

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

A. 510(k) Number:

K052250

B. Purpose for Submission:

Addition of the antibiotic tobramycin at concentrations of 0.5 – 16 µg/mL to the Gram Positive ID/AST and AST only Phoenix™ panels.

C. Measurand:

Tobramycin at 0.5 – 16 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 – Tobramycin 0.5 - 16 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):
BD Phoenix™ Automated Microbiology System:
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*.

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™ GP ID/AST and AST only panels are also intended for the quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria isolates from pure culture belonging to the genera *Staphylococcus*, *Streptococcus*, and *Enterococcus* when used with the BD Phoenix™ Automated Microbiology System.

2. Indication(s) for use:

This submission is for the addition of the tobramycin at concentrations of 0.5 – 16 µg/mL to the Phoenix™ GP ID/AST and AST only panels.

Tobramycin has been shown to be active *in vitro* and in clinical infections against most strains of *S. aureus*.

3. Special condition for use statement(s):

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, nine (9) had on-scale modes for tobramycin 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), although only nine isolates produced on-scale modes. Three organisms – one *Staphylococcus spp.*, one *S. aureus*, and one *S. hyicus* - produced off-scale results or no result, among the three sites.

b. Linearity/assay reportable range:

Not applicable

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

The CLSI recommended Quality Control strains *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 0.12 - 1 µg/mL	≤0.5	240	9
	1	7	233
	2	1	3
	4		
	8		1
	16		
	>16		

There is a trend for the mode for the Phoenix™ results to be more resistant than the mode for the reference method for the QC recommended organism *S. aureus* ATCC 29213, if only by one dilution, but still producing acceptable QC 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. Additional testing on 5 streptococcal strains was performed to demonstrate acceptable performance for streptococcal species.

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 1220 isolates were tested, 46 were Challenge isolates, and 1174 were Clinical isolates. The clinical isolates were comprised of 52.0% fresh, 33.0% recent and 15.0% stock organisms with the following performance (see table below).

Of the total number of isolates tested, 953 were appropriate strains for this panel. The remaining 267 strains of *S. epidermidis* were not included in the performance data evaluation; MIC's and SIR interpretation results for *S. epidermidis* will not be reported.

The FDA tobramycin drug insert provides breakpoints only for *S. aureus*. With the exception of *S. aureus*, SIR interpretation results from all other Gram positive organisms against tobramycin will be automatically suppressed from reporting by the Phoenix BDxpert Triggered Rules software; only MIC results will be reported.

Therefore, the table below contains the performance data for *S. aureus* and *Staphylococcus* CNS other than *S. epidermidis*, for EA and Eval EA, and *S. aureus* only for CA and the error rates.

Clinical and Challenge Data for *S. aureus* and *Staphylococcus* CNS other than *S. epidermidis*

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Clinical	914	855	93.5	87	74	85.1	769	757	98.4	269	5	1	6
Challenge	39	36	92.3	5	5	100.0	28	28	100.0	7	0	0	0
Combined	953	891	93.5	92	79	85.9	797	785	98.5	276	5	1	6

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

maj-major discrepancies

vmj-very 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 agrees exactly with the reference panel result interpretation. Evaluable (Eval) are results that are within the test range and on scale.

Because of the limited number of on-scale results, as compared to the total number of *S. aureus* tested, no real trending was observed.

The test device had a 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:

Interpretive criteria = ≤ 4 (S), 8 (I), ≥ 16 (R) for *Staphylococcus aureus*.

The expected value range, interpretive criteria and QC for tobramycin utilized in gram positive panels are the same for *Staphylococcus aureus* 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 for tobramycin against *S. aureus* only