic/10 Anaerobic/F)

Organism	% Recovery (# detected/# tested), [95% CI]				Time to Detection (hours)	
	Site 1	Site 2	Site 3	Overall	Mean	Range
Bacteroides fragilis	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	20.5	9.0 – 42.6
Clostridium perfringens	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	8.0	7.0 – 12.0
Enterococcus faecalis	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	9.9	9.2 – 10.5
Escherichia coli	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	8.9	8.0 – 9.9
Staphylococcus aureus	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	10.8	9.7 – 11.9
Streptococcus pneumoniae	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	15.3	6.0 – 37.1
Negative Controls	0% (0/20)	0% (0/20)	0% (0/20)	0% (0/60)	N/A	N/A

Table 4. Reproducibility Study Results (Plus Anaerobic/F)

Organism	% Recovery (# detected/# tested), [95% CI]				Time to Detection (hours)	
	Site 1			Overall	Mean	Range
	Instrument 1	Instrument 2	Instrument 3			
Bacteroides fragilis	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	23.0	19.3 – 81.2
Clostridium perfringens	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	9.2	8.2 – 10.6
Enterococcus faecalis	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	10.2	9.2 – 10.9
Escherichia coli	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	9.4	8.9 – 10.7
Staphylococcus aureus	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	10.9	9.6 – 13.6
Streptococcus pneumoniae	100.0% (20/20)	100.0% (20/20)	100.0% (20/20)	100.0% (60/60) [94.0%, 100.0%]	13.5	12.2 – 15.4
Negative Controls	0% (0/60)			0% (0/60)	N/A	N/A

(b) Within-Laboratory Precision Study

Testing was conducted with Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F culture vials in an in-house precision study for 20 days using multiple FXI instruments and multiple operators. Six vial replicates per organism, instrument, vial type and vial lot were tested for a minimum of 1440 vials tested per each organism and vial type. The target organism inoculum was between 10 and 100 CFU/vial. For simplicity, vials were tested without blood as the organisms evaluated in this study do not depend on blood for growth. The rate of detection and recovery as well as the mean time to detection was calculated for each organism and vial type evaluated. For calculation of percent recovery, positive results reflect a positive flag by the instrument. One positive vial from each unique inoculum preparation (one culture vial type per organism inoculum) per testing day was subcultured to confirm purity and the presence of the appropriate organism. Vials flagged negative at the end of the 5-day protocol were subcultured to assess false negative rates.

The within-laboratory precision study results were acceptable. Results are shown in **Tables 5-7** for Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F culture vials, respectively.

Table 5. Plus Aerobic/F Culture Vials: Within-Laboratory Precision

Sample Input	CFU/vial Range	% Recovery (# detected/# tested)				Time to Detection (hours)	
Organism		Lot 1	Lot 2	Lot 3	Overall	Mean	Range
Candida albicans	27 – 77	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	22.0	19.1 – 26.5
Escherichia coli	28 – 53	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	8.5	7.0 – 10.1
Staphylococcus aureus	31 - 59	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	13.6	11.7 – 15.6

Table 6. Lytic/10 Anaerobic/F Culture Vials: Within-Laboratory Precision

Sample Input	CFU/vial Range	% Recovery (# detected/# tested)				Time to Detection (hours)	
Organism		Lot 1	Lot 2	Lot 3	Overall	Mean	Range
Bacteroides fragilis	49 – 98	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	18.5	16.1 – 20.3
Escherichia coli	28 – 53	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	8.1	5.5 – 9.7
Streptococcus pneumoniae	13 - 94	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	13.5	11.6 – 15.8

Table 7. Plus Anaerobic/F Culture Vials: Within-Laboratory Precision

Sample Input	CFU/vial Range	% Recovery (# detected/# tested)				Time to Detection (hours)	
Organism		Lot 1	Lot 2	Lot 3	Overall	Mean	Range
Bacteroides fragilis	46 – 91	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	23.0	11.9 – 50.3
Escherichia coli	21 – 89	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	8.1	6.2 – 9.7
Streptococcus pneumoniae	15 - 98	100.0 (480/480)	100.0 (480/480)	100.0 (480/480)	100.0 (1440/1440)	12.3	9.6 – 14.7

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Not applicable.

