510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K173873

B. Purpose for Submission:

Update blood volume to 3.0 mL in intended use, remove current product limitation of fluconazole/*Candida albicans* for BD BACTEC Peds Plus/F Culture Vials (plastic)

C. Measurand:

Aerobic microorganisms from blood (bacteria and yeast)

D. Type of Test:

Liquid culture medium for recovery of microorganisms from blood using fluorescent technology to detect the increased CO_2 produced by the growth of microorganisms

E. Applicant:

Becton, Dickinson and Company

F. Proprietary and Established Names:

BD BACTEC Peds Plus/F Culture Vials Soybean-Casein Digest Broth with Resins in a Plastic Vial

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.2560 Microbial Growth Monitor

2. Classification:

   Class I

3. Product code:

   MDB System, Blood Culturing

4. Panel:

   83 Microbiology

H. Intended Use:

1. Intended use(s):

   BD BACTEC Peds Plus/F culture vials (enriched Soybean-Casein Digest broth with CO_2) are for aerobic blood cultures. Principal use is with the BD BACTEC fluorescent series instruments for the qualitative culture and recovery of aerobic microorganisms (mainly bacteria and yeast) from pediatric and non-pediatric blood specimens which are generally less than 3.0 mL in volume.

2. Indication(s) for use:

   Same as Intended Use

3. Special conditions for use statement(s):

   Prescription Use

   Updated limitation specific for antifungal agents/yeast combination under the Antimicrobial Activity section is:

   Studies have demonstrated that the resins present in this medium adequately neutralize the antifungal agent fluconazole with Candida albicans. However, other antifungal agent/yeast combinations have not been tested/evaluated.

4. Special instrument requirements:

   BACTEC fluorescent series instruments BACTEC FX, BACTEC FX40, BACTEC 9240 and BACTEC 9050 and were evaluated using software versions listed below:

Instrument	Software Version
BACTEC FX	V5.20
BACTEC 9240	V4.95
BACTEC 9050	V2.01
BACTEC FX 40	V2.51B

I. Device Description:

The blood sample to be tested is inoculated into one or more vials which are inserted into the BACTEC fluorescent series instrument for incubation and periodic reading. Each vial contains a chemical sensor which can detect increases in CO_2 produced by the growth of microorganisms. The sensor is monitored by the instrument every ten minutes for an increase

in its fluorescence, which is proportional to the amount of CO_2 present. A positive reading indicates the presumptive presence of viable microorganisms in the vial. Detection is limited to microorganisms that will grow in a particular type of culture medium.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   BD BACTEC Peds Plus/F Culture Vials (Plastic) Soybean-Casein Digest Broth with Resin in a plastic vial

2. Predicate 510(k) number(s):

   K151866

3. Comparison with predicate:

Table 1: Comparison with Predicate Device

Similarities		
Item	**Device** **BD BACTEC Peds Plus/F Culture Vials Soybean-Casein Digest Broth with Resins in a Plastic Vial** **K173873**	**Predicate** **BACTEC Peds Plus/F Culture Vials (Plastic) Soy Soybean-Casein Digest Broth with Resins in a Plastic Vial** **K151866**
Sample Type	Human blood	Same
Growth Medium	40 mL enriched soybean-casein digest broth with CO_2 and N_2	Same
Detection Technology	Continuous monitoring; measurement of CO_2 increase; resins for absorption of antimicrobials; rocking agitation parameters	Same
Incubation	35ºC (± 1.5ºC) up to 120 hours	Same
Vial Weight	20.9 gram	Same
Vial Height	5.0 inches	Same
Vial Sensor	Specific for the plastic vial geometry	Same
Sensor Adhesion Promotor	Required	Same

