

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

**A. 510(k) Number:**

k113558

**B. Purpose for Submission:**

To obtain a substantial equivalent determination for a premarket notification for the BD BACTEC Plus Aerobic/F blood culture medium in plastic bottles.

**C. Measurand:**

Aerobic bacteria and yeast

**D. Type of Test:**

Liquid culture medium for recovery of microorganisms (bacteria and yeast) from blood using fluorescent instruments to detect increased CO<sub>2</sub>

**E. Applicant:**

Becton Dickinson and Company

**F. Proprietary and Established Names:**

BD BACTEC Plus Aerobic /F (plastic)

**G. Regulatory Information:**

1. Regulation section:

21 CFR 866.2560

2. Classification:

Class I

3. Product code:

MDB

4. Panel:

83 Microbiology

**H. Intended Use:**

1. Intended use:

The BD BACTEC Plus Aerobic/F medium is used in a qualitative procedure for the aerobic culture and recovery of microorganisms (bacteria and yeast) from blood. The principal use of this medium is with the BD BACTEC fluorescent series instruments.

2. Indications for use:

The BD BACTEC Plus Aerobic/F medium is used in a qualitative procedure for the aerobic culture and recovery of microorganisms (bacteria and yeast) from blood. The principal use of this medium is with the BD BACTEC fluorescent series instruments.

3. Special conditions for use statement(s):

Prescription use

4. Special instrument requirements:

BD BACTEC fluorescent series instrument (BACTEC FX, 9240, 9050)

**I. Device Description:**

The 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<sub>2</sub> 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<sub>2</sub> 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 medium.

Resins have been described for the treatment of blood specimens both prior to and after their inoculation into culture media. Resins have been incorporated into BACTEC culture media to enhance recovery of organisms without a need for special processing.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

BD BACTEC Plus Aerobic /F medium

2. Predicate K number(s):

k921133

3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Intended Use	Qualitative procedure for the aerobic culture and recovery of microorganisms (bacteria and yeast) from blood, with the BD BACTEC fluorescent series instrument	Same
Specimen type	Human blood	Same
Instrumentation	BD BACTEC fluorescent series	Same
Detection Technology	Continuous monitoring; incorporate chemical sensor for detection of CO <sub>2</sub> increases produced by the growth of aerobic bacteria and yeast	Same
Incubation	35°C (±1.5°C) up to 120 hrs	Same

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Bottle	multilayer polycarbonate/nylon/polycarbonate plastic	Glass
Ingredients	Sugar concentration 0.2%	Sugar concentration 0%
Bottle weight	20.9g	113g
Bottle height	5.0 inches	5.6 inches
Sensor	2.6g specific for the plastic bottle geometry	1.75g
Indicator	Increase concentrations of indicator and dye for the sensor changes	Different indicator and dye ratios
Adhesive	Inert adhesion promoter for the adhesion of sensor to the polycarbonate surface of the	Adhesion promoter not required

Differences		
Item	Device	Predicate
	plastic bottles	

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

Not applicable

**L. Test Principle:**

If microorganisms are present in the test sample inoculated into the BACTEC vial, CO<sub>2</sub> will be produced when the organisms metabolize the substrates present in the vial. Increases in the fluorescence of the vial sensor caused by the higher amount of CO<sub>2</sub> are monitored by the BACTEC fluorescent series instrument. Analysis of the rate and amount of CO<sub>2</sub> increase enables the BACTEC fluorescent series instrument to determine if the vial is positive, i.e., that the test sample contains viable organisms.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

The reproducibility study was evaluated by time to detection and recovery, in the Instrument Time to Detection and Recovery studies by using three lots. Both Lots 1 and 3 exhibited no statistically significant difference in time to detection between the new and predicate devices. Lot 2 exhibited a statistically significant difference in time to recovery due to the performance of BACTEC 9050 with *Leuconostoc* spp.

b. *Linearity/assay reportable range:*

Not applicable

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

The range of time-to-detection in hours was  $\leq 72$  hours for each of the organisms listed below. The QC study was performed on three lots and the QC specifications were met.