4. Detection Limit and Assay Reportable Range:

   Limit of Detection

   The limit of detection (LoD) for Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F culture vials were evaluated for vials incubated on BACTEC FXI Culture System (candidate device) and FX Culture System (comparator device).

   Concentrations of organism suspensions used for vial inoculation were determined by plating and colony counts. Each vial was inoculated with organism suspensions prepared to yield 1 - 10 CFU/vial without blood. To support growth, 3 mL of human blood was added to vials inoculated with *H. influenzae* and *S. pneumoniae* (Plus Aerobic/F only). Once seeded, all vials were incubated on FXI and FX instruments until a final result of positive or negative was determined at the end of the protocol (five days or 120 hours). All vials flagged as positive by the instruments were subcultured to confirm purity and presence of the target organism. Vials flagged as negative at the end of the 5-day protocol were subcultured to assess false negative rates.

   A total of 90 replicates including three media lots were tested for each vial type/microorganism combination. The LoD for each organism/vial type/instrument was determined to be the organism concentration (CFU/vial) for which 95% of vials were flagged positive by the instrument and were also positive by subculture. The LoDs for the organisms evaluated in each vial type are shown in **Table 8** for testing on FXI and **Table 9** for testing on FX.

Table 8. Organism LoD (CFU/Vial) on FXI

Organism	CFU/Vial		
	Plus Aerobic/F	Lytic/10 Anaerobic/F	Plus Anaerobic/F
B. fragilis		2	3
C. albicans	6		
C. perfringens		4	2
E. faecalis	8	6	8
E. coli	2	2	3
H. influenzae	10*		
P. aeruginosa	7		
S. aureus	5	8	6
S. pneumoniae	7*	4	7

* 3 mL blood added

Table 9. Organism LoD (CFU/Vial) on FX

Organism	CFU/Vial		
	Plus Aerobic/F	Lytic/10 Anaerobic/F	Plus Anaerobic/F
B. fragilis		2	3
C. albicans	6		
C. perfringens		4	2
E. faecalis	8	6	8
E. coli	2	2	3
H. influenzae	10*		
P. aeruginosa	7		
S. aureus	5	8	6
S. pneumoniae	7*	4	7

* 3 mL blood added

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

(a) Quality Control

Internal Quality Control:
As internal quality control for the BACTEC FXI Culture System, normalization is performed for each vial position in the BACTEC FXI Analyzer Module. It is performed at the time of manufacture, and the normalization values are stored on the instrument.

External Quality Control:
During the clinical study, daily external quality control was conducted on the FXI system and included one positive and one negative control vial for each vial type tested. For the positive controls, two organisms were seeded into separate vials at target inoculum levels of 10-100 CFU/vial. Organism concentrations for vial seeding were confirmed by plate counting procedures. For Plus Aerobic/F vials, organisms evaluated included one obligate aerobe (*Pseudomonas aeruginosa* ATCC 27853) and one facultative organism (*Escherichia coli* ATCC 25922). For Lytic/10 Anaerobic/F vials, organisms evaluated included one obligate anaerobe (*Clostridium perfringens* ATCC 13124) and one facultative organism (*Escherichia coli* ATCC 25922). For each vial type, one organism was evaluated daily, alternating between the two quality control organisms. In addition, an uninoculated negative control vial was tested daily for each vial type. There were 925 positive controls for each vial type tested on FXI for all clinical sites combined. A total of 1845 positive controls (98.3% for Plus Aerobic/F and 96.9% for Lytic/10 Anaerobic/F vial types) generated the expected positive signal by FXI. There were 924 negative controls for each vial type tested on FXI for all sites combined and total 1817 negative controls (98.6% for Plus Aerobic/F and 98.1% for Lytic/10 Anaerobic/F vial types) were reported as negative.