Differences		
Item	Device	Predicate
Intended Use	BD BACTEC Peds Plus /F culture vials (enriched Soybean-Casein Digest broth with CO_2) are for aerobic blood cultures. Principal use is with the BD BACTEC fluorescent series instruments for the qualitative culture and recovery of aerobic microorganisms (mainly bacteria and yeast) from pediatric and non-pediatric blood specimens which are generally less than 3 mL in volume.	BD BACTEC Peds Plus /F culture vials (enriched Soybean-Casein Digest broth with CO_2) are for aerobic blood cultures. Principal use is with the BD BACTEC fluorescent series instruments for the qualitative culture and recovery of aerobic microorganisms (mainly bacteria and yeast) from pediatric and non-pediatric blood specimens which are generally less than 5 mL in volume.
Blood Volume	3.0 mL	0.5, 5.0 mL
Ingredient (Pyridoxal HCl (Vitamin B_6)	0.001% w/v	0.0006% w/v

K. Standard/Guidance Document Referenced (if applicable):

Not Applicable

L. Test Principle:

The BD BACTEC Peds Plus /F medium is an enriched soybean- casein digest broth, with each vial containing 40 mL of broth. Sodium polyanetholesulfonate (SPS) is added to the medium as an anticoagulant that inhibits bacteriocidal activities in the blood. The concentration of SPS has been adjusted to accommodate the low blood volumes of 0.5- 5.0 mL per vial.

Each BD BACTEC Peds Plus/F culture vial contains a chemical sensor in a silicon rubber base that can detect increases in CO_2 produced by the growth of microorganisms. Low volume (0.5- 5 mL) of blood is inoculated into the BD BACTEC Peds Plus/F blood culture vial, which is inserted into the BD BACTEC Fluorescent Series instrument for incubation, agitation and periodic measurement. When microorganisms are present in the blood sample, they metabolize nutrients in the culture medium, releasing CO_2 into the medium. A dye in the sensor reacts with the CO_2, modulating the amount of light that is absorbed by the fluorescent material in the sensor. The instrument's photo detectors monitor the sensor every 10 minutes and measure the level of fluorescence, which is proportional to the amount of CO_2 present in the vial. Positivity of a vial is determined by algorithms resident in the instrument rack's microprocessor. The algorithms use the rate of CO_2 production as well as the absolute increase in CO_2 to interpret the data.

Culture vials flagged as presumptively positive are removed from the instrument for

subculture and Gram stain in order to identify the microorganisms for further evaluation and proposed patient treatment. Culture vials that are not flagged as positive remain in the instrument until the test protocol has been completed and negative vials are discarded at the end of protocol (120 hours).

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The BD BACTEC Peds Plus/F vial (plastic) was evaluated across three lots of culture media vials in the Time To Detection (TTD) and the Percent Recovery studies using exactly 3.0 mL of blood per vial.

The TTD results with 95% confidence intervals (CI) stratified by vial lot (combining total results for organisms and instruments) are shown in Table 2.1.

Table 2.1: Time To Detection (hours) by Lots

Lot #	Total #	Median Time to Detection (TTD) in Hours (95% CI)			
		0-1 CFU	1-10 CFU	10-100 CFU	Overall
1	204	28.09(17.24, 40.72)	19.88(15.85,29.33)	17.05(15.41,17.61)	17.23(16.49,18.62)
2	208	19.62(12.31,26.08)	21.56(16.14,32.25)	17.09(15.82,17.93)	17.45(16.57,18.55)
3	203	40.57(14.24,88.11)	21.07(16.51,28.26)	17.05(15.78,17.74)	17.57(16.56,18.68)

The percent recovery results with 95%CI stratified by vial lot (combining total results for inoculum levels, organisms, and instruments) are shown in Table 2.2.

Table 2.2: Percent Recovery by Lots

Lot #	Total #	Positive	Percent Recovery (95% CI)
1	224	204	91.07% (88.84, 95.98)
2	224	208	92.86% (87.95, 95.09)
3	224	203	90.62% (88.83, 95.54)

The analysis was acceptable and there was no significant difference across the three lots evaluated with 3.0 mL blood in this study.

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Quality Control

An internal validation study across three lots with inoculum at 10-100 CFU and 3.0

mL of blood per vial was conducted using nine organisms: *Streptococcus pyogenes, Escherichia coli, Pseudomonas aeruginosa,* and *Streptococcus pneumoniae* were evaluated by testing nine vials each; *Haemophilus influenzae, Neisseria meningitidis, Candida albicans,* and *Alcaligenes faecalis* were evaluated by testing six vials each; *Staphylococcus aureus* was evaluated by testing three vials. All organisms were detected ≤72 hours, with mean ranges between 10 (*Escherichia coli*) to 36.5 (*Neisseria meningitidis*) hours.

