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

A. 510(k) Number:
K072668

B. Purpose for Submission:
The addition of the new formulation for the antibiotic Vancomycin to the VITEK®2 Antimicrobial Susceptibility Test (AST) System.

C. Measurand
VITEK ® 2 Gram Positive Vancomycin (≤ 0.5 - ≥ 32 µg/ml)

D. Type of Test:
Quantitative growth based detection algorithm using optics light detection

E. Applicant:
bioMerieux, Inc.

F. Proprietary and Established Names:
Vitek®2 Gram Positive Vancomycin.

G. Regulatory Information:
1. Regulation section:
   866.1645 Short-Term Antimicrobial Susceptibility Test 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 VITEK ® 2 Gram Positive Susceptibility Card is intended for use with VITEK ® 2 system in clinical laboratories as an *in vitro* test to determine the susceptibility of gram positive organisms to Vancomycin when used as instructed in the System Product Information manual.

   The VITEK® 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK® 2 and VITEK® 2 Compact Systems for the automated quantitative or qualitative susceptibility testing of isolated colonies for the most clinically significant aerobic gram negative bacilli, *Staphylococcus spp., Enterococcus spp., Streptococcus agalactiae,* and *S. pneumoniae.*

2. Indication(s) for use:
   This submission is for the addition of a new formulation of the antibiotic vancomycin at concentrations of 1, 2, 4, 8, and 16 µg/mL to VITEK® Gram Positive (AST-GP) panels. Vitek 2® Gram Positive Vancomycin is designed for antimicrobial susceptibility testing of *Enterococcus* spp., *Staphylococcus* spp., and *Streptococcus agalactiae.* VITEK 2® Gram Positive Vancomycin is a quantitative test. It is intended for use with the VITEK 2® and VITEK 2® Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents.

3. Special condition for use statement(s):
   The VITEK 2 AST cards cannot be used with direct clinical specimens or other sources containing mixed flora. Any change or modification in the procedure may affect the results.

   Prescription Use Only

4. Special instrument Requirements:
   Not Applicable

I. Device Description:

Each VITEK® 2 test card contains 64 microwells. A control well, that contains only microbiological culture medium is resident on all cards, with the remaining wells containing pre measured amounts of a specific antibiotic combined with culture medium. A suspension of organism from a pure culture is made in 0.45-0.5% sterile saline in a clear plastic polystyrene tube and standardized to a McFarland 0.5 standard using the DensiChek Turbidity meter. The desired card(s) are placed in the cassette along with an empty tube for the susceptibility card. The cassette is placed into the VITEK® 2 instrument where a susceptibility test will be automatically diluted from the ID suspension by the Vitek® 2. Alternately, a manual dilution specific for each AST product type card can be made. The cards are then automatically vacuum filled; the tubes are cut and the cards sealed prior to proceeding to the Incubator Loading Station. Cards are then transferred from the cassette into the carousel for incubation (35.5° C) and optical scanning during testing. Readings are performed every 15 minutes.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Vitek 2 Gram Positive Daptomycin

2. Predicate K number(s):
   K050075

3. Comparison with predicate

Similarities		
Item	**Device**	**Predicate**
Test Card	VITEK® 2 card format with base broth	same
Instrument	VITEK® 2 and VITEK ®2 Compact System	same
Dilution methods	Auto-dilution and manual	same
Differences		
Item	**Device**	**Predicate**
Antibiotic	Vancomycin	Daptomycin
Test Organisms	*Staphylococcus* spp., *Enterococcus* spp., and *Streptococcus agalactiae*	*Enterococcus faecalis, Staphylococcus aureus, Streptococcus agalactiae, Enterococcus faecium, Staphylococcus epidermidis* and *Staphylococcus haemolyticus*
Reading algorithm	Unique for new formulation of Vancomycin.	Unique for Daptomycin

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-S16) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard"

L. Test Principle:

Optics systems use visible light to directly measure organism growth. These transmittance optics are based on an initial light reading of a well before significant growth has begun. Periodic light transmittance samplings of the same well measure organism growth by how much light is prevented from going through the well. An interpretive call is made between 4 and 16 hours with the majority of the *S. pneumoniae* between 5 and 9 hours. The VITEK Susceptibility Card test is based on the microdilution minimum inhibitory concentration (MIC) technique with concentrations equivalent to standard method concentrations. Several parameters based on the growth characteristics observed are used to provide appropriate input for the MIC calculations. Discriminate analysis is used to develop the algorithm that determines the susceptibility result for all antimicrobials on the VITEK 2 system. The MIC result must be linked to an organism identification in order to determine a category interpretation. A category interpretation will be reported along with a MIC.

