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

A. 510(k) Number:

K173252

B. Purpose for Submission:

Addition of ceftolozane/tazobactam to the BD Phoenix Gram Negative ID/AST and AST only Phoenix panels

C. Measurand:

Ceftolozane/tazobactam 0.25/4 – 32/4 µg/mL

D. Type of Test:

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

E. Applicant:

Becton, Dickinson and Company

F. Proprietary and Established Names:

BD Phoenix Automated Microbiology System- GN Ceftazidime/tazobactam (0.25/4- 32/4 µg/mL)

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.1645 – Short-Term Antimicrobial Susceptibility Test System

2. Classification:

   Class II

3. Product code:

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

4. Panel:

   83 Microbiology

H. Intended Use:

1. Intended use(s):

   The BD Phoenix Automated Microbiology System is intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of Gram Negative aerobic and facultative anaerobic bacteria belonging to the family *Enterobacteriaceae* and non-*Enterobacteriaceae*.

2. Indication(s) for use:

   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 bacterial 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*.

   Ceftazidime/tazobactam has been shown to be active *in vitro* against most strains of microorganisms listed below, as described in the FDA-approved package inserts for this antimicrobial agent.

   Active i*n vitro* and in Clinical Infections Against:
   Gram-negative bacteria
   Enterobacter cloacae
   Escherichia coli
   Klebsiella oxytoca
   Klebsiella pneumoniae
   Proteus mirabilis
   Pseudomonas aeruginosa

   Active *in vitro* but clinical significance is unknown:
   Gram-negative bacteria
   Citrobacter koseri
   Morganella morganii
   Proteus vulgaris
   Providencia stuartii
   Serratia liquefaciens
   Serratis marcescens

3. Special conditions for use statement(s):
   For prescription use only

   Limitation:
   Results for the following antimicrobic/organism combination(s) are suppressed from reporting by the BD Phoenix System:
   - *Ceftolozane/tazobactam: Providencia rettgeri*

4. Special instrument requirements:

   BD Phoenix Instrument and software (V5.83A or higher)
   BD PhoenixSpec Nephelometer
   BD Phoenix AP instrument

I. Device Description:

This submission is for a single drug to be included in the gram negative "ID/AST" or "AST only" panel. The ID portion of the ID/AST combination panel was not subject for review in this submission.

The Phoenix AST method is a broth based microdilution test. The Phoenix panel is a sealed and self-inoculating molded polystyrene tray, with 136 micro-wells containing dried reagents. The ID/AST combination panel includes an ID side (51 wells) with dried substrates for bacterial identification and an AST side (85 wells). The AST panel contains a wide range of two-fold doubling dilution concentrations of antimicrobial agents and growth and fluorescent controls at appropriate well locations. The AST panel does not include wells for isolate identification.

The Phoenix System utilizes a redox indicator for the detection of organism growth in the presence of an antimicrobial agent. 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 ID broth, and equated to a 0.5 McFarland suspension using a nephelometer device. A further dilution is made into AST broth (a cation-adjusted formulation of Mueller-Hinton broth containing 0.010% Tween 80), to which the redox-buffered oxidation-reduction AST indicator solution is added producing a blue color in the wells. The concentration of organisms in the final AST broth suspension is approximately 5 X 10^5 CFU/mL.

The Phoenix AST Broth is poured into the inoculation port of the AST panel and the inoculum flows into the panel, filling panel wells. Polyethylene caps are applied to seal the inoculation ports. An air admittance port is located in the panel lid to ensure adequate oxygen tension in the panel for the duration of the test. Inoculated panels are barcode scanned and loaded into the BD Phoenix Automated Microbiology System instrument where panels are continuously incubated at 35˚C ± 1˚C.

Continuous measurements of changes to the indicator as well as bacterial turbidity are used in the determination of bacterial growth. The instrument takes readings every 20 minutes.