(b) Evaluation of Delay in Vial Entry
As stated in the labeling for Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F vials, it is recommended that vials are loaded onto the instrument as soon as possible. If a delay is inevitable, it is recommended that vials should be held at room temperature for no longer than 24 hours. The following statement is also included in each vial package insert:

*** CAUTION: Culture vials held at room temperature for longer than 24 hours before loading may not detect microorganisms and should be subcultured.**

An analytical study was performed to evaluate potential effects on vial/instrument performance for vials that are delayed between specimen collection and loading onto the BACTEC FXI and FX systems. The following delay conditions were evaluated:

- Control: no delay
- 20-25°C for 24 hours
- 20-25°C for 36 hours
- 35±1°C for 12 hours

Testing was conducted using vials containing 3 and/or 10 mL pooled fresh human blood seeded with target organism concentrations of 10-100 CFU/vial. The study included three lots for each vial type and a minimum of three vials for each combination of vial type, organism, hold time, temperature condition and blood volume for a total of 264 vials for aerobic and 144 vials for anaerobic culture vials. For calculation of percent recovery, positive results reflect a positive flag by the instrument. One positive vial from each unique inoculum preparation (vials inoculated at the same time with the same blood source and organism inoculum) was subcultured to confirm purity and the presence of the appropriate test organism. Vials flagged negative at the end of the 5-day protocol were subcultured to assess false negative rates.

The study demonstrated >95% recovery at the recommended conditions (20-25°C for 24 hours) for both FXI and FX instruments and the results support equivalency between the systems.

6. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

(a) Comparison Panel Growth Performance Study

The performance of the BACTEC FXI culture system (candidate device) and FX culture system (comparator device) was compared in an analytical study using a panel of microorganisms seeded into Plus Aerobic/F, Plus Anaerobic/F, and Lytic/10 Anaerobic/F vials. The growth performance study was conducted internally with seeded vials containing two different blood volumes (3 and 10 mL) and three media lots. A single strain was tested for each species evaluated at target inoculum levels of 1-10 and 10-100 CFU/vial. Each microorganism was tested in triplicate for each vial type, lot, inoculum level, and blood level on FXI and FX systems for a total of 36 vials per organism/vial type. One positive vial from each unique combination of inoculum preparation and blood volume was subcultured to determine purity and presence of the appropriate test organism. At the end of the 5-day protocol, all negative vials were subcultured to assess false negative rates.

Tables 10 and **11** list the strains evaluated for the aerobic and anaerobic vials in the Comparison Panel Growth Performance Study.

Table 10. Comparison Panel of Organisms for Plus Aerobic/F Culture Vial

Microorganism	ATCC #	Microorganism	ATCC #
Abiotrophia defectiva	49176	*Kingella kingae*	23330
Acinetobacter lwoffii	17925	*Klebsiella pneumoniae*	33495
Aerococcus viridans	11563	*Leuconostoc mesenteroides*	11449
Aggregatibacter actinomycetemcomitans	NCTC 9710	*Listeria monocytogenes*	19115
Alcaligenes faecalis	8750	*Micrococcus luteus*	4698
Bacillus subtilis	82	*Neisseria gonorrhoeae*	10150
Candida albicans	18804	*Neisseria meningitidis*	13090
Candida auris	2370	*Pediococcus acidilactici*	25740
Candida glabrata	66032	*Proteus mirabilis*	8259
Cardiobacterium hominis	15826	*Providencia stuartii*	25825
Citrobacter freundii	8090	*Pseudomonas aeruginosa*	27853
Corynebacterium jeikeium	43216	*Saccharomyces cerevisiae*	9763
Cryptococcus neoformans	32045	*Stomatococcus* (*Rothia*) *mucilaginosa*	NCTC 10663
Eikenella corrodens	23834	*Salmonella enterica*	13311
Enterobacter cloacae	35030	*Staphylococcus aureus*	25923
Enterococcus faecalis	29212	*Staphylococcus epidermidis*	12228
Escherichia coli	25922	*Stenotrophomonas maltophilia*	13637
Granulicatella adiacens	43205	*Streptococcus agalactiae* (Group B)	12928
Haemophilus influenzae	19418	*Streptococcus pneumoniae*	6305
Haemophilus influenzae, type a	9006	*Streptococcus pyogenes*	19615
Haemophilus influenzae, type b	10211	*Streptococcus sanguinis*	10556
Haemophilus parainfluenzae	33392		