M. Performance Characteristics (if/when applicable):

An external evaluation was conducted with fresh and stock clinical isolates and challenge strains. The external evaluations were designed to confirm the acceptability of the new formula of VITEK 2 Gram Positive Vancomycin, using both the auto-dilution and the manual dilution methods, by comparing its performance with the CLSI broth microdilution reference method read at 24 hours.

This submission is for the AST Panel only. The ID System was not reviewed.

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was demonstrated using a panel of 10 *Staphylococcus aureus* isolates in triplicate, each for three days at three sites with VITEK 2 AST-GP Vancomycin (VA2), for a total of 270 results. All results were > 95 % reproducible for both dilutions methods.

b. Linearity/assay reportable range:

Not Applicable

c. Traceability (controls, calibrators, or method):

The recommended QC isolates were tested by VITEK 2 AST cards containing Vancomycin, and broth microdilution plates containing Vancomycin. QC organisms *Staphylococcus aureus* ATCC 29212 and *Enterococcus faecalis* ATCC 29213 were tested at each clinical trial site. One *Streptococcus pneumoniae* ATCC 49619 quality control organism was tested throughout comparative testing with *Streptococcus agalactiae* by the reference method only (data not presented). This was done to perform further quality control of the broth microdilution panels supplemented with lysed horse blood. The VITEK 2 was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended range > 95% of the time. The following tables provide the frequency of the results in each concentration at each of the 3 testing sites for the manual and the auto-dilution (automated) dilution methods.

AUTO-DILUTION QC (Vancomycin – VA2)

QC ORGANISM	Concentration	Vitek 2	Reference
Enterococcus faecalis **ATCC 29212** **Expected Range 1 – 4 µg/mL**			
	≤0.125		
	0.25		
	0.5 *		
	1 *		2
	2 *	74	72
	4 *		
	8 *		
	16*		
	32*		
	≥64		

* VITEK 2 Card Result Range

MANUAL-DILUTION QC (Vancomycin – VA2)

QC ORGANISM	Concentration	Vitek 2	Reference
Enterococcus faecalis			
	≤0.125		
ATCC 29212	0.25 *		
	0.5 *		
	1 *		2
Expected Range	2 *	73	71
1 – 4 µg/mL	4 *		
	8 *		
	16*		
	32*		
	≥64		

* VITEK 2 Card Result Range

AUTO-DILUTION QC (Vancomycin – VA2)

QC ORGANISM	Concentration	Vitek 2	Reference
S. aureus			
	≤0.125		
ATCC 29213	0.25		
	0.5 *	69	28
Expected Range	1 *	21	62
0.5 – 2 µg/mL	2 *		
	4 *		
	8 *		
	16*		
	32*		
	≥64		

*VITEK 2 Card Result Range

MANUAL-DILUTION QC (Vancomycin – VA2)

QC ORGANISM	Concentration	Vitek 2	Reference
S. aureus			
	≤0.125		
ATCC 29213	0.25		
	0.5 *	72	28
Expected Range	1 *	18	62
0.5 – 2 µg/mL	2 *		
	4 *		
	8 *		
	16*		
	32*		
	≥64		

* VITEK 2 Card Result Range

***E. faecalis* ATCC 29212 QC performance:** The modes of the Reference result were the same as the modes of the device results for both dilution methods.

***S. aureus* ATCC 29213 QC performance:** The modes for the VITEK 2 results were one dilution more susceptible than the modes of the reference methods for both dilution methods.

No QC trending was observed.

