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

A. 510(k) Number:
K072038

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

C. Measurand
VITEK ® 2 Gram Negative Levofloxacin (≤0.12 - ≥8 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 Levofloxacin.

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 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.*
   The VITEK ® 2 Gram Negative Susceptibility Card is intended for use with VITEK ® 2 system in clinical laboratories as an *in vitro* test to determine the susceptibility of gram negative organisms to Levofloxacin when used as instructed in the System Product Information manual.

2. Indication(s) for use:
   VITEK® Gram Negative Levofloxacin is designed for antimicrobial susceptibility testing of *Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Serratia marcescens, Acinetobacter baumannii, Acinetobacter lwoffi, Citrobacter koseri, Citrobacter freundii, Enterobacter aerogenes, Enterobacter sakazakii, Klebsiella oxytoca, Morganella morganii, Pantoea agglomerans, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Pseudomonas fluorescens.* VITEK 2 Gram Negative Levofloxacin 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.

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 is made in 0.45-0.5% sterile saline from a pure culture and standardized to a McFarland 0.5 standard using the DensiChek Turbidity meter. The desired cards 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. (275 microliter/2.5ml for manual inoculations and 235 microliter/2.5 ml saline for gram positive cocci.). 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.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   Vitek 2 Gram Negative Ertapenenm

2. Predicate K number(s):
   K041982

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	Levofloxacin	Ertapenem
Reading algorithm	Unique for new formulation of Levofloxacin.	Unique for Ertapenem

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 four and 16 hours with the majority of the *S. pneumoniae* between five and nine hours. The VITEK 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 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 VITEK 2 Gram Negative Levofloxacin by comparing its performance with the CLSI broth microdilution reference method.

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 48 gram-negative isolates in triplicate, each for three days at three sites with VITEK 2 AST-GN Levofloxacin.

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 Levofloxacin, and broth microdilution plates containing Levofloxacin. QC organisms *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853 were tested at each clinical trial site. 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 three testing sites for the manual and the auto dilution reading methods.

AUTO-DILUTION QC (Levofloxacin -- LEV)

QC ORGANISM	Concentration	Vitek 2	Reference
E. coli	0.06		75
ATCC 25922	0.125 *	75	
	0.25 *		
Expected Range 0.008-0.06 µg/mL	0.5 *		
	1 *		
	2 *		
	4 *		
	8 *		
	16		

MANUAL-DILUTION QC (Levofloxacin -- LEV)

QC ORGANISM	Concentration	Vitek 2	Reference
E. coli	0.06		75
	0.125 *	75	
ATCC 25922	0.25 *		
	0.5 *		
Expected Range 0.008-0.06 µg/mL	1 *		
	2 *		
	4 *		
	8 *		
	16		

* VITEK 2 Card Result Range

AUTO-DILUTION QC (Levofloxacin -- LEV)

QC ORGANISM	Concentration	Vitek 2	Reference
P. aeruginosa	0.06		
	0.125 *		
ATCC 27853	0.25 *		
	0.5 *	1	10
Expected Range 0.5-4µg/mL	1 *	68	61
	2 *	6	4
	4 *		
	8 *		
	16		

MANUAL-DILUTION QC (Levofloxacin -- LEV)

QC ORGANISM	Concentration	Vitek 2	Reference
P. aeruginosa	0.06		
	0.125 *		
ATCC 27853	0.25 *		
	0.5 *	2	10
Expected Range	1 *	67	61
	2 *	9	4

0.5-4 µg/mL	4 *		
	8 *		
	16		

* VITEK 2 Card Result Range

***E. coli* ATCC 25922 QC performance:** The device dilutions present on the VITEK 2 card produced QC results which were outside the expected result range. Therefore, a secondary QC isolate, *Pseudomonas aeruginosa* ATCC 27853, which produced on scale results was also tested. The mode of the Reference result were one dilution lower than the mode of the device results.

***Pseudomonas aeruginosa* ATCC 27853 QC performance:** The modes for the VITEK 2 results were the same as the reference methods for both reading 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 596 clinical isolates of which 200 were fresh, along with a challenge set with known results. Two methods of inoculation (manual and automated) were evaluated by both VITEK 2 AST-GN Levofloxacin and agar dilution containing Levofloxacin. All isolates with the exception of 1 grew in the VITEK 2 AST-GN card in <16 hours. A panel of 95 organisms were used for Challenge testing at one site. Each challenge organism was tested one time by manual dilution, automatic dilution, and agar dilution. A comparison was provided to the reference method with the following agreement.

Clinical and Challenge Data - Automated Read Method comparison for Levofloxacin

	total	EA	%EA	Total evaluable	EA of evaluable	%EA	CA	%CA	#R	min	maj	vmj
Clinical	595	585	98.3	162	156	96.3	570	95.8	179	23	1	1
Challenge	95	95	100	40	40	100	91	95.8	12	4	0	0
Combined	690	680	98.6	202	196	97	661	95.8	191	27	1	1

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

Challenge Data - Manual Read Method comparison for Levofloxacin

	total	EA	%EA	Total evaluable	EA of evaluable	%EA	CA	%CA	#R	min	maj	vmj
Challenge	95	94	98.9	40	40	100	91	96.8	12	3	0	0

The performance characteristics of the antimicrobial agents included in VITEK 2 AST cards were established using the manual and auto dilution 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.

Clinical testing and challenge testing demonstrated one very major discrepancy (vmj), the test was Sensitive and the reference was Resistant. And only one major discrepancy (maj), the test was Resistant and the reference as Sensitive. A combined two minor errors were also recorded. A combined EA of 98.6% and CA of 95.8 % are both acceptable. 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

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range

Interpretative criteria: ≤ 2 (S), 4(I), ≥ 8 (R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC for the new formulation and new algorithm of Levofloxacin are the same as recommended by FDA and CLSI. All values will be included in the package insert.

O. Conclusion:

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