Streptococcus pyogenes	ATCC 19615
Escherichia coli	ATCC 25922
*Streptococcus pneumoniae**	ATCC 6305
Pseudomonas aeruginosa	ATCC 27853
Candida albicans	ATCC18804
Neisseria meningitidis	ATCC 13090
Alcaligenes faecalis	ATCC 8750
Haemophilus influenzae	ATCC 19418
Staphylococcus aureus	ATCC 25923

*CLSI recommended QC strain for blood culture media

d. *Detection limit:*

Microbial Detection Limit (MDL)

The microbial detection limit study was conducted to assess the capability of the culture media to detect low level of organisms (expected target level of 0-1 and 1-10 CFU/vial) when present in blood. The study included 15 organisms (12 bacteria and 3 yeast strains) tested with 3.0 mL of blood, at challenging target inoculum levels of 0-1 and 1-10 CFU/vial across three lots with BACTEC FX and BACTEC 9240 instruments:

15 strains x 1 blood volume (3.0 mL) x 2 inoculum levels x 3 lots x 2 instruments = 180 paired sets

For statistical analysis, 95% two-sided bootstrap confidence intervals for differences were used. The results were stratified by organism and are shown in Table 3.1 below.

Table 3.1: Percent Recovery Difference for 0-1 and 1-10 CFU Combined (by Organism) Using 3.0 mL of Blood

Organism	**Paired sets (#)**	**Percent recovery for** Peds Plus/F **(Plastic)**	**Percent recovery for** Peds Plus/F **(Glass)**	**Difference in percent recovery between Plastic and Glass (95% CI)**
Candida albicans	12	83.33%	75.00%	8.33% (-16.67%, 33.33%)
Candida glabrata	12	58.33%	75.00%	-16.67% (-41.67%, 0%)
Crytococcus neoformans	12	83.33%	66.67%	16.67% (-16.67%, 50%)

Organism	Paired sets (#)	Percent recovery for Peds Plus/F (Plastic)	Percent recovery for Peds Plus/F (Glass)	Difference in percent recovery between Plastic and Glass (95% CI)
Enterococcus faecalis	12	83.33%	91.67%	-8.33% (-25.00%, 0%)
Escherichia coli	12	66.67%	83.33%	-16.67% (-58.33%, 25.00%)
Haemophilus influenzae	12	75.00%	66.67%	8.33% (-16.67%, 33.33%)
H. parainfluenzae	12	83.33%	83.33%	0.00% (-25.00%, 25.00%)
Micrococcus luteus	12	50.00%	58.33%	-8.33% (-25.00%, 0%)
Neisseria gonorrhoeae	12	75.00%	83.33%	-8.33% (-33.33%, 16.67%)
Neisseria meningitidis	12	58.33%	66.67%	-8.33% (-33.33%, 16.67%)
Pseudomonas aeruginosa	12	75.00%	91.67%	-16.67% (-41.67%, 0%)
Staphylococcus aureus	12	75.00%	83.33%	-8.33% (-41.67%, 25%)
Staphylococcus epidermidis	12	66.67%	41.67%	25.00% (8.13%, 50%)
Streptococcus pneumoniae	12	41.67%	33.33%	8.33% (-67.67%, 41.67%)
Streptococcus sanguinis	12	50.00%	58.33%	-8.33% (-25.00%, 0%)
Total	180	68.33%	70.56%	-2.22% (-9.44%, 4.44%)

There were 180 paired sets tested; 104 sets were positive in both the predicate glass and the modified plastic vials, 23 were positive in the glass vial only, and 19 were positive in the plastic vial only. Of the 104 paired sets that were positive, 18 were at the target inoculum level of 0-1 CFU/vial and 86 at the target inoculum level of 1-10 CFU/vial. These paired sets were further evaluated by Time To Detection (TTD) in hours with 95% CI using bootstrap percentile method. The performance is noted in the table below:

