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

A. 510(k) Number:

k131331

B. Purpose for Submission:

Modification of a portion of the algorithm for Vancomycin (VA_18, 0.5 - 32µg/mL) with *Enterococcus* species and *Staphylococcus* species and updates for software from the last software cleared by FDA under k040099 through version 6.01

C. Measurand:

Vancomycin 0.5-32µg/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- Vancomycin 0.5-32µg/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):

   The BD 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,* other gram positive cocci and gram positive bacilli. The BD Phoenix Automated Microbiology System is also intended for the quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most gram positive bacteria isolates from pure culture belonging to the genera *Staphylococcus* and *Enterococcus.*

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 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.*

   This premarket notification is for a modification of a portion of the algorithm for Vancomycin (0.5-32 μg/mL) with *Enterococcus* species and *Staphylococcus* species and updates for software from the last software cleared by FDA under K040099 through version 6.01.

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

   Active *In Vitro* and in Clinical Infections Against:

   Enterococci (e.g., *Enterococcus faecalis*)
   Staphylococci, including *Staphylococcus aureus* and *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains).

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   BD Phoenix™ Automated Microbiology System, software version 6.01

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 BD nephelometer devices. A further dilution is made into an AST broth, which turns to blue after AST broth indicator is added prior to inoculating the panel. The AST broth is a cation-adjusted formulation of Mueller-Hinton broth containing 0.01% Tween 80, and has a final inoculum of approximately 5×10^5 CFU/mL. After inoculation and incubation, the color 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 incubated at 35°C and continuously measured of changes to the indicator as well as bacterial turbidity to determine the bacterial growth in the presence of an antimicrobial agent. 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 CLSI 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
Intended Use	The BD Phoenix™ Automated Microbiology System 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 VITEK System is intended for the determination of *in vitro* susceptibility to antimicrobial agents for rapidly growing, aerobic and/or facultative anaerobic Gram-negative and Gram-positive bacteria.
Sample	Isolated colonies from culture	Same
Result reported	Minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
Incubation Time	<16 hours	<16 hours
Type of Test	Automated	Same

Differences		
Item	Device	Predicate
Results achieved (MIC)	Serial twofold dilutions of antimicrobial	Computer-assisted 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 Systems; Guidance for Industry and FDA"

CLSI M7-A8, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically"

CLSI M100, S22 "Performance Standards for Antimicrobial Susceptibility Testing"

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" which contains no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility testing was performed at three sites (one internal and two external) in triplicate on three separate days using inoculum prepared manually and inoculum using the BD Phoenix AP. Inter-site and Intra-site testing demonstrated best-case reproducibility of ≥95%.

b. Linearity/assay reportable range:

Not applicable

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

The FDA and CLSI recommended QC isolates, *E. faecalis* ATCC 29212 and *S. aureus* ATCC 29213 were with the reference method and the BD Phoenix™ Automated Microbiology System. Inoculum density was standardized by manual (CrystalSpec or BD PhoenixSpec) or automated (BD Phoenix AP) methods. The BD Phoenix™ was tested sufficient number of times to demonstrate that the system can produce acceptable range results >95% of the time by both inoculum preparation methods.

Vancomycin QC Table

ORGANISM	conc. (µg/mL)	Manual (CrystalSpec/ PhoenixSpec)		BD Phoenix™ AP	
		Ref	Phoenix	Ref	Phoenix
E. faecalis ATCC 29212 Expected Range: 1-4µg/mL	1				
	2	75	116	75	84
	4	1		1	
	8				
	16				
	32		1		
S. aureus ATCC 29213	≤0.5	22	24	22	21
	1	54	93	54	62

Expected Range: ≤ 0.5-2 µg/mL	2	1		1	
	4				

Inoculum density control: The organism suspension density of the ID broth was standardized using BD nephelometer device which was verified each day of testing. Internal validation data was used to demonstrate that the use of BD nephelometer devices would produce reproducible results.

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 CLSI recommendation and was used to compare with the BD Phoenix™ results. Clinical testing was performed at three sites. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. The test device had a growth rate of >90%. A comparison was provided to the reference method with the following agreement.

GP Accuracy Summary Clinical and Challenge

	EA Tot	**EA N**	**EA %**	**Eval EA Tot**	**Eval EA N**	**Eval EA %**	**CA Tot**	**CA N**	**CA %**	**#R**	**min**	**maj**	**vmj**
Clinical	1425	1411	99.0	821	809	98.5	1425	1422	99.8	100	1	0	2
Challenge	113	112	99.1	52	51	98.1	113	110	97.3	25	3	0	0
Combined	1538	1523	99.0	873	860	98.5	1538	1532	99.6	125	4	0	2

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 EA is when the MIC result is on scale for both the BD Phoenix™ and the reference and have on-scale EA.

There were a total of two very major discrepancies (1.6% discrepancy rate). However, the acceptable number of discrepancy for 125 resistant isolates is three and the two vmj discrepancies were within the acceptable limit.

The performance of the BD Phoenix AP was also evaluated in the challenge study:

Comparison challenge Data- Manual and automated Phoenix AP

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Manual	113	112	99.1	52	51	98.1	113	110	97.3	25	3	0	0
Phoenix AP	114	114	100	56	56	100	114	112	98.2	25	2	0	0

Validation study

An additional validation study comprising of stock, recently acquired, and Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) isolates was conducted internally. The recently acquired isolates were clinical isolates obtained from four external clinical sites. There were a total of 435 stock, 482 recently acquired and 10 NARSA isolates. A comparison was provided to the reference method with the following agreement:

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Validation	927	917	98.9	410	403	98.3	927	904	97.5	366	19	4	0

E. faecalis: There were four major discrepancies with false resistance of >32µg/mL; the major error rate was within the acceptable rate of 3%, at 1.6% (4/256).

E. faecium and other *Enterococcus* spp.: There were 304 *E. faecium,* five other *Enterococcus* spp. isolates of >32µg/mL and one 32µg/mL for *E. faecium*. No major or very major discrepancies were observed. The performance data met the acceptance criteria.

Staphylococcus aureus: There were ten vancomycin resistant *S. aureus* (VRSA) tested in the validation study, resulting in no very major discrepancies or major discrepancies. However, there were five minor discrepancies at the breakpoint (BP) of 4µg/mL for vancomycin intermediate (VI); the Phoenix result was one dilution lower at 2µg/mL (susceptible) 27.8% (5/18) of the time. The following was included in the Expert triggered rule when reporting vancomycin of 2µg/mL for *S. aureus*:

> "Vancomycin intermediate isolates of *S. aureus* (VISA) with a reference method MIC value of 4mcg/mL may be reported as having an MIC of 2mcg/mL. *S. aureus* isolates with an MIC of 2 mcg/mL (susceptible) should have susceptibility confirmed using a non-automated MIC method or by submission of the isolate to a reference laboratory as appropriate."

The results for *S. epidermidis* and coagulase-negative *Staphylococci* were acceptable.

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:

Enterococci:	≤4, 8-16, ≥32
S. aureus:	≤2, 4-8, ≥16
Coagulase-negative Staphylococcus:	≤4, 8-16, ≥32

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.