Organisms growing in the presence of a given antimicrobial agent reduce the indicator (changing it to a pink color). This signals organism growth and resistance to that antimicrobial agent. Organisms killed or inhibited by the antimicrobial agent do not cause reduction of the indicator and therefore do not produce a color change. The Phoenix instrument reads and records the results of the antimicrobial tests contained in the panel and interprets the reactions (based on the organism identification) to give a minimal inhibitory concentration (MIC) value and category interpretations (susceptible, intermediate, resistant or not susceptible). AST results are available within 4 to 16 hours. This is an autoread result; no manual readings are possible with this system.

Additional comments concerning specific organism/antimicrobial combinations is provided from the software-driven "EXPERT" system, using rules derived from CLSI documentation.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   BD Phoenix Automated Microbiology System Tigecycline

2. Predicate 510(k) number(s):

   K132909

3. Comparison with predicate:

Table 1: Similarities and Differences of the BD Phoenix Ceftolozane/Tazobactam and the Predicate

Item	Device: BD Phoenix Automated Microbiology System (Ceftolozane/Tazobactam)	Predicate: BD Phoenix Automated Microbiology System Tigecycline (K132909)
Similarities		
Intended Use	Determination of *in vitro* antimicrobial susceptibility testing of aerobic and facultative anaerobic Gram-negative and Gram-positive bacteria	Same
Source of Microorganisms for Testing	Bacterial colonies isolated from culture	Same
Results Achieved	Antimicrobials in serial doubling dilutions	Same
Results Reported	Minimum inhibitory concentration (MIC) and interpretive criteria (i.e., susceptible, intermediate, resistant and non-susceptible)	Same
Incubation Time	Short-term (<16 hours)	Same
Results	MIC and interpretive criteria (i.e., susceptible, intermediate, resistant and non-susceptible)	Same

Item	Device: BD Phoenix Automated Microbiology System (Ceftolozane/Tazobactam)	Predicate: BD Phoenix Automated Microbiology System Tigecycline (K132909)
Technology	Automated growth-based detection	Same
Inoculum Preparation	Manual: PhoenixSpec nephelometer Automated: BD Phoenix AP instrument	Same
Differences		
Antimicrobial	Ceftolozane/Tazobactam	Tigecycline
Reporting Range	• *P. aeruginosa* and *Enterobacteriaceae* (except *Providencia stuartii,* and *Proteus* spp., other than *P. mirabilis*)*:* 0.25/4- 32/4 µg/mL • *Proteus* spp. other than *P. mirabilis:* 1/4- 32/4 µg/mL • *Providencia stuartii*: 0.5/4- 32/4µg/mL	0.25- 16 µg/mL

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

- CLSI M7-A10 "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically"
- CLSI M100-S27 "Performance Standards for Antimicrobial Susceptibility Testing"
- Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA

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" that contain no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Reproducibility testing was conducted at three clinical trial sites. Testing was performed using inocula prepared manually using the PhoenixSpec nephelometer and the automated BD Phoenix AP instrument. The mode MIC value was determined and the reproducibility was calculated based on MIC values falling within ± 1 dilution of the mode MIC value.

   Thirteen strains with known Ceftolozane/tazobactam modal MIC values were provided to the testing sites by BD with isolate identification and expected MIC result

blinded to the testers. The reproducibility set included: *C. freundii* (2), *C. koseri* (1), *E. cloacae* (2), *E. coli* (1), *K. pneumoniae* (2), and *P. aeruginosa* (5). Isolates were tested in triplicate on three separate days as follows:

13 strains x 3 replicates x 3 sites x 3 days= 351 results

Because there were three off-scale results, reproducibility was calculated for best case and worst case scenarios as described in the AST Special Controls Guidance. Results of the inter-site and intra-site reproducibility studies were acceptable and demonstrated best case and worst case results of greater than 95%. A summary of the reproducibility study performance is shown in Table 2 below.

