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

A. 510(k) Number:
k040845

B. Purpose of Submission:
Addition of ESBL Test to the VITEK®2 Antimicrobial Susceptibility Test System

C. Analyte
The following antimicrobial concentrations will be included in the VITEK®2 ESBL Test.

Cefepime	Cefepime/Clavulanic Acid
Cefotaxime	Cefotaxime/Clavulanic Acid
Ceftazidime	Ceftazidime/Clavulanic Acid

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

E. Applicant:
bioMerieux, Inc.

F. Proprietary and Established Names:
VITEK®2 ESBL Test

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 (AST) 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 ESBL Test is intended for use with the VITEK®2 Antimicrobial Susceptibility Test System (AST) as a laboratory aid in the determination of in vitro susceptibility to antimicrobial agents.

2. Indication(s) for use:
   This will include the testing of VITEK®2 ESBL Test as a confirmatory test to detect the presence of extended-spectrum beta-lactamase (ESBLs) in *Escherichia coli, Klebsiella pneumoniae,* and *Klebsiella oxytoca*.
3. Special condition for use statement(s):
   For ESBL positive strains, the test interpretation should be reported as resistant
   for all penicillins, cephalosporins and aztreonam.

   A negative ESBL Test result does not rule out the presence of an ESBL masked by an AMPC beta-lactamase

   Prescription use only

4. Special instrument Requirements:
   Not applicable

I. Device Description:

The ESBL analysis for the VITEK 2 system is based on monitoring organism activity (growth) in seven different wells on the test card. One well is a control containing only growth media. The other six are cefepime, cefotaxime, and ceftazidime, each with and without clavulanic acid.

Organism activity is monitored in the control well to determine whether sufficient activity is present to complete the analysis and to determine the length of incubation. No ESBL result is reported unless the organism reaches predetermined growth thresholds. Once the organism reaches the exponential phase, incubation is extended a set amount of time to evaluate the activity in the antimicrobial wells with and without clavulanic acid.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   VITEK ESBL Test
2. Predicate K number(s):
   N50510/S081
3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended Use	Same	Same
Test organism	Colonies of Gram-Negative bacilli	Same
	<16 hours	<16 hours

Differences		
Item	**Device**	**Predicate**
Instrument	VITEK®2 System	VITEK® System
Test Card	VITEK®2 card	VITEK® card
Antibiotic	Contains additional antimicrobial, cefepime	Contains only cefotaxime and ceftazidime

K. Standard/Guidance Document Referenced (if applicable):

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA"; NCCLS M7 (M100-S14) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard".

L. Test Principle:

The detection of an ESBL is based on the inhibition of activity in the presence of clavulanic acid. The VITEK® 2 analysis looks for growth patterns that exhibit activity in the well containing the antimicrobial without clavulanic acid and limited activity in the corresponding antimicrobial well containing clavulanic acid. Each of the three pairs of wells is evaluated independently. If any one of the three pairs demonstrates the expected growth pattern (difference in activity with and without clavulanic acid) a positive test result is reported.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:
   - *a. Precision/Reproducibility:*
     Ten gram-negative organisms were tested at three sites with >95% reproducibility. These same organisms were tested at one site nine times to determine the 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):*

ORGANISM	**Test Results**	***VITEK®2*** ***AUTO-DIL***	***Reference*** ***AUTO-DIL***	***VITEK®2*** ***MAN-DIL***	***Reference*** ***MAN-DIL***
E. coli ATCC 25922 Expected Result: Neg	Negative	78	15	74	15
	Positive				
K. pneumoniae ATCC 700603 Expected Result: Pos	Negative	3	1	3	1
	Positive	77	14	73	14

Quality Control was performed during the studies using both the auto-dilution and the manual method of diluting the organisms. The false negative QC results were due to an incorrect QC organism that was used for QC testing.

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 ESBL test and the NCCLS reference agar dilution method prepared as recommended in NCCLS M7 approved standard. Inoculum was prepared with direct colony suspension. 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. Greater than 99% of the isolates grew in the VITEK®2 ESBL test in less than 16 hours.

The following table provides the results from the automated testing.

	Total	**Number Neg**	**Number Pos**	**CA**	**%CA**	**maj**	**vmj**
Clinical	318	162	156	312	98.1	3	3
Challenge	29	0	29	27	93.1	0	2
Combined	347	162	185	339	97.7	3	5

CA-Category Agreement

maj-major discrepancies
vmj-very major discrepancies

CA is when the interpretation of the reference method agrees exactly with the interpretation of the VITEK®2 results.

The 5 vmj errors were due to *K. pneumoniae* with a vmj error rate of 4.4% (5/113) for this report group. All clinical vmj errors were from one site. Two of the clinical vmj errors were very resistant as reflected in their antibiograms and were further characterized as an ESBL producer with AmpC. It was observed in these vmj errors that AmpC masked the detection of ESBL producers.

Three of the 5 vmj errors would be recommended to be resistant by the Expert System as if it was an ESBL producer. This expert system interpretation included comments to the user further describing this phenomenon and providing reporting option to the user.

Furthermore, a limitation statement will also be added to the package insert "A negative ESBL Test result does not rule out the presence of an ESBL masked by an AMPC beta-lactamase" alerting the user to this possibility.

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 was no difference between the two inoculation methods.

	Total	**Number Neg**	**Number Pos**	**CA**	**%CA**	**maj**	**vmj**
Challenge	29	0	29	28	96.6	0	1

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:
   Negative – Strain does not produce ESBLs.
   Positive – Strain produces ESBLs. Test interpretation should be reported as resistant for all penicillins, cephalosporins, and aztreonam.

   The interpretative criteria and QC are the same as recommended in NCCLS. The expected results will be included in the package insert.

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