Table 11. Comparison Panel of Organisms for Lytic/10 Anaerobic/F and Plus Anaerobic/F Culture Vials

Microorganism	ATCC #	Microorganism	ATCC #
Bacteroides fragilis	25285	*Fusobacterium nucleatum*	10953
Bacteroides ovatus	8483	*Klebsiella pneumoniae*	33495
Bacteroides thetaiotaomicron	29741	*Porphyromonas asaccharolytica*	25260
Bacteroides vulgatus	8482	*Staphylococcus aureus*	25923
Hathewaya histolytica	19401	*Staphylococcus epidermidis*	12228
Clostridium novyi	17861	*Streptococcus agalactiae* (Group B)	12928
Clostridium perfringens	13124	*Streptococcus pneumoniae*	6305
Enterococcus faecalis	29212	*Streptococcus pyogenes*	19615
Enterococcus faecium	19434	*Veillonella parvula*	10790
Escherichia coli	25922		

Tables 12-14 include stratified results for Plus Aerobic/F, Plus Anaerobic/F, and Lytic/10 Anaerobic/F vials, tested with blood (3 and 10 mL) added. For each vial type, vials were seeded with applicable organisms and incubated/monitored on both FXI and FX systems.

In summary, results of the growth performance study demonstrated an overall comparable performance for FXI and FX systems for detection and recovery of representative organisms in Plus Aerobic/F, Lytic/10 Anaerobic/F, and Plus Anaerobic/F culture vials. The study

demonstrated >95% detection for the organisms evaluated at target 10-100 CFU with blood in each vial type for both systems.

Table 12. Plus Aerobic/F: Growth Performance on FXI and FX with Blood

BACTEC FXI				BACTEC FX			
Target CFU/vial	**% Recovery (n)**	**Mean TTD (hours)**	**Range TTD (hours)**	**Target CFU/vial**	**% Recovery (n)**	**Mean TTD (hours)**	**Range TTD (hours)**
10-100	100.0 (773/773)	19.9	7.2 – 73.9	10-100	100.0 (769/769)	20.1	8.8 – 64.2
1-10	97.7 (754/772)	22.1	8.2 – 104.2	1-10	96.9 (748/772)	22.0	9.6 – 82.8

Table 13. Lytic/10 Anaerobic/F: Growth Performance on FXI and FX with Blood

BACTEC FXI				BACTEC FX			
Target CFU/vial	**% Recovery (n)**	**Mean TTD (hours)**	**Range TTD (hours)**	**Target CFU/vial**	**% Recovery (n)**	**Mean TTD (hours)**	**Range TTD (hours)**
10-100	100.0 (342/342)	18.4	6.9 – 57.3	10-100	98.8 (338/342)	20.2	7.6 – 69.2
1-10	89.1 (304/341)*	19.9	7.2 – 119.6	1-10	88.3 (301/341)*	21.6	8.6 – 73.1

* One paired set inoculated with *S. aureus* was excluded due to database technical issue.

Table 14. Plus Anaerobic/F: Growth Performance on FXI and FX with Blood

BACTEC FXI				BACTEC FX			
Target CFU/vial	**% Recovery (n)**	**Mean TTD (hours)**	**Range TTD (hours)**	**Target CFU/vial**	**% Recovery (n)**	**Mean TTD (hours)**	**Range TTD (hours)**
10-100	96.2 (329/342)	21.0	7.2 – 108.4	10-100	97.4 (333/342)	24.1	8.3 – 105.3
1-10	88.8 (302/340)*	21.0	8.4 – 111.7	1-10	86.2 (293/340)*	23.2	9.6 – 112.1

* Two paired sets inoculated with *S. aureus* were excluded due to database technical issue.

(b) <u>Clinical Study to Evaluate Blood Cultures on FXI and FX</u>

A multi-center clinical study was conducted to compare the performance of the BACTEC FXI Culture System (candidate device) and FX Culture System (comparator device) with blood cultures collected in BACTEC Plus Aerobic/F and Lytic/10 Anaerobic/F culture vials. Based on the acceptability of the media equivalency study (as described in VII. B. 2), BACTEC Lytic/10 Anaerobic/F culture vials were used to support performance of BACTEC Plus Anaerobic/F culture vials in the clinical study.