Table 2: Summary of Reproducibility Studies- BD Phoenix Ceftolozane/Tazobactam

Inoculation Method	**Reproducibility**	
	Best Case	Worst Case
Manual PhoenixSpec Nephelometer	99.4% (349/351)	98.9% (347/351)
Phoenix AP Instrument	99.7% (350/351)	98.6% (346/351)

b. Linearity/assay reportable range:

Not applicable

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

Testing of the FDA and CLSI recommended quality control (QC) strains, *E. coli* ATCC 25922, *E. coli* ATCC 35218, *K. pneumoniae* ATCC 700603, and *P. aeruginosa* ATCC 27853 were performed each day of the challenge and clinical study testing with the reference method and with the BD Phoenix Systems. The inocula were standardized using both the Phoenix AP instrument and PhoenixSpec Nephelometer (manual). A sufficient number of tests were performed and all quality control results for the BD Phoenix fell within the acceptable ranges as per the FDA drug label, demonstrating that the BD Phoenix System can consistently produce quality control results in the recommended range for ceftazidime/avibactam. Results demonstrate that acceptable results were achieved >95% of the time by both Phoenix AP and manual inoculum preparation methods as shown in Table 3 below.

Table 3: Summary of Quality Control Results- Ceftolozane/Tazobactam

ORGANISM	**conc.[a] (µg/mL)**	**Reference**	**Inoculum Preparation**	
			Manual (PhoenixSpec)	**Phoenix AP**
E. coli ATCC 25922 Expected Range: Reference: 0.12/4-0.5/4 µg/mL	≤0.25 [b]	117	37	14
	0.5	13	96	71
	1		1	
	2			
	4			

ORGANISM	conc.[a] (µg/mL)	Reference	Inoculum Preparation	
			Manual (PhoenixSpec)	Phoenix AP
Phoenix: ≤0.25/4-0.5/4 µg/mL	8			
	16		1	
	32			
	>32			
E. coli ATCC 35218 Expected Range: Reference: 0.06/4-0.25/4 µg/mL Phoenix: ≤0.25/4µg/mL	≤0.25 [b]	128	131	81
	0.5	1	1	
	1			
	2			
	4		1	
	8			
	16		1	
	32			
	>32	1	1	1
K. pneumoniae ATCC 700603 Expected Range: 0.5/4 – 2/4 µg/mL	≤0.25	1		
	0.5	20		
	1	92	104	70
	2	17	24	14
	4		1	
	8			
	16		2	1
	32			
	>32			
P. aeruginosa ATCC 27853 Expected Range: 0.25/4 – 1/4 µg/mL Phoenix: ≤0.25/4- 1/4 µg/mL	≤0.25 [b]			
	0.5	127	124	76
	1	4	10	6
	2			
	4			
	8			
	16			
	32		1	
	>32			

[a] MIC for ceftolozane in the presence of a fixed concentration of 4µg/mL of tazobactam

[b] The lowest dilution of the BD Phoenix Automated Microbiology System ceftolozane/tazobactam MIC range is ≤0.25 µg/mL. Obtaining this value was considered as an indicator that the quality control test results were acceptable.

The expected range of *K. pneumoniae* ATCC 700603 is 0.5/4 – 2/4µg/mL. This QC isolate has on-scale results for the reporting range of Phoenix Ceftolozane/tazobactam. However, the reporting range on the Phoenix Ceftolozane/tazobactam is 0.25/4 to 32/4 µg/mL and does not provide results lower than 0.25/4 µg/mL. Hence, the expected ranges is not fully covered for: *E. coli* ATCC 25922 (0.12/4 to 0.5/4 µg/mL), *E. coli* ATCC 35218 (0.06/4 to 0.25/4 µg/mL), and *P.*

aeruginosa ATCC 27853 (0.25/4 to 1/4 µg/mL). A MIC value of ≤0.25/4 µg/mL was used to indicate that the results for these three QC organisms were acceptable. The footnote below is included in *Table 1*, *Quality Control Organisms and Expected Results* of the Package Insert for Phoenix GN Panels (Section 3).