Table 3.2: Median TTD Difference for 0-1 and 1- 10 CFU/Vial in Hours

Target Inoculum Level	Paired Sets (#)	Median TTD (Plastic)	Median TTD (Glass)	Median of TTD Differences (Platic-Glass)
0- 1 CFU	18	22.02 (15.09, 38.13)	23.02 (15.44, 37.56%)	-0.34 (-1.17, 0.25)
1-10 CFU	86	20.84 (18.5, 23.24)	21.73 (17.77, 24.84)	-0.5 (-0.67, -0.17)

The MDL study demonstrated that the Peds Plus/F vial (plastic) performed equivalently when compared to the comparator glass device at the challenging low target inoculum levels of 0-1 and 1-10 CFU/vial with 3.0 mL of blood.

e. Analytical specificity:

Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

Performance of the BD BACTEC Peds Plus/F (plastic) blood culture vials was evaluated in seeded internal analytical studies to demonstrate equivalent performance to the comparator device, the BD BACTEC Peds Plus/F (glass) blood culture vials. The comparisons were made using the following parameters: Time to detection, percent recovery, false negative rate, and antimicrobial neutralization capability. For statistical analysis, 95% two-sided bootstrap confidence intervals for differences were used.

a. Method comparison with predicate device:

Instrument Time to Detection (TTD) study

The TTD (in hours) was recorded as part of the combined Percent Recovery and the Microbial Detection Limit (MDL) studies. MDL studies were conducted using the BD BACTEC FX and 9240 instruments at challenging inoculum levels 0- 1 and 1- 10 CFU per vial. The Percent Recovery study represented by the standard inoculum of 10 to 100 CFU per vial across four instruments (9050, 9240, FX, and FX40). Studies were conucted with 3.0 mL of blood over three media lots.

TTD result stratified by target inoculum levels is shown in Table 4.1 below.

Table 4.1: Median TTD Difference By Inoculum Levels in Hours

Target Inoculum Level	Median TTD (Plastic)	Median TTD (Glass)	Median of TTD Differences (Plastic-Glass)
0- 1 CFU	22.02 (15.09, 38.13)	23.02 (15.25, 38.05)	-0.34 (-1.08, 0.25)
1-10 CFU	20.84 (18.02, 23.24)	21.73 (17.93, 24.91)	-0.5 (-0.67, -0.17)
10-100 CFU	17.07 (16.56, 17.56)	17.52 (17.00, 18.01)	**-0.50 (-0.50, -0.33)**

TTD results in hours with 95% CI for the standard inoculum level of 10- 100 CFU/vial were evaluated by testing 41 isolates (32 bacteria and 3 yeasts noted in Table 4.2 below), across three lots tested with four BACTEC instruments. The results stratified by organisms and lots are shown in Table 4.2 and 4.3 below.

Table 4.2: Median TTD Difference for 10- 100 CFU/Vial in Hours (by Organism)

Organism	Paired Sets (#)	Median TTD (Plastic)	Median TTD (Glass)	Median of TTD Differences (Plastic-Glass)
Abiotrophia defectiva	12	16.84 (16.54, 17.53)	17.67 (17.00, 18.15)	-1.08 (-1.50, 0.16)
Acinetobacter lwoffii	12	21.02 (20.3, 21.82)	22.06 (22.02, 22.57)	-1 (-1.75, -0.5)
Aerococcus viridans	12	13.36 (13.00,13.82)	13.89 (13.43, 14.57)	-0.50 (-1, -0.08)
Aggregatibacter actinomycetemcomitans	12	25.07 (24.05, 26.52)	25.82 (25.31, 27.02)	-1 (-1.5, -0.5)
Alcaligenes faecalis	12	20.91 (20.49, 21.96)	22.49 (21.99, 23.05)	-1.5 (-1.59, -1)
Bacillus subtilis	12	21.54 (21.08, 22.57)	22.55 (22.01, 23.16)	-0.75 (-2, 0)
Candida albicans	12	28.56 (27.26, 29.25)	27.59 (26.78, 28.54)	0.50 (-0.50, 1.42)
Candida glabrata	12	44.64 (39.53, 46.04)	40.41 (36.86, 44.77)	2.25 (-1.00, 4.58)
Cardiobacterium hominis	12	39.94 (39.11, 41.4)	41.45 (40.58, 41.98)	-1.17 (-2.34, -1.00)
Corynebacterium jeikeium	12	29.02 (28.55, 29.57)	29.30 (28.51, 29.63)	-0.08 (-1.08, 0.17)