The study included evaluation of matched pairs of the same vial type with one vial incubated on FXI and the other incubated on FX. Samples were considered compliant based on achieving volume requirements (3-10 mL) for each collection as well as if the blood volume of the vial with the smallest volume was within 50% of the blood volume of the vial with the largest volume.

For each vial type, the performance of FXI was considered substantially equivalent to the FX if the ratio of the true positive rate was above 0.9 based on all compliant samples with isolates characterized as significant. An additional condition also needed to be met regarding the upper limit of the 95% confidence interval for the ratio of system agreement with positive clinical determination (true positive rate) for the total compliant samples/isolates (significant, contaminated and unknown). The range between lower confidence limit and upper confidence limit must cross a value of 1.

The target sample quantity for vials (Plus Aerobic/F and Lytic/10 Anaerobic/F) was 3-10 mL per vial. Overfilled vial test pairs, in which either vial of a pair were filled with a volume greater than the maximum 10 mL of blood, were excluded from the analysis.

All vials that were flagged as positive by each system were gram stained, subcultured, and all recovered organisms identified using matrix-assisted laser desorption/ionization (MALDI) mass spectrometry. A minimum of 30% of all negative blood cultures were subcultured. A clinical determination was defined as "Positive" when viable organisms were present from the subculture of FXI- or FX-incubated vials and defined as "Negative" when no viable organisms were present from both subcultures of FXI- and FX-incubated vials. A culture vial was determined to be a "True Positive" if flagged positive by the instrument with viable organisms present in the subculture and the clinical determination was positive. True positive rates were calculated for each vial and specimen type on FXI and on FX, and the ratio of FXI true positives to FX true positives was calculated to compare performance between systems. Clinical isolates recovered from each subcultured vial were classified as significant, contaminant, or unknown. Classification was performed by clinicians at each clinical site and was based on patient chart review in conjunction with predetermined criteria.

A culture vial was determined to be false negative if the clinical determination was positive and the vial result was negative by the instrument or the vial result was positive by the instrument but no growth upon subculture of the vial. A culture vial was determined to be false positive if clinical determination was negative, but the instrument signaled the vial as positive.

Results are shown below for blood culture specimens collected in Plus Aerobic/F and Lytic/10 Anaerobic/F vial pairs of which one vial was tested on FXI, and the other vial was tested on FX.

(i) BACTEC Plus Aerobic/F Culture Vials Clinical Performance:
A total of 1407 Plus Aerobic/F culture vial pairs obtained from 1139 adult patients suspected of blood stream bacterial/yeast infections were tested on both the FXI and FX culture systems. Of these, 939 vial pairs from 804 patients were determined to be compliant.

A total of 124 isolates were recovered from all compliant Plus Aerobic/F culture vial pairs with a positive status. At least a single isolate was recovered by subculture from 114 Plus Aerobic/F culture vial pairs incubated on FXI and/or FX. Two isolates were recovered from ten vial pairs. A total of 87 isolates were recovered from Plus Aerobic/F culture vials on FXI, and a total of 92 isolates were recovered from Plus Aerobic/F culture vials on FX. Of the significant isolates, a total of 62 isolates were recovered from Plus Aerobic/F culture vials on FXI compared to a total of 64 isolates recovered from Plus Aerobic/F culture vials on FX.

One false positive Plus Aerobic/F culture vial was observed on FXI (1/949; 0.1%) and five were observed on FX (5/949; 0.5%).

Terminal subcultures were performed on 569 Plus Aerobic/F culture vial pairs that were negative on both FXI and FX. False negative results were observed for both FXI and FX vials of one vial pair. For negative vial pairs for which both vials were subcultured, the false negative rate based on instrument negative and subculture positive was 0.2% (1/569) for the FXI and 0.4% (2/569) for the FX.