> "*The lowest dilution of the BD Phoenix Automated Microbiology System ceftazidime/avibactam MIC range is ≤0.25/4 µg/mL. Obtaining this value was considered as an indicator that the quality control test results were acceptable.*"

In addition, special instruction is noted in FDA approved drug labeling and the most recent CLSI M100 to ensure the β-lactamases production integrity of *E. coli* ATCC 35218 and *K. pneumoniae* ATCC 700603. The footnote below is also included in Table 1:

> "*Refer to the current CLSI M100 table, "MIC: Quality Control Ranges (µg/mL) for Nonfastidious Organisms (Unsupplemented Mueller-Hinton Medium [Cation-Adjusted if Broth]" for additional information on maintaining the integrity of these QC isolates.*"

Growth Rate: Six isolates failed to grow during the clinical study. The overall growth rate during the clinical studies was 99.5%.

Purity Check Plates**:** Purity check plates were inoculated from the standardized organism suspensions for both the Phoenix and reference methods. Any isolate that showed mixed growth on the purity check plate was considered noncompliant and not included in result analysis.

Inoculum Density Control: The PhoenixSpec Nephelometer was used to prepare the inocula for testing of the clinical, challenge, reproducibility and QC isolates. The same inoculum suspension was used for both the Phoenix System and the reference method testing. The BD Phoenix AP instrument was used to standardize the inocula for challenge, QC, and reproducibility isolates. Validation data for both the PhoenixSpec and the Phoenix AP instrument was provided and found to be acceptable.

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 accuracy of results obtained with the Phoenix System was determined by comparison to the CLSI-recommended broth dilution method (reference method). Reference panels were prepared according to CLSI M07-A10 guidelines. During the comparative studies, the reference results were read after 16 to 18 hours of incubation. Sites performed testing on Gram negative isolates using BD Phoenix and reference panel formats as appropriate for gram negative organisms. Antimicrobial agents in the test and reference panels had identical dilution ranges which were appropriate for the interpretive breakpoints of the drug. Testing was performed using at least two different production lots of Phoenix panels, AST broth and AST indicator at each study site. A minimum of three different lots of the Phoenix panel were used across all sites for the entire study. Phoenix and reference panels were inoculated using the same organism suspension.

Growth in the Phoenix panels was determined from data recorded by the instrument. Performance was analyzed using FDA breakpoints for ceftolozane/tazobactam, and results were compared to results obtained by the broth microdilution reference method based on the guidelines provided in the *Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems.*

Clinical and Challenge:

A total of 1210 clinical isolates were tested at the three study sites and included both fresh and stock isolates. Stock isolates comprised 11.6% of total isolates tested. Clinical isolates tested included representatives of species listed in the FDA pharmaceutical drug label and were tested using inocula prepared by the PhoenixSpec nephelometer (manual method).

A total of 135 unique challenge isolates with expected results (expected MIC value of each isolate was the mode after testing with the reference broth dilution multiple times) were also supplied to the testing sites by the sponsor. Challenge isolates were obtained from BD's internal collection and from external laboratories. The challenge isolates were randomized and divided equally among the testing sites. Results obtained for Challenge isolates using the Phoenix System were compared to expected MIC results. Identification and expected results were masked to the study sites. The inocula for the challenge isolates were prepared using both the PhoenixSpec Nephelometer (manual method) and the Phoenix AP (automated method).

The performance evaluation summary of essential and categorical agreement results for clinical and challenge isolates with inocula prepared using the PhoenixSpec nephelometer (manual method) is shown in Table 4.1 below.

Table 4.1: Performance ‡ of Phoenix System with Clinical and Challenge Isoaltes (Manual Preparation)

Ceftolozane/ tazobactam	EA Total	EA N	EA %	Eval EA Total	Eval EA N	Eval EA %	CA N	CA %	#R	Min	Maj	Vmj
Enterobacteriaceae ≤2/4 (Susceptible), 4/4 (Intermediate), ≥8/4 (Resistant)												
Clinical	928	892	96.1	233	215	94.7	896	96.6	47	24	6	2
Challenge	106	106	100	32	32	100	105	99.1	52	1	0	0
Combined	1034	998	96.5	265	247	95.4	1001	96.8	99	25	6	2
P. aeruginosa ≤4/4 (Susceptible), 8/4 (Intermediate), ≥16/4 (Resistant)												
Clinical	116	111	95.7	106	104	98.1	114	98.3	0	2	0	0
Challenge	29	29	100	19	19	100	29	100	11	0	0	0
Combined	145	140	96.6	125	123	98.4	143	98.6	11	2	0	0
Enterobacteriaceae + P. aeruginosa	**1179**	**1138**	**96.5**	**390**	**370**	**94.9**	**1144**	**97.0**	**110**	**27**	**6**	**2**