Organism	Paired Sets (#)	Median TTD (Plastic)	Median TTD (Glass)	Median of TTD Differences (Plastic-Glass)
Cryptococcus neoformans	12	61.81 (59.73, 63.80)	65.86 (63.92, 69.43)	-4.67 (-7.08, -2.5)
Eikenella corrodens	12	28.57 (27.54, 28.67)	29.38 (28.60, 29.91)	-1.08 (-1.66, -0.42)
Enterobacter cloacae	12	9.58 (9.29, 9.80)	9.75 (9.49, 9.93)	-0.08 (-0.33, 0)
Enterococcus faecalis	12	9.66 (9.50, 9.74)	9.87 (9.57, 10.03)	-0.25 (-0.42, 0)
Escherichia coli	12	10.07 (9.79, 10.29)	10.24 (9.87, 10.46)	-0.08 (-0.25, 0.08)
Granulicatella adiacens	12	15.04 (14.52, 15.29)	15.1 (14.93, 15.5)	-0.25 (-0.66, 0.08)
Haemophilus influenzae	12	17.09 (16.95, 17.39)	17.62 (17.32, 18.12)	-0.5 (-1.00, 0)
H. influenzae, type b	12	17.31 (17.12, 17.56)	17.55 (17.06, 18.06)	-0.09 (-0.50, 0)
H. influenzae, type a	12	16.02 (15.64, 17.13)	16.34 (16.00, 17.38)	-0.25 (-0.92, 0.25)
H. parainfluenzae	12	33.04 (31.41, 34.84)	30.73 (28.99, 33.55)	1.5 (-0.09, 4)
Kingella kingae	12	17.6 (17.09, 18.12)	17.82 (17.19, 18.27)	0 (-0.92, 0.75)
Klebsiella pneumoniae	12	9.12 (8.91, 9.24)	9.17 (9.07, 9.41)	-0.25 (-0.33, 0.08)
Leuconostoc citreum	12	17.46 (17.05, 18.37)	18.06 (17.57, 18.71)	-0.5 (-1, 0)
Micrococcus luteus	12	38.74 (38.34, 39.95)	39.89 (39.3, 41.37)	-1.08 (-2.92, 0.5)
Neisseria gonorrhoeae	12	21.12 (20.09, 21.38)	22.12 (21.25, 22.55)	-1.08 (-1.50, 0.42)
Neisseria meningitidis	12	19.44 (18.88, 19.96)	21.51 (20.80, 22.09)	-2.27 (-2.92, -0.75)
Pediococcus acidilactici	12	19.52 (19.45, 20.11)	19.66 (19.45, 20.11)	0 (-0.66, 0.66)
Proteus mirabilis	12	13.37 (13.11, 13.54)	13.91 (13.68, 14.17)	-0.58 (-0.92, -0.16)
Providencia stuartii	12	11.54 (11.42, 11.61)	11.87 (11.64, 12.02)	-0.33 (-0.58, -0.08)
Pseudomonas aeruginosa	12	14.54 (14.26, 14.85)	15.05 (14.91, 15.43)	-0.75 (-1, -0.25)
Rothia mucilaginosa	12	16.49 (15.82, 16.95)	17.17 (16.74, 17.45)	-0.58 (-1.42, 0.08)
Staphylococcus aureus	12	11.26 (10.91, 11.61)	11.38 (11.16, 11.61)	-0.16 (-0.34, 0)
Staph epidermidis	12	17.63 (17.29, 17.88)	18.04 (17.62, 18.60)	-0.5 (-1, 0.16)
Stenotrophomonas maltophilia	12	35.06 (32.94, 37.48)	34.52 (33.98, 36.27)	0.5 (-2.83, 1.84)
Streptococcus agalactiae (Group B Strep)	12	8.95 (8.79, 9.18)	9.04 (8.75, 9.35)	-0.08 (-0.17, 0.17)
Streptococcus pneumoniae	12	12.53 (12.14, 12.86)	12.96 (12.60, 13.05)	-0.25 (-0.50, 0)
Streptococcus pneumoniae	12	11.38 (11.28, 11.54)	11.59 (11.41, 11.77)	-0.25 (-0.42, -0.17)
Streptococcus pneumoniae	12	11.78 (11.57, 11.96)	11.82 (11.70, 12.03)	0.00 (-0.42, 0.17)
Streptococcus pneumoniae	12	13.45 (13.12, 13.84)	14.29 (13.71, 14.62)	-0.75 (-1.25, 0)
Streptococcus pyogenes (Group A Strep.)	12	12.08 (11.77, 12.66)	12.72 (12.34, 12.93)	-0.66 (-0.92, -0.08)
Streptococcus sanguinis	12	14.00 (13.58, 14.11)	14.58 (14.33, 14.33)	-0.58 (-1, -0.33)
Total	492	17.07 (16.53, 17.56)	17.52 (17.00, 18.00)	**-0.50 (-0.50, -0.33)**