The following tables compare results of true positive blood cultures incubated on FXI and FX for all compliant Plus Aerobic/F culture vials yielding any number of isolates on subculture (**Table 15**), a single isolate on subculture (**Table 16**), and multiple isolates on subculture (**Table 17**). The comparative yield of microorganisms from vials incubated on FXI and FX is summarized in **Table 18**.

In summary, the clinical study results demonstrate equivalent performance for paired culture specimens in Plus Aerobic/F Culture Vials tested on the BACTEC FXI and FX Culture Systems.

Table 15. Plus Aerobic/F – Compliant – Single and Multiple Isolates Combined

Clinical Determination	FXI True Positives	% of FXI True Positives in Population	FX True Positives	% of FX True Positives in Population	Ratio of True Positives (FXI/FX)	95% CI (LCL, UCL)*
Significant	62	6.5% (62/949)	64	6.7% (64/949)	0.969	(0.814, 1.150)
Contaminant	24	2.5% (24/949)	26	2.7% (26/949)	0.923	(0.582, 1.461)
Unknown	1	0.1% (1/949)	2	0.2% (2/949)	0.500	(0.066, 3.816)
Total	87	9.2% (87/949)	92	9.7% (92/949)	0.946	(0.790, 1.131)

* LCL (Lower Confidence Limit), UCL (Upper Confidence Limit)

Table 16. Plus Aerobic/F – Compliant – Single Isolates

Clinical Determination	FXI True Positives	% of FXI True Positives in Population	FX True Positives	% of FX True Positives in Population	Ratio of True Positives (FXI/FX)	95% CI (LCL, UCL)*
Significant	55	5.9% (55/929)	58	6.2% (58/929)	0.948	0.788, 1.135
Contaminant	16	1.7% (16/929)	20	2.2% (20/929)	0.800	0.464, 1.370
Unknown	1	0.1% (1/929)	2	0.2% (2/929)	0.500	0.066, 3.816
Total	72	7.8% (72/929)	80	8.6% (80/929)	0.900	0.743, 1.086

* LCL (Lower Confidence Limit), UCL (Upper Confidence Limit)

Table 17. Plus Aerobic/F – Compliant – Multiple Isolates

Clinical Determination	FXI True Positives	% of FXI True Positives in Population	FX True Positives	% of FX True Positives in Population	Ratio of True Positives (FXI/FX)	95% CI (LCL, UCL)*
Significant	7	35.0% (7/20)	6	30.0% (6/20)	1.167	(0.619, 2.284)
Contaminant	8	40.0% (8/20)	6	30.0% (6/20)	1.333	(0.548, 3.284)
Unknown	0	0.0% (0/20)	0	0.0% (0/20)	N/A	N/A
Total	15	75.0% (15/20)	12	60.0% (12/20)	1.250	(0.728, 2.186)

* LCL (Lower Confidence Limit), UCL (Upper Confidence Limit)

Table 18. Plus Aerobic/F: Comparative Yield of Microorganisms (Number of Isolates)

Group	FXI	FX
Enterobacterales	22	19
Enterococcus spp.	2	2
Non-fermentative Gram-Negative Bacilli	4	8
Other Gram-Positive	2	3
Coagulase-Negative *Staphylococcus*	31	29
Staphylococcus aureus	12	14
Streptococcus species	11	13
Yeasts	3	4
Total	87	92

NOTE: Isolate table includes polymicrobic cultures.

(ii) BACTEC Lytic/10 Anaerobic/F Culture Vials Clinical Performance:

A total of 1402 Lytic/10 Anaerobic/F culture vial pairs obtained from 1136 adult patients suspected of blood stream bacterial/yeast infections were tested on both the FXI and FX culture systems. Of these, 982 vial pairs from 833 patients were determined to be compliant.

A total of 134 isolates were recovered from all compliant Lytic/10 Anaerobic/F culture vial pairs with a positive status. At least a single isolate was recovered by subculture from 116 Lytic/10 Anaerobic/F culture vial pairs incubated on FXI and/or FX. Two isolates were recovered from 16 vial pairs, and three isolates were recovered from one vial pair. A total of 92 isolates were recovered from Lytic/10 Anaerobic/F culture vials on FXI and FX each. Of the significant isolates, a total of 67 isolates were recovered from Lytic/10 Anaerobic/F culture vials on FXI compared to a total of 72 isolates recovered from Lytic/10 Anaerobic/F culture vials on FX.