‡ **EA** – Essential Agreement (+/- 1 doubling dilution)
CA – Category Agreement
EVAL – Evaluable isolates
R – Resistant isolates
Min – Minor discrepancies
Maj – Major discrepancies
Vmj – Very major discrepancies

Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of BD Phoenix within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on scale for both the BD Phoenix panel and the reference method. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the BD Phoenix result.

The phoenix ceftolozane/tazobactam performance met the acceptance criteria. For *Enterobacteriaceae*, the EA and CA were at 96.5% and 96.8%, respectively. For *Pseudomonas aeruginosa* the EA and CA were at 96.6% and 98.6%, respectively. Because of similar performance, the combined *Enterobacteriaceae* + *P. aeruginosa* performance was presented in the final labeling with the footnote below:

> *"Enterobacteriaceae (1034) and Pseudomonas aeruginosa (145) were included in the above combined performance, and performance was similar and acceptable for both.*"

However, a high very major (vmj) discrepancy rate (18.2%, 2/11) was observed with *E. coli* when analyzed separately. The EA and CA observed for 277 *E. coli* during the clinical study were at 98.6% and 98.9%, respectively. To address the observed vmj discrepancy, two additional studies were conducted. In the first study, reference method was tested in replicates on the two vmj *E. coli* isolates. In the second study, a new set of 66 additional resistant *E. coli* isolates were tested by both the reference method and the BD Phoenix panel. No vmj errors observed in these two studies. The footnote below is included for the overall ceftolozane/tazobactam CA in the labeling:

> *"A very major (vmj) error rate of 18.2% (2/11) was observed with E. coli. EA and CA for E. coli were ≥ 98.5%. Reference method testing performed in replicates on the two vmj error E. coli isolates showed no vmj errors. An additional comparative study that included 66 resistant E. coli isolates showed no vmj errors."*

Inoculum Preparation Methods:

A total of 135 challenge organisms (106 *Enterobacteriaceae* and 29 *P. aeruginosa*) were evaluated at one site. The inoculum for the challenge organisms were prepared either manually (using PhoenixSpec) or by using the Phoenix AP instrument. The comparison between manual (PhoenixSpec) method and Phoenix AP is shown in Table 4.2 below. The overall % EA and % CA met the acceptance criteria of greater than or equal to 90%. There were no very major or major discrepancies with either inoculation method.

Table 4.2: Performance of Manual PhoenixSpec and Automated Phoenix AP Inocula

	EA Total	EA N	EA %	Eval EA Total	Eval EA N	Eval EA %	CA N	CA %	#R	Min	Maj	Vmj
Manual	135	135	100	51	51	100	134	99.3	63	1	0	0
Automated	135	133	98.5	51	49	96.1	132	97.8	63	2	1	0

MIC Trending:

Combined *Enterobacteriaceae* + *Pseudomonas aeruginosa*, *P. aeruginosa*, and *Enterobacteriaceae* were evaluated for trending. This trending calculation takes into account MIC values that are determined to be ≤1 and ≥1 doubling dilutions compared to the reference method irrespective whether the device MIC values are on-scale or not. The trending analysis is shown in Table 4.3.