Table 4.3: Median TTD Difference for 10- 100 CFU/Vial in Hours (by Lots)

Lot #	Paired Sets (#)	Median TTD (Plastic)	Median TTD (Glass)	Median of TTD Differences (Plastic-Glass)
1	164	17.05 (15.45, 17.61)	17.61 (16.00, 18.45)	-0.5 (-0.67, -0.5)
2	164	17.09 (15.67, 18.00)	17.55 (16.11, 18.11)	-0.5 (-0.67, -0.42)
3	164	17.05 (15.54, 17.63)	17.19 (15.97, 18.27)	-0.16 (-0.33, 0)

When stratified by organisms, it was noted that there were only four organisms that favored the compartor glass vial: *Candida glabrata, Haemophilus parainfluenzae, Candida albicans,* and *Stenotrophomonas maltophilia.*

The TTD study demonstrated that the modified plastic device performed equivalently compared to the comparator glass device when stratified by target inoculum level, organisms or lot numbers. It was observed that the median TTD for the modified plastic vial and the predicate glass was 17.07 and 17.52 hours respectively. The median difference was -0.50 hours (95% CI -0.50, -0.33), favoring the plastic vial by approximately 30 minutes as noted in Tables 4.1 and 4.2 above.

Percent Recovery (Detection) Study

The percent recovery (detection) was evaluated in a study of 492 paired sets (41 strains x 3 lots x 4 instruments= 492) at the standard inoculum level of 10 to 100 CFU/vial on four instruments across three lots with 3.0 mL of blood using a diverse set of 41 strains that are commonly isolated from blood. The strains tested is listed in Table 4.2 above.

At standard inoculum level of 10-100 CFU/mL, the detection rate was 100% for both predicate glass and modified plastic devices. Difference in percent recovery was 0%. 95% CI is calculated using a score method for correlated proportion, shown in Table 5.1 for overall performance and in Table 5.2 stratified by lots.

Table 5.1: Overall Percent Recovery Difference for 10- 100 CFU/Vial

Paired Sets (#)	Percent Recovery (Plastic)	Percent Recovery (Glass)	Difference between Percent Recovery of Plastic and Glass
492	100%	100%	0% (-0.77%, 0.77%)

Table 5.2: Percent Recovery Difference for 10- 100 CFU/Vial by Lots

Lot#	Paired Sets (#)	Percent Recovery (Plastic)	Percent Recovery (Glass)	Difference between Percent Recovery of Plastic and Glass
1	164	100%	100%	0% (-2.29%, 2.29%)
2	164	100%	100%	0% (-2.29%, 2.29%)
3	164	100%	100%	0% (-2.29%, 2.29%)

The study demonstrated that the modified plastic device performed equivalently when compared to the comparator glass device. The detection rate was 100% for organisms listed in Table 4.2 at standard inoculum level of 10-100 CFU/vial with 3.0 mL of blood for both the comparator glass and the plastic vials.