Two false positive Lytic/10 Anaerobic/F culture vials were observed on FXI (2/1000; 0.2%) and one was observed on FX (1/1000; 0.1%).

Terminal subcultures were performed on 588 Lytic/10 Anaerobic/F culture vial pairs that were negative on both FXI and FX. False negative results were observed for both FXI and FX vials of two vial pairs. For negative vial pairs for which both vials were subcultured, the false negative rate based on instrument negative and subculture positive was 0.7% (4/588) for the FXI and 1.2% (7/588) for the FX.

The following tables compare results of true positive blood cultures incubated on FXI and FX for all compliant Lytic/10 Anaerobic/F culture vials yielding any number of isolates on subculture (**Table 19**), a single isolate on subculture (**Table 20**), and multiple isolates on subculture (**Table 21**). The comparative yield of microorganisms from vials incubated on FXI and FX is summarized in **Table 22**.

In summary, the clinical study results demonstrate equivalent performance for paired culture specimens in Lytic/10 Anaerobic/F Culture Vials tested on BACTEC FXI and FX Culture Systems.

Table 19. Lytic/10 Anaerobic/F – Compliant – Single and Multiple Isolates Combined

Clinical Determination	FXI True Positives	% of FXI True Positives in Population	FX True Positives	% of FX True Positives in Population	Ratio of True Positives (FXI/FX)	95% CI (LCL, UCL)*
Significant	67	6.7% (67/1000)	72	7.2% (72/1000)	0.931	(0.795, 1.082)
Contaminant	22	2.2% (22/1000)	18	1.8% (18/1000)	1.222	(0.702, 2.134)
Unknown	3	0.3% (3/1000)	2	0.2% (2/1000)	1.500	(0.300, 7.502)
Total	92	9.2% (92/1000)	92	9.2% (92/1000)	1.000	(0.841, 1.189)

* LCL (Lower Confidence Limit), UCL (Upper Confidence Limit)

Table 20. Lytic/10 Anaerobic/F – Compliant – Single Isolates

Clinical Determination	FXI True Positives	% of FXI True Positives in Population	FX True Positives	% of FX True Positives in Population	Ratio of True Positives (FXI/FX)	95% CI (LCL, UCL)*
Significant	48	5.0% (48/965)	57	5.9% (57/965)	0.842	(0.700, 0.991)
Contaminant	16	1.7% (16/965)	12	1.2% (12/965)	1.333	(0.691, 2.590)
Unknown	2	0.2% (2/965)	1	0.1% (1/965)	2.000	(0.262, 15.262)
Total	66	6.8% (66/965)	70	7.3% (70/965)	0.943	(0.774, 1.146)

* LCL (Lower Confidence Limit), UCL (Upper Confidence Limit)

Table 21. Lytic/10 Anaerobic/F – Compliant – Multiple Isolates

Clinical Determination	FXI True Positives	% of FXI True Positives in Population	FX True Positives	% of FX True Positives in Population	Ratio of True Positives (FXI/FX)	95% CI (LCL, UCL)*
Significant	19	54.3% (19/35)	15	42.9% (15/35)	1.267	(0.898, 1.873)
Contaminant	6	17.1% (6/35)	6	17.1% (6/35)	1.000	(0.364, 2.744)

Clinical Determination	FXI True Positives	% of FXI True Positives in Population	FX True Positives	% of FX True Positives in Population	Ratio of True Positives (FXI/FX)	95% CI (LCL, UCL)*
Unknown	1	2.9% (1/35)	1	2.9% (1/35)	1.000	(0.104, 9.579)
Total	26	74.3% (26/35)	22	62.9% (22/35)	1.182	(0.813, 1.741)

* LCL (Lower Confidence Limit), UCL (Upper Confidence Limit)

Table 22. Lytic/10 Anaerobic/F: Comparative Yield of Microorganisms (Number of Isolates)

Group	FXI	FX
Anaerobe	5	6
Enterobacterales	26	23
Enterococcus spp.	4	4
Other Gram-Negative	4	4
Other Gram-Positive	1	1
Coagulase-Negative *Staphylococcus*	26	24
Staphylococcus aureus	10	10
Streptococcus species	15	19
Yeasts	1	1
Total	92	92

NOTE: Isolate table includes polymicrobic cultures.

