

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

A. 510(k) Number:
K053241

B. Purpose for Submission:
Addition of the antibiotic cefoxitin at concentrations of 1-32 µg/mL to the Gram Positive ID/AST and AST only Phoenix™ panels.

C. Measurand:
Cefoxitin at 1 - 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 – Cefoxitin 1 - 32 µg/mL Gram Positive 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):
Cefoxitin at concentrations of 1 – 32 µg/mL on the Phoenix™ Gram Positive ID/AST and AST only panel is intended for use with the Phoenix™ system in clinical laboratories as an *in vitro* test to determine the susceptibility of *Staphylococcus species* to antimicrobial agents when used as instructed in the Phoenix™ system user's manual.

The BD Phoenix™ Gram Positive (GP) Panel: The Phoenix™ Automated Microbiology System is intended for the *in vitro* rapid identification (ID) of gram positive bacteria from pure culture belonging to the genera *Staphylococcus*, *Enterococcus*, *Streptococcus* and other gram positive cocci.

The BD Phoenix™ Automated Microbiology System is intended 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 - *Enterobacteriaceae* and gram-positive bacteria belonging to the genera *Staphylococcus*, *Streptococcus* and *Enterococcus*.

2. Indication(s) for use:

This submission is for the addition of the antibiotic cefoxitin at concentrations of 1-32 µg/mL to the Phoenix™ GP ID/AST and AST only panels. It will also be used as an *in vitro* test to predict *mecA*-mediated resistant *Staphylococcus aureus* in these panels.

3. Special condition for use statement(s):

Staphylococci resistant to methicillin/oxacillin should be considered resistant to cefoxitin.

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 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 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 Clinical and Laboratory Standards Institute (CLSI).

Readings are taken every 20 minutes with an ID result available between 2-12 hours and 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 <i>in vitro</i> rapid identification (ID) and 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.

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-S15) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.”

L. Test Principle:

The system employs conventional, colorimetric, fluorogenic and chromogenic substrates to identify the genus and species of the isolate. 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:

Of the nineteen isolates included in the reproducibility study, eleven (11) had on-scale modes for cefoxitin that were evaluated for site to site and inter site reproducibility; Intersite and Intrasite testing both 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 method):

The CLSI recommended Quality Control strain *S. aureus* 29213 was tested a sufficient number of times with acceptable results on most testing days with the reference method. The Phoenix™ results demonstrated that the system can produce QC results in the recommended range.

The following table provides the frequency of the results in each concentration tested with the expected range stated.

Organism	Concentration µg/mL	Reference results	Phoenix™ results
<i>S. aureus</i> ATCC 29213 Expected range 1 - 4 µg/mL	≤0.5		
	1		
	2	31	125
	4	205	124
	8		
	16		
	>16		1

The QC results for the Phoenix™ are bimodal within the expected range; Phoenix™ produced acceptable QC results as compared to the reference method results >95% of the time.

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. The testing included both fresh clinical isolates and stock isolates along with a challenge set with

known results. A total of 1164 isolates were tested, 47 were Challenge isolates, and 1117 were Clinical isolates. The clinical isolates were comprised of 53.2% fresh, 31.6% recent and 15.2% stock organisms with the following performance (see table below).

Following CLSI guidelines and the BDXpert software driven rules System, the cefoxitin results for *Staphylococcus* would normally be interpreted as “Resistant” when the oxacillin result is resistant. The overall performance data for all *Staphylococcus* isolates, with the influence of the oxacillin interpretation result, demonstrated an EA rate of 96.3%, an Evaluable EA rate of 95.1% and a CA rate of 96.5%.

The table below contains the performance data for *Staphylococcus* species.

Clinical and Challenge Data for *Staphylococcus* species with oxacillin interpretation and BDXpert Rules applied

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Clinical	1117	1075	96.2	751	714	95.1	1117	1077	96.4	472	35	1	4
Challenge	47	46	97.9	11	11	100.0	47	46	97.9	17	1	0	0
Combined	1164	1121	96.3	762	725	95.1	1164	1123	96.5	489	36	1	4

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

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.

maj-major discrepancies

vmj-very major discrepancies

min- minor discrepancies

There is a slight trend for the test device results to be more susceptible than the reference method results.

The test device had a growth rate of >95%.

Evaluation of Cefoxitin to predict *mecA*-mediated resistance in *S. aureus*:

A comparative internal study was performed which evaluated 553 *S. aureus* strains (298 *mecA* positive and 255 *mecA* negative characterized by PCR) to Phoenix™ cefoxitin (FOX) test results. Using ≥ 8 µg/ml as the cefoxitin breakpoint, the Phoenix™ FOX was able to show 100% sensitivity for detection of *mecA*-mediated resistance (212/212) and demonstrated 99.2% specificity (127/128) for *S. aureus*, when compared to PCR. BDXpert software driven rules will indicate this resistance marker only for *S. aureus*.

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:

Interpretive criteria = ≤ 8 (S), 16 (I), ≥ 32 (R) for *Staphylococcus species*.

Cefoxitin at a breakpoint of ≥ 8 $\mu\text{g/ml}$ will be used to predict *mecA*-mediated resistance in *S. aureus* only.

The expected value range, interpretive criteria and QC for cefoxitin utilized in gram positive panels are the same as those recommended by FDA and CLSI. All values will be included in the package insert.

O. Conclusion:

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