***Haemophilus* spp. Detection Re-calculation**

There were four *Haemophilus* spp. tested in the percent recovery (detection) study with 3.0 mL of blood at the inoculum level of 10-100 CFU/vial. The detection rate was 100% (Table 5.1 above) due to the increased blood volume of 3.0 mL in this study.

The *Haemophilus* spp. detection rate was evaluated originally (K151866) for three

target inoculum levels (0-1, 1-10, and 10-100) at 0.5 mL blood with the detection rate range of 8% - 40%. When stratified, the dataset of standard inoculum level 10- 100 CFU/vial with 0.5 and 5.0 mL blood was re-calculated and presented separately in the current submission.

There were a total of 96 paired sets (4 strains x 2 blood vol. x 3 lots x 4 instruments =96) in this re-calculation. The detection rate was 69% (33/48) and 100% (48/48) for 0.5 mL blood and 5.0 mL blood respectively. The detection rate is updated and presented separately according to blood volume at inoculum level of 10- 100 CFU/vial:

The Haemophilus species detection rates were 69% with 0.5 mL blood, and 100% with 5.0 mL

False Negative Rates (Instrument-negative, subculture-positive)

A false negative was defined as a vial that was instrument-negative at the end of protocol (120 hours) yet contains viable organisms by subcultured onto appropriate culture media. The data for this study was generated from the Instrument Time to Detection, Percent Recovery, and Microbial Detection Limit studies.

A total of 110 instrument negative vials were sub-cultured at the end of protocol; 53 glass and 57 plastic vials. All subcultures were negative. There were no false negatives observed in either the glass or plastic device.

False Positive Rate ((Instrument-positive, subculture-negative)

A false positive was defined as instrument positive but subculture negative. False positivity of the BACTEC Peds Plus/F plastic vial was assessed with 0.5, 3, and 5 mL fresh human blood in the previous submission (K151866). No instrument false positive signals were detected in the evaluation.

The plastic device performed equivalently when compared to the glass device in the false positive study.

BD BACTEC Instrument Compatibility

The BACTEC instrument compatibility study was evaluated from the MDL and Percent Recovery studies (180+492= 672 paired sets) across four fluorescent series instruments: BD BACTEC FX, FX40, 9240, and 9050. The study included target inoculum levels of 0-1, 1-10, and 10-100 CFU/mL with 3.0 mL of blood. All four instruments were tested for standard inoculum level of 10-100 CFU/vial; FX and 9240 were tested for inoculum levels of 0-1, 1-10 CFU/mL. Of the 672 paired sets, 596 sets recovered organisms in both the comparator glass and plastic vials. The BACTEC instrument compatibility study is shown in Tables 6.1 and 6.2.

Table 6.1: Summary of Compatibility Study

Instrument	Paired Sets (#)	Median of Time to Detection (TTD) in Hours (95% CI)		
		Plastic	Glass	Median of TTD differences
FX 40	123	17.15 (15.57, 18.1)	17.62 (15.94, 18.6)	-0.50 (-0.50, -0.17)
FX	174	17.59 (16.59, 19.48)	17.78 (17.14, 19.63)	-0.50 (-0.75, -0.33)
9050	123	17.00 (16.00, 18.83)	17.50 (15.67, 19)	-0.33 (-0.50, -0.17)
9240	176	17.45 (16.52, 19.32)	17.63 (16.53, 20.23)	-0.33 (-0.50, -0.17)