2. Matrix Comparison:

Media Equivalency Study

A media equivalency study was conducted to assess compatibility of the BACTEC FXI and FX cultures systems with anaerobic blood culture vial types, Lytic/10 Anaerobic/F and Plus Anaerobic/F. A total of 21 organisms were inoculated into each vial type. Testing was conducted using vials containing 3 and/or 10 mL pooled fresh human blood at target organism concentrations of 10-100 CFU/vial. Paired testing was conducted with one vial from each media lot, receiving the same organism inoculum and blood source, with one vial placed on the FXI culture system and the other vial placed on the FX culture system. The study included three lots of paired vials for a total of 126 vials per instrument. For calculation of percent recovery, positive results reflect a positive flag by the instrument. One positive vial from each unique inoculum preparation (vials inoculated at the same time with the same blood source and organism inoculum) was subcultured to confirm purity and the presence of the appropriate test organism. Vials flagged negative at the end of the 5-day protocol were subcultured to assess false negative rates.

Table 23 lists the strains evaluated for the anaerobic vials in the media equivalency study.

Table 23. A List of Organisms Tested for Media Equivalency Study

Microorganism	ATCC #	Microorganism	ATCC #
Bacteroides fragilis	25285	*Escherichia coli*	25922
Bacteroides ovatus	8483	*Fusobacterium nucleatum*	10953
Bacteroides thetaiotaomicron	29741	*Klebsiella pneumoniae*	33495
Bacteroides vulgatus	8482	*Porphyromonas asaccharolytica*	25260
Candida albicans	18804	*Staphylococcus aureus*	25923

Microorganism	ATCC #	Microorganism	ATCC #
Candida glabrata	66032	*Staphylococcus epidermidis*	12228
Clostridium novyi	17861	*Streptococcus agalactiae* (Group B)	12928
Clostridium perfringens	13124	*Streptococcus pneumoniae*	6305
Enterococcus faecalis	29212	*Streptococcus pyogenes*	19615
Enterococcus faecium	19434	*Veillonella parvula*	10790
Hathewaya histolytica	19401		

The media equivalency study results were acceptable. The results support equivalent recovery between Plus Anaerobic/F and Lytic/10 Anaerobic/F culture vials on both the FXI and FX culture systems. This study supports using Lytic/10 Anaerobic/F Culture Vials to represent Plus Anaerobic/F vials in clinical trial testing to support performance of both vial types. Results are shown in **Table 24**.

Table 24. Percent Recovery Anaerobic Media: Media Equivalency Study

Instrument	Blood Volume	Number of Paired Sets	Lytic/10 Anaerobic/F Positive Vials (% recovery)	Plus Anaerobic/F Positive Vials (% recovery)	Ratio of Positive Yields
FXI	3 mL	63	61 (96.8%)	63 (100.0%)	1.03
	10 mL	63	59 (93.7%)	60 (95.2%)	1.02
FX	3 mL	63	61 (96.8%)	62 (98.4%)	1.02
	10 mL	63	60 (95.2%)	57 (90.5%)	0.95

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Clinical Cut-Off

   Not applicable.

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not applicable.

D Expected Values/Reference Range:

The expected positive percentage of culture vials will vary based on factors such as patient population, specimen type prevalence of significant organisms, site location, and contamination rates. The expected values shown below are based on the clinical study conducted to evaluate Plus Aerobic/F and Lytic/10 Anaerobic/F Culture Vials on the BACTEC FXI Culture System for blood cultures:

- Plus Aerobic/F Culture Vial (Blood): The average percent positive blood cultures observed from this study at three clinical trial sites were 9.8% and 10.2% for Plus Aerobic/F Culture Vial and Lytic/10 Anaerobic/F Culture Vial, respectively.

E Other Supportive Instrument Performance Characteristics Data:

Not applicable.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.