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

A. 510(k) Number:
   K063811

B. Purpose for Submission:
Removal of the limitations for *Klebsiella oxytoca* and *Proteus mirabilis* with the antimicrobial agent cefazolin at concentrations of 0.5 - 32 µg/mL, for the Gram Negative ID/AST or AST only Phoenix™ panel.

C. Measurands:
Cefazolin at 0.5 - 32 µg/mL

D. Type of Test:
Antimicrobial Susceptibility Test (Quantitative and Qualitative) colorimetric oxidation-reduction, growth-based

E. Applicant:
Becton, Dickinson & Company

F. Proprietary and Established Names:
BD Phoenix™ Automated Microbiology System – Cefazolin at 0.5 - 32 µg/mL, Gram Negative (GN) panel

G. Regulatory Information:

   1. Regulation section:
      21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial
   2. Classification:
      Class II
   3. Product Code:
      LON
   4. Panel:
      83 Microbiology

H. Intended Use:

   1. Intended use(s):
   Cefazolin at 0.5 - 32 µg/mL on the Phoenix™ Gram Negative ID/AST and AST only panels are intended for use with the BD Phoenix™ Automated Microbiology System for the *in vitro* quantitative determination of antimicrobial

susceptibility by minimal inhibitory concentration (MIC) of most gram-negative aerobic and facultative anaerobic bacteria belonging to the family *Enterobacteriaceae* and non – E*nterobacteriaceae* and gram-positive bacteria belonging to the genera *Staphylococcus, Streptococcus* and *Enterococcus*.

2. Indication(s) for use:
Removal of the limitations for *Klebsiella oxytoca* and *Proteus mirabilis* with the antimicrobial agent cefazolin at concentrations of 0.5 - 32 µg/mL for the Gram Negative ID/AST or AST only Phoenix™ panel, using a new cefazolin formulation.

3. Special condition for use statement
Prescription Use Only

4. Special instrument Requirements:
Not Applicable

I. Device Description:

This submission is for the AST panel only. The ID system was not reviewed.

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 the 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 broth containing Tween 80. After adding the indicator solution to the AST inoculum, the color is blue, and after inoculation and incubation, it changes to pink then 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 resulting AST has a final inoculum of 5×10^5 CFU/ml. The instrument incubates, reads and records the results of the biochemical substrates and antimicrobial agents and interprets the reactions to give a 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 software driven "EXPERT" System using rules derived from the Clinical and Laboratory Standards Institute (CLSI). Readings are taken every 20 minutes with an AST result available between 4-16 hours. This is only an autoread result; there are no manual readings possible.

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**
Intended use	Intended for the *in vitro* rapid quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria.	Same
Isolates	Isolated colonies from culture used	Isolated colonies from culture used
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)
Incubation conditions	<16 hours	<16 hours
Type of Test	Automated	Automated

Differences		
Item	**Device**	**Predicate**
Reading algorithm	Results are determined from serial twofold dilutions of antimicrobial agents	Results are determined from extrapolation of doubling dilutions
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.
Sample Preparation	Inoculum density equated to 0.5 McFarland standard	Inoculum density equated to 1.0 McFarland standard

K. Standard/Guidance Document Referenced (if applicable):
"Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA"; CLSI M7 (M100-S16) "Methods

for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard."

L. Test Principle:

The AST portion of 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 contain no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility*
      Fourteen isolates were evaluated. The overall inter-site demonstrated >95% reproducibility and an overall intra-site of > 95%. 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 method*
      The FDA recommended Quality Control isolate *E. coli* ATCC 25922 was performed during the testing of all isolates on each day of testing with the following results. The table below includes the concentrations tested around the expected range with the frequency of the reference and the Phoenix™ results at each concentration. The Phoenix™ was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended ranges most of the time.

Organism	Concentration µg/ml	Reference Results	Phoenix™ Results
Cefazolin			
E. coli ATCC 25922	<=0.5		
Expected Range	1	1	
1-4 µg/mL	**2**	**79**	**94**
	4	4	
	8		1
	NC	1	

   Phoenix produced acceptable QC results as compared to the expected results >95% of the time. The mode for the Phoenix™ is the same as the mode generated by the reference method.

   No trending has been observed.

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 the CLSI recommendation and used to compare with the Phoenix™ results. Clinical testing was performed at four sites on 874 clinical isolates and compared with the reference method results performed at the same time. An additional 182 challenge isolates were tested and compared to an expected result, determined by repeated reference testing. The test device had a growth rate of >95%. A comparison was provided to the reference method with the following agreement.

CZ GN 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	874	841	96.2	609	577	94.7	874	838	95.9	286	28	5	3
Challenge	182	178	97.8	81	78	96.3	182	175	96.2	105	3	2	2
Combined	1056	1019	**96.5**	690	655	94.9	1056	1013	**95.9**	391	31	7	5

EA-Essential Agreement   **maj**-major discrepancies
CA-Category Agreement   **vmj**-very major discrepancies
R-resistant isolates   **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 (Eval) are results that are within the test range and on scale.

The EA and CA were within acceptable limits. The overall vmj rate was 1.3% (5/391), maj rate was 1.1% (7/627) and the min rate was 2.9% (31/1056). Of the 31 min, 22 were within 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:
        Enterobacteriacae ≤ 8 (S), 16(I), ≥ 32(R)

    The expected value range, interpretive criteria and QC are included in the package insert. The labeling is sufficient and it satisfies the requirement of 21 CFR Part 809.10.

N. Conclusion:

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