Table 4.3: Trending Analysis of Evaluable Clinical and Challenge Isolates

Ceftolozane/Tazobactam ≤ 0.25 – ≥32µg/mL	Total * (Total # tested)	Difference in MIC as Compared to the CLSI Reference Method				
		≥2 dil. lower	1 dil. lower	Exact	1 dil. higher	≥2 dil. higher
Enterobacteriaceae + *P. aeruginosa*	636 (1179)	21	62	224 (35.22%)	121	208
		83 (13.05%) [a]			329 (51.73%) [a]	
P. aeruginosa	132 (145)	5 (3.79%) [b]		72 (54.55%)	55 (41.67%) [b]	
Enterobacteriaceae	504 (1034)	13	65	152 (30.16%)	249	25
		78 (15.48%) [c]			274 (54.37%) [c]	

* Total number of evaluable results for trending analysis

[a] Difference between isolates trending higher and isolates trending lower for *P. aeruginosa* + *Enterobacteriaceae*: 38.68%; 95% CI (33.87% to 43.22%)

[b] Difference between isolates trending higher and isolates trending lower for *P. aeruginosa:* 37.88%; 95% CI (28.51% to 46.88%)

[c] Difference between isolates trending higher and isolates trending lower for *Enterobacteriaceae*: 38.89%; 95% CI (33.34% to 44.07%)

A trend towards higher MIC was observed with claimed *Enterobacteriaceae* isolates and *P. aeruginosa* when compared to the CLSI broth microdilution reference method. This trending and the potential for occurrence of major discrepancies when testing clinical and challenge isolate results with the Phoenix Ceftolozane/tazobactam was addressed by adding the following footnote:

BD Phoenix Ceftolozane/Tazobactam MIC values tended to be in exact agreement or at least one doubling dilution higher when testing Enterobacteriaceae or P. aeruginosa compared to the reference broth micro-dilution.

Reportable Ranges:

Different reportable ranges for Ceftolozane/tazobactam were evaluated with acceptable performance for the organimsm groups below:

≤0.25/4 - ≥32/4 µg/mL for *Enterobacteriaceae* and *Pseudomonas aeruginosa*
≤0.5/4 - ≥32/4 µg/mL for *Providencia stuartii*
≤1/4 - ≥32/4 µg/mL for *Proteus* spp. other than *Proteus mirabilis*

Enzyme Group Characterization/Resistance Markers Information:

Third-two *Enterobacteriaceae* with beta-lactamases were included in the ceftolozane/tazobactam comparative studies. They were AmpC (2), KPC (14), OXA (7), CTX-M (8), TEM (10), and SHV (7). The *Enterobacteriaceae* included *Enterobacter cloacae, E. coli, Klebsiella oxytoca,* and *Klebsiella pneumoniae.*

The study indicated that in the presence of ESBL β-lactamase TEM, *E. coli* (7) were susceptible to Ceftolozane/Tazobactam with MIC <2/4 µg/mL; *K. pneumoniae* (6) demonstrated MIC values ranging from ≤0.25/4 to >32/4 µg/mL in the presence of β-lactamase CTX-M, OXA, TEM, and/or SHV. For KPC, *K. pneumoniae* (8) had MIC ranging from ≤0.25/4 to >32/4 µg/mL; however, *Enterobacter cloacae* (5) and *K. oxytoca* (1) were susceptible with MIC <2/4 µg/mL.

In addition, seven metallo-beta-lactamase producing *Pseudomonas aeruginosa* were tested and demonstrated resistance (≥32/4µg/mL) to Ceftolozane/tazobactam. The following limitation was added to the Ceftolozane/tazobactam labeling regarding other resistance markers and enzyme characterization:

"*Enzyme group characterization was not available at the time of comparative testing, and therefore the performance of the BD Phoenix Ceftolozane/Tazobactam is unknown for the following: Pseudomonas aeruginosa (chromosomal AmpC, loss of OprD, and up-regulation MexXY, MexAB); Enterobacteriaceae (metallo-beta-lactamases).*"

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:

The FDA susceptibility interpretive criteria for Ceftolozane/tazobactam are as listed in Table 5.

Table 5. Interpretive Criteria for Ceftolozane/tazobactam (µg/mL)

	Susceptible (S)	Intermediate (I)	Resistant (R)
Enterobacteriaceae	≤2/4	4/4	≥8/4
P. aeruginosa	≤4/4	8/4	≥16/4

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.