Inoculum density control: A turbidity meter was used (DensiCheck) for the turbidity inoculation method. DensiChek Calibration verification procedure was also included.

a. *Detection limit:*
   Not Applicable
b. *Analytical specificity:*
   Not Applicable
c. *Assay cut-off:*
   Not Applicable

2. Comparison studies:
   a. *Method comparison with predicate device:*
   Clinical testing was conducted at 3 sites. The new formulation and new algorithm testing included 963 clinical isolates of which 280 were fresh, along with a challenge set with known results. Two methods of inoculation (manual and automated) were evaluated by both VITEK 2 AST-GP Vancomycin and broth microdilution containing Vancomycin. All isolates with the exception of 2 completed incubation in the VITEK 2 AST-GP card in <16 hours. A panel of 105 organisms were used for Challenge testing at one site. Each challenge organism was tested one time by manual dilution, automatic dilution, and broth microdilution, and the Disk Approximation Test (data not presented). A comparison was provided to the reference method with the following agreement.

Clinical and Challenge Data - Automated Dilution Method comparison for new formula Vancomycin (VA2)

	Total	EA	%EA	Total evaluable	EA of evaluable	Eval %EA	CA	%CA	#R	min	maj	vmj
Clinical	**858**	**858**	**100**	**509**	**509**	**100**	**858**	**100**	**34**	**0**	**0**	**0**
Challenge	**105**	**104**	**99.0**	**88**	**87**	**98.9**	**101**	**96.2**	**4**	**4**	**0**	**0**
Combined	**963**	**962**	**99.9**	**597**	**596**	**99.8**	**959**	**99.6**	**38**	**4**	**0**	**0**

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies

Challenge Data - Read Method comparison for Vancomycin (VA2)

	total	EA	%EA	Total evaluable	EA of evaluable	Eval %EA	CA	%CA	#R	min	maj	vmj
Manual	**105**	**103**	**98.1**	**83**	**82**	**98.8**	**99**	**94.3**	**4**	**5**	**1**	**0**
Auto-dilution	**105**	**104**	**99.0**	**88**	**87**	**98.9**	**101**	**96.2**	**4**	**4**	**0**	**0**

The performance characteristics of the antimicrobial agents included in VITEK 2 AST cards were established using the manual and automated modes at multiple clinical laboratories. The VITEK 2 AST card results were compared to results from a reference method prepared according to CLSI. Essential Agreement (EA) represents VITEK 2 results which agree exactly with the Reference method or are within a +/- one two-fold dilution of the reference result. Category Agreement (CA) occurs when the VITEK 2 and the reference interpretative result agree as Susceptible, Intermediate, and Resistant (S-I-R) exactly.

There were 4 minor (min) discrepancies generated by the in the Challenge set using the automated dilution method, and there were 5 min and 1 major discrepancy (maj) produced using the manual dilution method. The EA% and the CA% for both dilution methods were both very good.

Clinical testing and challenge testing using the automated method demonstrated no very major discrepancies (vmj) and no major discrepancies. A combined EA % of 99.8 and CA % of 99.6 are both very good.

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):

Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) Vancomycin Resistant *Staphylococcus aureus* (VRSA) strains

Five of the glycopeptides resistant NARSA strains (VRS1 through VRS5) were tested at each clinical site by automatic dilution and by broth microdilution. To mitigate the potential loss of plasmid, day-2 subcultures fresh from the freezer were used for testing. These results, provided below, are not included in the performance data for the new formula Vancomycin (VA2).

NARSA Isolates combined performance for Vancomycin (VA2)

	Total	EA	%EA	Total evaluable	EA of evaluable	Eval %EA	CA	%CA	#R	min	maj	vmj
	15	15	100.0	0	0	0	15	15	15	0	0	0

4. Clinical cut-off:
   Not Applicable

5. Expected values/Reference range

   Interpretative criteria: ≤ 4 (S), 8 – 16 (I), ≥ 32 (R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC for the new formulation and new algorithm of Vancomycin (VA2) are the same as recommended by FDA. All values will be included in the package insert. The package insert will contain additional information for VA2, to differentiate the new from the original vancomycin formula (VA1):

- The new Vitek 2 AST-GP Vancomycin name will appear as: Vancomycin^{VA2}
- VA2 = See performance characteristics identified by "VA2" Comment in Systems Product Information

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 support a substantial equivalence decision.