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

A. 510(k) Number:
k063597

B. Purpose of Submission:

Addition of Amoxicillin to the VITEK®2 and VITEK®2 Compact Systems Antimicrobial Susceptibility Test (AST) System

C. Measurand
Amoxicillin ≤0.06 - ≥8 μg/mL

D. Type of Test:
Quantitative growth based detection algorithm using predetermined growth thresholds

E. Applicant:
bioMerieux, Inc.

F. Proprietary and Established Names:
VITEK®2 Gram Positive Amoxicillin

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

     The VITEK®2 Gram Positive Susceptibility Card is intended for use with the VITEK®2 system in clinical laboratories as an in vitro test to determine the susceptibility of *Streptococcus pneumoniae* to antimicrobial agents when used as instructed in the Online Product Information.

2. Indication(s) for use:
   This submission is for the addition of the VITEK® 2 Gram Positive Amoxicillin for *Streptococcus pneumoniae* at a concentration of 0.06, 0.25, 1, and 2 µg/mL and a calling range of range of ≤0.06, and ≥8 µg/mL.

3. Special condition for use statement(s):
   Prescription use only

4. Special instrument Requirements:
   Not applicable

I. Device Description:

The VITEK® 2 AST card containing the test is inoculated with a standardized organism suspension. The card is incubated within the instrument and optically monitored throughout the incubation cycle. Results are automatically calculated once a predetermined growth threshold is reached and a report is generated that contains the final result.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   VITEK® 2 Gram Positive Telithromycin for *Streptococcus pneumoniae*
2. Predicate K number(s):
   k053186
3. Comparison with predicate

Similarities		
Item	**Device**	**Predicate**
Intended Use	Determine antimicrobial susceptibility to antimicrobial agents	Same
Instrument	VITEK®2 System	Same
Test Card	VITEK®2 card, including the base broth	Same
Test organism	Colonies of Gram-Positive cocci	Same
Differences		
Item	**Device**	**Predicate**
Antibiotic	Amoxicillin at specific concentrations	Telithromycin at specific concentrations
Reading algorithm	Unique for amoxicillin	Unique for telithromycin

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 for a "rapid" read but may be extended to 18 hours in some instances. The VITEK®2 Susceptibility Card test is based on the microdilution minimum inhibitory concentration 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 organism identification in order to determine a category interpretation. A category interpretation (SIR) will be reported along with a MIC.

M. Performance Characteristics (if/when applicable):
1. <u>Analytical performance:</u>

   a. *Precision/Reproducibility:*
      Ten *S. pneumoniae* on-scale organisms were tested at three sites with >95% reproducibility. These same organisms were tested at one site three times to determine within site reproducibility of >95% also. This testing was performed using both the manual dilution of the inoculum and also the automatic dilution method.

   b. *Linearity/assay reportable range:*
      Not applicable

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

      The recommended QC isolate, *S. pneumoniae* ATCC 49619, was tested on every test occasion with the reference method and the VITEK®2. The reference method QC results were in range for every day tested. The VITEK®2 was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended range.

      Quality Control was performed during the studies using both the auto-dilution and the manual method of diluting the organisms. Results demonstrated that methods were comparable with the same mode.

Amoxicillin QC Table

ORGANISM	Test Results	VITEK®2 AUTO-DIL	VITEK®2 MAN-DIL	Reference Conc. (ug/mL)	Reference
S. pneumoniae ATCC 49619 Expected Range: 0.03125 – 0.125 µg/mL	≤0.625	73	75	≤0.03125	31
	0.125	6	4	0.0625	47
				0.125	1

Inoculum density control was monitored using the DensiChek instrument. This was standardized weekly with all results recorded and in the expected range. Verification was performed during internal testing.

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:*
A clinical study was conducted at three sites using the VITEK®2 gram positive cards with amoxicillin and the broth microdilution method using cation-adjusted Mueller Hinton (MH) broth with lysed horse blood prepared as recommended by CLSI. Inoculum was prepared with direct colony suspension and incubated in ambient air at 35°C. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. Two methods of inoculation (manual and automated) were evaluated. Clinical testing was performed using the automated method of inoculation and the challenge set was tested using both the manual and the automated method. The test device had a growth rate of >90%. A comparison was provided to the reference method with the following agreement.

Summary Table for *S. pneumoniae*

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	Min	maj	vmj
Clinical	381	365	95.8	73	58	79.5	374	98.2	4	7	0	0
Challenge	58	57	98.3	25	25	100	52	89.7	1	5	1	0
Combined	439	422	96.1	98	83	84.7	426	97	5	12	1	0

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

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one well variability. EA is when there is agreement between the reference method and the VITEK®2 within plus or minus one serial two-fold dilution of antibiotic. CA is when the interpretation of the reference method agrees exactly with the interpretation of the VITEK®2 results.

Manual Dilution:
The challenge set of organisms was also tested at one site using the manual method of inoculation with the following performance that demonstrated that there is minimal difference between the two inoculation methods.

Summary Table for *S. pneumoniae*

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Challenge	58	58	100	28	28	100	54	93.1	1	4	0	0

A slight trend is observed in the clinical trials where the VITEK®2 appears to be more susceptible than the reference method. There are no vmj errors encountered in the clinical trial. Major and minor error rates are 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:
        S. pneumoniae $\leq$2 (S), 4 (I), $\geq$8 (R)

N. 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.