

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

A. 510(K) Number:
K063824

B. Purpose for Submission:
Removal of the limitation for *Pseudomonas aeruginosa*, the removal of the truncation for *Providencia stuartii* and the addition of organisms groups with Aztreonam 0.5-64 µg/mL – Gram Negative ID/AST or AST only Phoenix™ panels.

C. Measurands:
Aztreonam 0.5-64µg/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 –
Aztreonam (GN) 0.5-64µg/mL.

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):
The testing of aztreonam is for use with the BD Phoenix™ Automated Microbiology System. BD Phoenix is intended for the rapid identification and *in vitro* antimicrobial susceptibility testing of isolates from pure culture of most

aerobic and facultative anaerobic Gram-negative and Gram-positive bacteria of human origin. The BD Phoenix™ Automated Microbiology System is intended 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 for aztreonam at concentrations of 0.5-64 µg/mL to Gram-negative ID/AST or AST only Phoenix™ panels for the removal of the limitations for *Pseudomonas aeruginosa*, the removal or the truncation for *Providencia stuartii* and the addition of organism groups using a new formulation of aztreonam.

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 final inoculum of 5×10^5 CFU/ml. The Phoenix™ AST Broth is poured into the inoculation port of the 51-well side (left side) of the Phoenix Combo (ID/AST) panel. This side contains the ID substrates. The Phoenix AST Broth is poured into inoculation port of the 85-well side (right) of the Phoenix Combo panel. This side contains the antimicrobial agents. The inocula flow down the panel in serpentine fashion, filling the panel wells as the liquid front progresses toward the pad at the bottom of the panel. The pad absorbs excess inoculum. Polyethylene caps are applied to seal the inoculation

ports. An air admittance port is located in the divider area of the panel lid to ensure adequate oxygen tension in the panel for the duration of the test. The instrument reads and records the results of the biochemical substrates and antimicrobial agents contained in the panel and interprets the reactions to give an identification (ID) of the isolate, minimal inhibitory concentration (MIC) values and category interpretations, S, I, or R (sensitive, intermediate, and resistant). The instrument takes readings 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
BD Phoenix ™ System
2. Predicate number (s):
N50510
K020321 (Gatifloxacin)
K020323 (Ofloxacin)
K020322 (Levofloxacin)
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	Rapid ID and <i>in vitro</i> antimicrobial susceptibility testing of isolates of most aerobic and facultative anaerobic Gram positive and Gram negative bacteria.	Same
Sample	Isolated colonies from culture used	Same
Inoculum	Inoculum density to 0.5 McFarland standard	Same
Results Reported	Minimum Inhibitory Concentration (MIC) and categorical interpretation (S/I/R)	Same
Incubation Time	<16 hours	Same
Technology	Automated	Automated

Differences		
Item	Device	Predicate
Results Achieved	Serial two fold dilutions of antimicrobial	Extrapolation of doubling dilutions
Antibiotic	Aztreonam at 0.5-64 µg/mL	Different concentrations depending on antibiotic

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

Inter-site and Intra-site testing demonstrated >95% reproducibility for aztreonam. One site had to repeat testing on one organism due to an instrument error. The ten isolate study described in the guidance document was used (at least 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)

Quality Control was performed in the Phoenix™ System each day of the accuracy study. The tables below include the concentrations tested around the expected range with the frequency of the reference and the Phoenix™ System results at each concentration.

AZTREONAM – Gram Negative (*E. coli* ATCC 25922) – QC Results

<u>Organism</u>	<u>Concentration</u>	<u>Reference Results</u>	<u>Phoenix™ Results</u>
<i>E. coli</i> ATCC 25922 Expected Result Concentration ≤ 0.5 µg/mL	≤0.5	83	95
	1		
	2		
	4		
	8		
	16		
	32		
	64	1	
	≥64		
	No Counts	1	

AZTREONAM – Gram Negative (*P. aeruginosa* ATCC 27853) – QC Results

<u>Organism</u>	<u>Concentration</u>	<u>Reference Results</u>	<u>Phoenix™ Results</u>
<i>P. aeruginosa</i> ATCC 27853 Expected Result Concentration 2-8 µg/mL	≤0.5		
	1		
	2		
	4	73	90
	8	12	4
	16		
	32		
	64		
	≥64		

Phoenix™ System produced acceptable QC results for aztreonam as compared to the reference method results. The results were within the expected result range. The mode for the Phoenix™ results is the same as the mode produced by the reference method.

No QC trending was observed.

Inoculum density control: The organism suspension density of the ID broth was equivalent to a 0.5 McFarland standard using BBL CrystalSpec™ or BD PhoenixSpec™ nephelometer which was verified each day of testing.

- 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. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. There were 1403 isolates overall tested, 1110 were clinical isolates and 293 were challenge isolates. The clinical isolates were comprised of 799 (72.0%) fresh isolates, 245 (22.0%) recent isolates, and 66 (6.0%) stock isolates. The performance data is shown in the table below:

Aztreonam (ATM) –GN Clinical and Challenge Data

	EA TOT	EA N	EA %	Eval EA TOT	Eval EA N	Eval EA %	CA N	CA %	TOTAL R	Vmj N	TOTAL S	Maj N	Min N
Clinical	1110	1084	97.7	248	227	91.5	1021	96.0	105	3	930	5	34
Challenge	293	285	97.3	93	89	95.7	267	91.4	114	1	152	1	23
Combined	1403	1369	97.6	341	316	92.7	1288	95.1	219	4	1082	6	57

EA- Essential Agreement

CA- Category Agreement

R – Resistant isolates

S – Sensitive isolates

Maj – Major discrepancies

Vmj – Very major discrepancies

Min - Minor discrepancies

Eval - Evaluable

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 results (Eval) are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one well variability.

The overall performance of the clinical and challenge is acceptable with acceptable discrepancy rates according to the acceptance criteria in AST Guidelines. There is a slight trending for the Phoenix™ System to be more resistant than the reference method. However, the EA of the Evaluable data showed a combined value of 92.7% which is acceptable.

The device had an acceptable overall growth rate of >95%.

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:

Enterobacteriaceae and Non-*Enterobacteriaceae* :

≤ 8 (S) = Susceptible ; 16 (I) = Intermediate; ≥32 (R) = Resistant

The expected value range, interpretative 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:

This demonstrates acceptable performance as described in the FDA guidance document, “Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA” and therefore the testing of aztreonam 0.5- 64 µg/mL on the BD Phoenix™ Automated Microbiology System for the removal of the limitation for *Pseudomonas aeruginosa*, the removal of the truncation for *Providencia stuartii* and the addition of organism groups is substantially equivalent.