Table 6.2: Median of TTD for All Inoculum Levels

Target Inoculum Level	Instrument	Paired Sets (#)	Median Time to Detection (TTD) in Hours (95% CI)		
			Plastic	Glass	Median of TTD differences
0 to 1	FX	9	17.09 (11.65, 40.72)	18.58 (12.15, 37.55)	-0.50 (1.33, 2.17)
	9240	9	25.91 (17.24, 51.71)	25.91 (18.39, 56.87)	-0.17 (-5.00, 3.5)
1 to 10	FX	42	21.56 (17.11, 28.50)	22.59 (17.18, 28.58)	-0.50 (-0.83, 0.09)
	9240	44	19.74 (16.41, 29.29)	20.74 (17.45, 29.51)	-0.34 (-0.67, -0.17)
10 to 100	FX40	123	17.15 (15.57, 18.1)	17.62 (17.07, 18.60)	-0.50 (-0.50, -0.17)
	FX	123	17.14 (15.32, 17.64)	17.57 (15.77, 18.62)	-0.50 (-0.83, -0.33)
	9050	123	17.00 (15.33, 18.83)	17.50 (16.00, 19.00)	-0.50 (-0.50, -0.33)
	9240	123	16.70 (14.87, 17.58)	16.53 (15.07, 18.01)	-0.33 (-0.50, -0.17)

The study demonstrated that the four instruments performed equivalently when the plastic vials were compared to the comparator glass vials.

Antimicrobial Neutralization Capability

The Antimicrobail Neutralization Capability is to support the removal of the current limitation listed in the BACTEC Peds Plus/F Culture Vials (plastic) package insert, "*Based on the neutralization study with Candida albicans and fluconazole, the media showed some degree of neutralization; however the results were inconclusive. The adequacy of antifungal neutralization by resins in the BD BACTEC Peds Plus/F vial (plastic) in unknown.*"

In the antimicrobial neutralization study, fluconazole was evaluated at 1.0 and 2.0 µg/mL with two susceptible strains of *Candida albicans* (expected fluconazole MIC: 0.5 µg/mL) at target inoculum of 10- 100 CFU/vial with 3.0 mL of blood in the Peds Plus/F Culture Vials Soybean-Casein Digest Broth with Resins. Each paired set was tested in triplicates for each strain at each fluconazole concentration:

2 strains x 2 test concentration x 3 (triplicates) = 12 paired-sets

One set of non-resin vials (BACTEC Standard/10 Aerobic/F) with and without fluconazole were tested as controls for each strain at each fluconazole concentration. The non-resin vial with fluconazole served as negative (no growth) and the non-resin vial without fluconazole served as positive (growth) controls. The results are shown in Table 7.

Table 7: Fluconazole/*Candida albicans* Combination Neutralization

Organism	Fluconazole (µg/mL)		Resin Peds Plus/F (# Detected /# tested)		Non-resin Aerobic (# Detected /# tested)	
	Expected MIC	Test Conc.	Plastic	Glass	With Antifungal	w/o Antifungal (Growth Control)
C. albicans #1	0.5	1.0	3/3	3/3	0/1	1/1
		2.0	3/3	3/3	0/1	1/1
C. albicans #2	0.5	1.0	3/3	3/3	0/1	1/1
		2.0	3/3	3/3	0/1	1/1

The study demonstrated that resins in the Peds Plus/F media adequately neutralize fluconazole when testing *Candida albicans* at 10- 100 CFU/vial with 3.0 mL of blood. It upports the removal of the limitation. The following information specific for the antifungal agent/yeast combination is included in the Antimicrobial Activity section under limitation of the product labeling:

"*Studies have demonstrated that the resins present in this medium adequately neutralize the antifungal agent fluconazole with Candida albicans. However, other antifungal agents/yeast combination have not been tested/evaluated*."

b. Matrix comparison:

In seeded analytical studies, the performance of BD BACTEC Peds Plus/F culture medium in plastic vial was compared to that in glass vial, with 3.0 mL of blood, 32 common blood bloodstream bacteria and three yeast species across four fluorescent series instruments (BACTEC FX, FX40, BACTEC 9240, and BACTEC 9050).

3. Clinical studies:

Not applicable; seeded analytical studies to compare the plastic blood culture vials to the glass blood culture vials (comparator).

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Seeded analytical studies demonstrated equivalent performance of the BD BACTEC Peds Plus/F (plastic) blood culture medium when compared to the BD BACTEC Peds Plus/F (glass) blood culture medium.

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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