**Aerobic Medium Organisms**

*Neisseria meningitidis*

ATCC 13090

*Haemophilus influenzae*

ATCC 19418

*Candida glabrata*

ATCC 66032

*Staphylococcus aureus*

ATCC 25923

<i>Streptococcus pneumoniae</i> *	<i>Escherichia coli</i>
ATCC 6305	ATCC 25922
<i>Streptococcus pyogenes</i>	<i>Alcaligenes faecalis</i>
ATCC 19615	ATCC 8750
<i>Pseudomonas aeruginosa</i>	
ATCC 27853	

\*CLSI recommended strain

d. *Detection limit:*

**Microbial Detection Limit study**

The test includes 15 strains tested at two blood volumes, each with three low inoculum levels (0 to 1 and 1 to 10 CFU per bottle) over three lots for a total of 270 paired sets:

$$15 \text{ strains} \times 2 \text{ blood volumes} \times 3 \text{ inoculum levels} \times 3 \text{ lots} = 270$$

Microbial Detection Limit Comparison summary

Condition	Number of Bottles
Growth and detection in both the new and predicate device	200 per device
Growth and detection in the predicate device (glass) only	26 (9.6%)
Growth and detection in the new device (plastic) only	20 (7.4%)
No growth and detection in the both new and predicate devices	24 (8.9%)

There were 26 cultures positive only in the glass device, 20 of the negative cultures in the new plastic device were from the low inoculum (0 to 1 CFU per bottle) level. There were six failures at the 1 to 10 CFU per bottle inoculum level:

*Micrococcus luteus*, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae* and 2 *Candida glabrata*.

There were four false negative cultures that contributed to the overall difference. Two false negatives were with *Leuconostoc* species in the predicate device. Two false negatives were in the new device, one with *Leuconostoc* species and one with *Staphylococcus epidermidis*. The *Staphylococcus epidermidis* was a low inoculum and the inoculum plate count was culture negative.

The study demonstrated that the inoculum was 10- 100 CFU per bottle for the new BD BACTEC Plus Aerobic /F Plastic vial.

e. *Analytical specificity:*

Not applicable

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

Performance of the BD BACTEC Plus Aerobic/F medium in plastic bottles was evaluated during internal analytical studies to demonstrate comparable performance to the predicate device – the BD BACTEC Plus Aerobic/F medium in glass bottles.

**Instrument Time to Detection (TTD) study**

The study included blood volumes, organism and BACTEC fluorescent-series blood culture instrument (BACTEC FX, 9240, 9050). Each organism was inoculated at 10 to 100 CFU per bottle, across two blood volumes (3 mL and 10 mL) over three lots of media for paired sets of the new and predicate devices. This testing was repeated in each BACTEC fluorescent-series blood culture instrument (BACTEC FX, 9240, 9050). There were 726 (98.4%) pair sets positive in both the new and predicate devices.

3 lots x 2 blood volumes x 3 instruments x 41 isolates = 738 pair sets

Organisms with median TTD greater than one hour were summarized in the table below:

Organism	Median TTD Difference (hours)
<i>Candida glabrata</i>	-2.83 Earlier in new device (plastic)
<i>Cryptococcus neoformans</i>	-1.67 Earlier in new device (plastic)
<i>Haemophilus parainfluenzae biotype I</i>	1.33 Earlier in predicate device (glass)
<i>Micrococcus luteus</i>	2.83 Earlier in predicate device (glass)
<i>Leuconostoc spp.</i>	8.00 Earlier in predicate device (glass)

## Percent Recovery (Sensitivity) study

A total of 738 paired sets were evaluated in the Percent Recovery comparison. There were nine paired sets failed to recover organisms in both the new and predicate device (1.6%) in the percent recovery study. One paired set recovered in the predicate device only (the paired new device was negative) and two paired sets recovered in the new device only (the predicate device was negative).

Condition	Number of Bottles
Detected in both the new and predicate devices	726 per device
Detected in the predicate device only	1
Detected in the new device only	2
Not detected in either device	9 per device

The recovery failure included *S. pneumoniae*, *Eikenella corrodens*, and *Leuconostoc* spp. The observed failures of *S. pneumoniae* and *Eikenella corrodens* were replicates in a single instrument type. An additional study was conducted using the failed recovery strains; there were no recovery failure.

