

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

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

k073589

**B. Purpose for Submission:**

Addition of Daptomycin to the BD Phoenix™ Automated Microbiology System

**C. Measurand:**

Daptomycin 0.0313 – 16 µg/mL

**D. Type of Test:**

Antimicrobial Susceptibility Test (AST) (Qualitative) colorimetric oxidation-reduction, growth-based

**E. Applicant:**

Becton, Dickinson & Company

**F. Proprietary and Established Names:**

BD Phoenix™ Automated Microbiology System – Daptomycin 0.0313 – 16 µg/mL

**G. Regulatory Information:**

1. Regulation section:

21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System

2. Classification:

II

3. Product code:

LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation

4. Panel:

83 Microbiology

**H. Intended Use:**

1. Intended use(s):

Daptomycin at a concentration of 0.0313 – 16 µg/mL on the Streptococcus ID/AST or AST only Phoenix panels is intended for use with the BD Phoenix Automated Microbiology System for *in vitro* quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most Gram-negative aerobic and facultative anaerobic bacteria isolates from pure culture for Enterobacteriaceae and non – Enterobacteriaceae and most Gram-positive bacteria isolates from pure culture belonging to the genera Staphylococcus, Enterococcus, and Streptococcus.

2. Indication(s) for use:

This premarket notification is indicated for the addition of the antimicrobial agent Daptomycin at concentrations of 0.0313 – 16µg/mL to Streptococcus ID/AST or AST only Phoenix panels for testing *Streptococcus agalactiae*, *Streptococcus dysgalactiae* subsp. *equisimilis*, and *Streptococcus pyogenes*.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Not Applicable

**I. Device Description:**

The BD Phoenix™ Automated Microbiology System includes instrumentation and software, sealed and self-inoculating molded polystyrene trays with 136 micro-wells containing dried reagents, and specific inoculum broth formulations for ID and AST indicator. The organism to be tested must be a pure culture and be preliminarily identified as gram positive or gram negative. Colonies are then suspended in broth, and equated to a 0.5 McFarland with the recommendation to use the BD CrystalSpec™ Nephelometer. A further dilution is made into an AST broth, which contains an AST indicator, prior to inoculating the panel. The AST broth is a cation-adjusted formulation of Mueller-Hinton broth containing 0.01% Tween 80, a wetting agent. After adding the indicator solution to the AST inoculum the color turns to blue. After inoculation and incubation, the color changes to pink then to colorless as reduction in the panel well proceeds.

Inoculated panels are barcode scanned and loaded into the BD Phoenix™ Automated Microbiology System instrument where the panels are incubated at 35°C. The AST has a final inoculum of 5 x 10<sup>5</sup> CFU/ml. The instrument incubates, reads and records the results of the biochemical substrates and antimicrobial agents and interprets the reactions to give an ID of the isolate and MIC value and category interpretation of the antimicrobial agents. Organisms growing in the presence of a given antimicrobial agent reduce the indicator, signaling organism growth and resistance to the antimicrobial agent. Organisms killed or inhibited by a given antimicrobial do not cause reduction of the indicator and therefore do not produce a color change. Additional interpretation is done using software driven “EXPERT” System using rules derived from the CLSI documentation.

Readings are taken every 20 minutes however, the AST result is only available between 4-16 hours. This is only an autoread result; no manual readings are possible with this system.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

VITEK® System

2. Predicate K number(s):

N50510

3. Comparison with predicate:

<b>Similarities</b>		
Item	Device	Predicate
1. Intended Use	Intended for the <i>in vitro</i> rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria.	Same
2. Isolates	Isolated colonies from culture used	Isolated colonies from culture used
3. Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)
4. Incubation Time	<16 hours	<16 hours

Similarities		
Item	Device	Predicate
5. Type of Test	Automated	Automated

Differences		
Item	Device	Predicate
1. Results achieved	Results are determined from serial twofold dilutions of antimicrobial agents	Results are determined from extrapolation of doubling dilutions
2. Sample Preparation	Inoculum density equated to 0.5 McFarland standard	Inoculum density equated to 1.0 McFarland standard
3. Technology	Automated growth based enhanced by use of a redox indicator (colorimetric oxidation-reduction) to detect organism growth.	Automated growth based with detection using an attenuation of light measured by an optical scanner.

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA”; CLSI M7 (M100-S18) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.”

**L. Test Principle:**

The BD Phoenix™ Automated Microbiology System is a broth based microdilution method that utilizes a redox indicator (colorimetric oxidation-reduction) to enhance detection of organism growth. The MIC is determined by comparing growth in wells containing serial two-fold dilutions of an antibiotic to the growth in “growth control wells” which contains no antibiotic.

