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

A. 510(k) Number:
K080107

B. Purpose for Submission:
The addition of Piperacillin/tazobactam to the VITEK ® 2 and VITEK®2 Compact Systems Antimicrobial Susceptibility Test (AST) System.

C. Measurand
VITEK ® 2 Gram Negative Piperacillin/tazobactam (≤ 4- ≥ 128 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 Negative Piperacillin/tazobactam

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):

   Piperacillin/tazobactam at concentrations of ≤ 4- ≥ 128 μg/mL on the Gram Negative Susceptibility Card is intended for use with the VITEK®2 Systems 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*, *S. pneumoniae*, and yeast.

2. Indication(s) for use:

This submission is indicated for the addition of Piperacillin/tazobactam at concentrations of 4/4, 16/4, 32/4, 64/4 for a calling range of ≤4 - ≥128 µg/mL on the VITEK®2 Gram Negative Susceptibility Cards for use with the VITEK®2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Acinetobacter baumanii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa*, *Citrobacter koseri, Morganella morganii*, *Proteus mirabilis*, *Proteus vulgaris*, *Providencia stuartii, Providencia rettgeri, Salmonella enterica*, and *Serratia marcescens* to antimicrobial agents when used as instructed in the Online Product Information.

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 Negative Levofloxacin

2. Predicate K number(s):
   K072038

3. Comparison with predicate

Similarities		
Item	**Device**	**Predicate**
Test organism	Gram Negative Rods Colonies	same
Test Card	VITEK® 2 card format with base broth	same
Instrument	VITEK® 2 and VITEK ®2 Compact System	same
Differences		
Item	**Device**	**Predicate**
Antibiotic	Piperacillin/tazobactam	Levofloxacin
Reading algorithm	Unique for new formulation of Piperacillin/tazobactam	Unique for Levofloxacin

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-S18) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard"

L. Test Principle:
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 premeasured amounts of a specific antibiotic combined with culture medium. A suspension of organism is made in 0.45-0.5% sterile saline from a pure culture and standardized to a McFarland 0.5 standard using the DensiChek. The desired cards are placed in the cassette along with an empty tube for the susceptibility card. The cassette is placed in the VITEK®2 instrument where a susceptibility test will be automatically diluted from the ID suspension by the VITEK®2. 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^{o} C) and optical scanning during testing. Readings are performed every 15 minutes. In addition to the automatic dilution, there is also a manual inoculation dilution procedure described in the packager insert.

M. Performance Characteristics (if/when applicable):
Two AST (TZP1 and TZP2) will be identified in the product labeling (package inserts and the VITEK®2 System Product Information, Susceptibility Performance Characteristics). TZP1 will identify information related to the original test (N50510/S119) and TZP2 will identify information related to this submission.

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

1. Analytical performance:

   a. Precision/Reproducibility:
   Reproducibility was demonstrated using 10 isolates at 3 sites on 3 separate days in triplicates. The study included the Auto-dilution and the Manual dilution. All results were >95% reproducible and acceptable.

   b. Linearity/assay reportable range:
   Not Applicable

   c. Traceability (controls, calibrators, or method):
   Three recommended QC (*E. coli* ATCC 25922, *E. coli* ATCC 35218 and *P. aeruginosa* ATCC 27853) were tested a minimum 20 times/site by the automatic dilution and the manual dilution. The organisms were tested by the VITEK 2 AST cards and the reference (broth microdilution) methods.

The following table provides the frequency of results for all sites in each concentration with the expected range stated. Both the Auto dilution and the Manual dilution methods are within the expected range >95% of the time. The Reference Results are similar to the test results. In instances where any organism was out of range for the reference method, all testing data was invalid and repeated.

Organism	Conc in µg/ml	Auto-dilution		Manual dilution	
E. coli ATCC 25922 Range 1- 4 µg/ml		**Ref.**	**Test**	**Ref.**	**Test**
	≤ 4	108	108	85	85
	8				
	16				
	32				
	64				
	128				
	≥256				
E. coli ATCC 35218 Range 0.5- 2 µg/ml	≤ 4	105	104	83	82
	8				
	16				
	32				
	64	1		1	
	128	1	4	1	2
	≥256	1		1	
P. aeruginosa ATCC 27853 Range 1- 8 µg/ml	≤ 4	84	104	72	84
	8	18		13	
	16	2		1	
	32				
	64				
	128				1
	≥256				

Inoculum density control:
A turbidity meter (VITEK 2 DensiChek) was used to adjust the inoculum to the turbidity of 0.5 McFarland. The VITEK 2 DensiChek instrument 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:*
Clinical study was performed at three external sites using the VITEK 2 AST-GN Piperacillin/tazobactam and broth microdilution panels containing Piperacillin/tazobactam. The study included 483 clinical isolates (269 fresh, 214 stock) and a challenge set of 79 isolates. The clinical stock isolates were <50%. Two methods of inoculation (manual and automated) were evaluated. Clinical testing was performed by the automated method of inoculation and the challenge set was by both the manual and the automated methods. All isolates grew in the VITEK®2 cards in less than 16 hours. The test device had a growth rate of >95% for the clinical and the challenge study.

The vmj was 2.3% (4/176). *Pseudomonas aeruginosa, Acinetobacter baumannii, E. coli* and *K. pneumoniae* each had one vmj. There is no intermediate category in the interpretative criteria for *P. aeruginosa* so all discrepant results are either very major error (vmj) or a major error (maj), even the result is within EA. The vmj was within EA. The vmj for *Acinetobacter baumannii* and *K. pneumoniae* were 1.3% (1/76) and 1.4% (1/71) respectively. They all had an acceptable EA and CA of >90%.

Summary Table for *Acinetobacter baumannii, Enterobacteriaceae* and *Pseudomonas aeruginosa* (Auto Dilution)

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Clinical	483	469	97.1	68	67	98.5	470	97.3	169	7	2	4
Challenge	79	74	93.7	19	17	89.5	73	92.4	7	3	3	0
Combined	562	543	96.6	87	84	96.6	543	96.6	176	10	5	4

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

Manual Dilution:
The challenge set of 109 organisms was also tested at one site using the manual method of inoculation with the following performance. There was no difference in the overall CA agreement.

Comparison Challenge Data - Auto vs Manual dilution

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Auto	109	103	94.5	24	22	91.7	98	90	14	7	3	1
Manual	109	101	92.7	22	19	86.4	97	90	14	7	3	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):*

4. Clinical cut-off:
Not Applicable

5. Expected values/Reference range

The interpretative criteria and the recommended Quality Control ranges are the same as the FDA and CLSI and will appear in the Package Insert and software. Interpretative criteria used for the evaluation and that will appear in the Package Insert are as follows:

Enterobacteriaceae and *Acinetobacter baumanii*

≤ 16 (S)	32-64(I)	≥ 128 (R)

Pseudomonas aeruginosa

≤ 64 (S)	----	≥ 128 (R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC are included in the package insert. The labeling is sufficient and it satisfies the requirement of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision