

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

A. 510(k) Number:

k062207

B. Purpose for Submission:

To add additional organism groups to cefuroxime on the BD Phoenix™ gram-negative ID/AST or AST only Phoenix panels and to remove limitation for *Klebsiella pneumoniae*

C. Measurand:

Cefuroxime 1 – 64 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 – Cefuroxime 1 – 64 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):
Cefuroxime at 1 – 64 µg/mL on the BD Phoenix™ Gram Negative (GN) ID/AST or AST only panel 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 application is indicated for cefuroxime with additional organism groups at concentrations of 1 – 64 µg/mL to Gram-negative ID/AST or AST only Phoenix panels and removal of the limitation for *Klebsiella pneumoniae* from the original premarket notification (k033362).

3. Special conditions for use statement(s):

For prescription use only

This submission is not intended for the removal of a limitation with *Providencia rettgeri* which remains as: “Results for *Providencia rettgeri* have been excluded in the Phoenix™ System and therefore no results will be reported. An alternate method should be performed when these combinations are identified.”

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 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 is blue and after inoculation and incubation 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 35⁰C. The AST has a final inoculum of 5 x 10⁵ 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 NCCLS 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 510(k) number(s):
N50510
3. Comparison with predicate:

Similarities		
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
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	Automated growth based with detection using an attenuation of light

Differences		
Item	Device	Predicate
	(colorimetric oxidation-reduction) to detect organism growth.	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-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 contains no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

The data included in this submission were acquired during the clinical studies performed at multiple sites and described in the previous submission for cefuroxime (k033362). The accuracy performance data for the additional organism report groups for clinical and challenge isolates and each antimicrobial agent are contained in this submission. The Reproducibility studies and Quality Control (QC) performance data as previously submitted are presented for reference purposes only.

In addition to the above clinical trial study, a supplemental study using challenge isolates of resistant *Klebsiella pneumoniae* were evaluated to remove the limitation for this report group in the previous submission for Cefuroxime - 1-64 µg/mL (k033362, April 13, 2004). The accuracy performance data for this supplemental study are contained in this submission. The QC performance was within the expected ranges as shown under the “Traceability, Stability.... section (c)”.

a. *Precision/Reproducibility:*

Intersite and Intrasite testing demonstrated >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):*
Quality Control was performed on every test occasion with the following results. BD Phoenix™ produced acceptable QC results as compared to the reference method results >95% of the time.

Cefuroxime Gram Negative QC Table

ORGANISM	conc. (µg/mL)	Reference	BD Phoenix™
<i>E. coli</i> ATCC 25922 Exp. Range : 2 – 8 µg/mL	4	202	361
	8	178	22
	16	3	1
	32		1
	>64	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 the CLSI recommendation and used to compare with the BD Phoenix™ results. 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. Performance chart below includes all data, original with additional organisms and *K. pneumoniae*.

GN Accuracy Summary Clinical and Challenge with Additional Organisms and *K. pneumoniae* Included

Report Group	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Additional Organisms	232	226	97.4	78	74	94.9	225	97	185	6	1	0
<i>K. pneumoniae</i>	155	150	96.8	45	44	97.8	151	97.4	155	0	0	4
Combined (Original Data, Additional Org including <i>K. pneumoniae</i>)	1868	1786	95.6	1189	1140	95.9	1743	93.3	689	103	9	13

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates

vmj – very major discrepancies
maj - 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 (SIR) 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.

A trend was observed with the *K. pneumoniae* group where the BD Phoenix™ appears to be more susceptible when compared to expected results of the challenge strains.

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 ≤8(S), 16(I), ≥32(R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC for gram negative panels are included in the package insert. The labeling is sufficient and 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.