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

1. Analytical performance:

a. *Precision/Reproducibility:*

Thirty-three isolates were evaluated for site to site and inte-site reproducibility demonstrating >95% reproducibility. The ten isolate study described in the guidance document was used (10 organisms tested 3 times on 3 days at 3 sites).

b. *Linearity/assay reportable range:*

Not applicable

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

The FDA and CLSI recommended Quality Control (QC) isolate, *S. pneumoniae* ATCC 49619 was tested on every test occasion with the reference method and the BD Phoenix™. The mode of the BD Phoenix™ was one well dilution higher than the reference method. The reference method QC results were in range for every day tested. The BD Phoenix™ was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended ranges.

**Daptomycin QC Table**

<b>ORGANISM</b>	<b>conc. (µg/mL)</b>	<b>Reference</b>		<b>BD Phoenix™</b>	
<i>S. pneumoniae</i> ATCC 49619 Expected Range: 0.0625 – 0.5 µg/mL	0.0625	1			
	0.125	71		17	
	0.25	47		100	
	0.5	5		4	
	1			1	

Inoculum density control: The organism suspension density of the ID Broth was equivalent to a 0.5 McFarland standard using the BBL™ CrystalSpec™ Nephelometer which was verified each day of testing. Internal data was used to demonstrate that the use of the BBL™ CrystalSpec™ Nephelometer would produce reproducible results. Five different instruments were used.

d. *Detection limit:*

Not Applicable

e. *Analytical specificity:*

Not Applicable

f. *Assay cut-off:*

Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The broth dilution reference panel was prepared according to FDA and CLSI recommendation and was used to compare with the BD Phoenix™ results. The broth reference panel for *Streptococcus* spp. other than *S. pneumoniae* was set up on Mueller Hinton broth adjusted to a calcium content of 50 mg/mL, supplemented with 2% to 5% lysed horse blood, inoculated with a direct colony suspension and incubated in ambient air at 35°C for 20 – 24 hours as recommended by FDA and CLSI. Clinical testing was performed at several sites. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. The test device had a growth rate of >90%. A comparison was provided to the reference method with the following agreement.

**Strep Accuracy Summary Clinical and Challenge**

	<b>EA Tot</b>	<b>EA N</b>	<b>EA %</b>	<b>Eval EA Tot</b>	<b>Eval EA N</b>	<b>Eval EA %</b>	<b>CA N</b>	<b>CA %</b>	<b>#NS</b>
<b>Clinical</b>	<b>649</b>	<b>615</b>	<b>94.8</b>	<b>644</b>	<b>610</b>	<b>94.7</b>	<b>647</b>	<b>99.7</b>	<b>1</b>
<b>Challenge</b>	<b>19</b>	<b>19</b>	<b>100</b>	<b>19</b>	<b>19</b>	<b>100</b>	<b>19</b>	<b>100</b>	<b>0</b>
<b>Combined</b>	<b>668</b>	<b>634</b>	<b>94.9</b>	<b>663</b>	<b>629</b>	<b>94.9</b>	<b>666</b>	<b>99.7</b>	<b>1</b>

**EA-Essential Agreement**

**CA-Category Agreement**

**NS-Not susceptible; there is only a susceptible category**

Essential agreement (EA) is when the BD Phoenix™ panels agree with the reference test panel results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the BD Phoenix™ panel result interpretation agrees exactly with the reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the BD Phoenix™ and the reference and have on-scale EA.

There appears to be a slight trend where the test device is more susceptible than the reference method as reflected in the Accuracy study. There is one not susceptible isolate due to *S. pyogenes*.

*b. Matrix comparison:*

Not Applicable

3. Clinical studies:

*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:

*S. pyogenes*, *S. agalactiae*, and *S. dysagalactiae* subsp. *equisimilis*  $\leq 1$  (S)

The MIC interpretive criteria for Streptococcus spp. other than *S. pneumoniae* are applicable only to tests performed by broth dilution using Mueller Hinton broth adjusted to a calcium content of 50 mg/mL, supplemented with 2% to 5% lysed horse blood, inoculated with a direct colony suspension and incubated in ambient air at 35°C for 20 – 24 hours as recommended by CLSI.

The current absence of data on Daptomycin resistant isolates precludes defining any categories other than “Susceptible.” Isolates yielding test results suggestive of a “Non-susceptible” category should be retested, and if the result is confirmed, the isolate should be submitted to a reference laboratory for further testing.

**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.