## False Positive Rate Study

False positivity was assessed with bottles inoculated with freshly drawn human blood (i.e. 2, 4, 6, and 8 mL). No organisms were added to the bottle. There were 240 paired sets comprised of 80 bottles from each of the three lots. There were two false positive plastic bottles observed but they were inoculated outside of the recommended usage range for the device (<3 mL).

## False Negative Rate Study

The data for this study was generated from the Instrument Time to Detection, Percent Recovery (Sensitivity), and Microbial Detection Limit studies. Bottles from that study that are expected to be positive (i.e., those inoculated with viable organisms) will form the dataset for the False Negative Rate.

A total of 82 paired sets were evaluated to determine the false negatives, with the following results:

Detected in predicate device only	27
Detected in new device only	22
Detected in neither devices (Negatives)	33 paired sets

There was one false negative result with the new device: *Leuconostoc* spp. with 3 mL of blood (plate count 35 CFU).

## BACTEC Instrument Platform Compatibility

Data for this study were from a subset of organisms included in the Instrument Time to Detection study. A total of 246 paired sets (new and predicate devices) were tested in each the BACTEC FX, BACTEC 9240 and BACTEC 9050 fluorescent-series blood culture instruments. There were nine paired sets that failed to recover in both the new and predicate devices in the BACTEC FX instrument.

### Recovery Failures in the BACTEC FX

Device	Organism	Blood Volume	Replicates
New (Plastic) and Predicate Devices (Glass)	<i>S. pneumoniae</i>	3 mL	3
New (Plastic) and Predicate Devices (Glass)	<i>S. pneumoniae</i>	10 mL	3
New (Plastic) and Predicate Devices (Glass)	<i>E. corrodens</i>	10 mL	3

A total of three recovery failures were observed with the BACTEC 9050 instrument. All three recovery failures were associated with *Leuconostoc* spp.

The BACTEC 9050 exhibited a statistically significant difference in time to detection between the new and predicate devices. In the BACTEC 9050, the Wilcoxon median time to detection difference estimate is 0.417 hours (25 minutes) in favor of the predicate device.

### Recovery Failures in the BACTEC 9050

Device	Organism	Blood Volume	Replicates
Predicate Device (Glass)	<i>Leuconostoc</i> spp.	3 mL	1
Predicate Device (Glass)	<i>Leuconostoc</i> spp.	10 mL	1
New Device (Plastic)	<i>Leuconostoc</i> spp.	3 mL	1

There was no recovery failures observed with the BACTEC 9240 instrument.

## Antimicrobial Neutralization Capability

The amount of antimicrobial added to each bottle represents the amount found in 7 mL of blood at or near the peak serum level. The antimicrobials were:

Amoxicillin/Clavulanate	Aztreonam	Ceftazidime
Ciprofloxacin	Ceftriaxone	Cefotaxime
Ertapenem	Fluconazole	Cefepime
Gentamicin	Imipenem	Levofloxacin
Meropenem	Tetracycline	Tigecycline
Ticarcillin/Clavulanate	Piperacillin/Tazobactam	Vancomycin

A supplemental antimicrobial neutralization study, at a lower concentration was conducted with a representative drug in each antimicrobial class: Aztreonam, Ciprofloxacin, Cefotaxime, Cefepime, Gentamicin, Meropenem, Piperacillin, and Tazobactam.

No statistically significant difference was observed in the studies.

*a. Method comparison with predicate device:*

Performance of the new BD BACTEC Plus Aerobic /F Plastic was compare to that of the BACTEC Plus Aerobic/F medium in glass bottles.

*b. Matrix comparison:*

BD BACTEC Plus culture media, human blood volume, common bloodstream pathogens

3. Clinical studies:

Not Applicable, analytical seeded studies for comparison between the new BD BACTEC Plus Aerobic /F Plastic and the BACTEC Plus Aerobic/F medium in glass bottles

*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:

Not Applicable

**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.