510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION

DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K082913

B. Purpose for Submission:

Addition of Doxycycline to the BD Phoenix™ Automated Microbiology System

C. Measurand:

Doxycycline 0.25-16 µg/mL

D. Type of Test:

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

E. Applicant:

Becton, Dickinson & Company

F. Proprietary and Established Names:

BD Phoenix™ Automated Microbiology System – Doxycycline 0.25-16 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):

   Doxycycline at a concentration of 0.25-16 µg/mL on the Phoenix ™ Gram Positive 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 doxycycline at concentrations of 0.25-16 µg/mL to the Phoenix ™ Gram Positive ID/AST or AST only for testing *S. aureus* (Doxycycline is not the drug of choice in the treatment of any type of staphylococcal infections) and *Enterococcus* group (*Streptococcus faecalis* or *Streptococcus faecium*).

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. 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 continuously incubated at 35°C. The AST has a final inoculum of 5 x 10^5 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 antimicrobic agent reduce the indicator, signaling organism growth and resistance to the antimicrobic agent. Organisms killed or inhibited by a given antimicrobic do not cause reduction of the indicator and therefore do not produce a color change. Additional interpretation is done using a software driven "EXPERT" System using rules derived from the CLSI documentation.

Readings are taken every 20 minutes with an AST result 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:

Similarities		
Item	Device	Predicate
1. Intended Use	Intended for the *in vitro* 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)

Similarities		
Item	Device	Predicate
4. Incubation Time	<16 hours	<16 hours
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:*

   Twelve on-scale isolates were evaluated for site to site and inter 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) isolates, *E. faecalis* ATCC 29212 and *S. aureus* ATCC 29213 were tested on every test occasion with the reference method and the BD Phoenix™. BD Phoenix produced acceptable QC results as compared to the reference method results >95% of the time. 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.

Doxycycline QC Table

ORGANISM	**conc. (µg/mL)**	**Reference**	**BD Phoenix™**
E. faecalis ATCC 29212 Expected Range: 2 – 8 µg/mL	0.5		3
	1		
	2	29	61
	4	56	21
S.aureus ATCC 29213 Expected Range: ≤ 0.5 µg/mL	≤0.25	84	84
	0.5	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 CLSI recommendation and was used to compare with the BD Phoenix™ results. Clinical testing was performed at three 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.

GP Accuracy Summary Clinical and Challenge

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Clinical	932	889	95.4	256	231	90.2	932	879	94.3	23	52	1	0
Challenge	279	277	99.3	82	80	97.6	279	269	96.4	14	10	0	0
Combined	1211	1166	96.3	338	311	92.0	1211	1148	94.8	37	62	1	0

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies

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 were 38 min errors with *E. faecalis* with a min error rate of 19.6% (38/194). Of these min errors, 37 were in essential agreement. If the min errors that are in essential agreement were removed, then the min error rate would be 0.5% which is acceptable.

There were 11 min errors with *E. faecium* with a min error rate of 9.9% which is still acceptable. All 11 min errors were in essential agreement.

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:

<=4(S), 8(I), >= 16(R)

N. Proposed Labeling:

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

O. Conclusion:

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