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

A. 510(k) Number:

K112228

B. Purpose for Submission:

To obtain a substantial equivalence determination for this premarket notification for the addition of Levofloxacin to the VITEK 2 and VITEK 2 Compact Antimicrobial Susceptibility Test (AST) Systems.

C. Measurand:

Levofloxacin concentrations of 1, 2, 4 and 16 µg/mL are included in the VITEK® 2 Streptococcus Levofloxacin card.

D. Type of Test:

The minimum inhibitory concentration (MIC) is determined using qualitative growth based detection algorithm using predetermined growth threshold. The MIC reporting result range of the card is ≤ 0.25 – ≥ 16 µg/mL.

E. Applicant:

bioMerieux, Inc.

F. Proprietary and Established Names:

VITEK® 2 Streptococcus Levofloxacin

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LON	Class II	21 CFR 866.1645	Microbiology

H. Intended Use:

1. Intended use(s):

VITEK® 2 Streptococcus Levofloxacin is designed for antimicrobial susceptibility testing of Streptococcus species. VITEK 2 Streptococcus

Levofloxacin is a quantitative test 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. Levofloxacin has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial.

Active *in vitro* and in clinical infections
Streptococcus pneumoniae (including multi-drug resistant strains [MDRSP])
Streptococcus pyogenes

Active *in vitro* but clinical significance unknown
β-hemolytic *Streptococcus (Group C/F)*
β-hemolytic *Streptococcus (Group G)*
Streptococcus agalactiae
Streptococcus milleri
Viridans group Streptococci

2. Indication(s) for use:

VITEK® 2 Streptococcus Levofloxacin is designed for antimicrobial susceptibility testing of Streptococcus species. VITEK 2 Streptococcus Levofloxacin is a quantitative test 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. Levofloxacin has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial.

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Streptococcus agalactiae
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Viridans group Streptococci

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 the most clinically significant aerobic gram-negative bacilli, *Staphylococcus spp*., *Enterococcus spp*., *Streptococcus spp.* and clinically significant yeast.

3. Special conditions for use statement(s):

For prescription use only.

The ability of the VITEK 2 Streptococcus to detect resistance to Levofloxacin in *S. pneumoniae* and *S. pyogenes* is unknown because resistant organisms were not available at the time of comparative testing.

4. Special instrument requirements:

For use with the VITEK® 2 and VITEK® 2 Compact Systems

I. Device Description:

The VITEK 2 AST card is essentially a miniaturized, abbreviated and automated version of the doubling dilution technique for determining the minimum inhibitory concentration (MIC). Each VITEK 2 AST card contains 64 wells. A control well which only contains microbiological culture media is resident on all cards. The remaining wells contain premeasured portions of a specific antibiotic combined with culture media. The bacterial or yeast isolate to be tested is diluted to a standardized concentration with 0.45 – 0.5% saline before being used to rehydrate the antimicrobial medium within the card. The VITEK 2 System automatically fills, seals and places the card into the incubator/reader. The VITEK 2 Compact has a manual filling, sealing and loading operation. The VITEK 2 Systems monitor the growth of each well in the card over a defined period of time. At the completion of the incubation cycle, a report is generated that contains the MIC value along with the interpretive category result for each antibiotic contained on the card.

The VITEK 2 Streptococcus Levofloxacin has the following concentrations in the card: 1, 2, 4 and 16 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK 2 card is ≤ 0.25 – ≥ 16µg/mL.

The MIC ranges, interpretive criteria and equivalent concentrations are as follows:

VITEK 2 Streptococcus Levofloxacin	Equivalent Standard Method Concentration by Efficacy in µg/mL	FDA Interpretive Categories MIC in µg/mL:		
		S	I	R
Levofloxacin	1, 2, 4, 16	≤ 2	4	≥ 8

S = Susceptible, I = Intermediate, R = Resistant.

J. Substantial Equivalence Information:

1. Predicate device name(s):

VITEK 2 AST-GP Amoxicillin for *S. pneumoniae*

2. Predicate K number(s):

   k063597

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Determining susceptibility to antimicrobial agents	Same
Inoculation and test organism	Isolated colonies of *Streptococcus* species	Same
Instrument	Test are run on both the VITEK 2 and VITEK 2 Compact Systems	Same
Test Card	The VITEK 2 card, including base broth	Same

Differences		
Item	Device	Predicate
Test Method	Automated qualitative antimicrobial susceptibility test for use with the VITEK® 2 and VITEK® 2 Compact Systems to determine the *in vitro* susceptibility of *Streptococcus* species.	Automated quantitative antimicrobial susceptibility test for use with the VITEK® 2 and VITEK® 2 Compact Systems to determine the *in vitro* susceptibility of *Streptococcus* species.
Antibiotic	Levofloxacin-specific concentrations	Amoxicillin-specific concentrations
Reading algorithm	Unique to Levofloxacin	Unique to Amoxicillin

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

"Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA"

http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071462.pdf

Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, Approved Standard -8th Edition, Document M7-A8.

Performance Standards for Antimicrobial Susceptibility Testing – 19th Informational Supplement, M100-S19.

L. Test Principle:

Automated growth based detection using attenuation of light measured by an optical scanner. The optics used in the systems use visible light to directly measure organism growth. 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. The VITEK 2 System monitors the growth of each well in the card over a defined period of time. An interpretive call is made between 4 and 16 hours for a "rapid" read but may be extended to 18 hours in some instances. At the completion of the incubation cycle, a report is generated that contains the MIC value along with the interpretive category result for each antibiotic on the card. The VITEK 2 Streptococcus Levofloxacin has the following concentrations in the card: 1, 2, 4 and 16 μg/mL (equivalent standard method concentration by efficacy in μg/mL). The MIC result range for the VITEK 2 card is ≤ 0.25 – ≥ 16 μg/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A reproducibility study was conducted at three external clinical sites. Ten *Streptococcus* species isolates were tested at each site and testing was performed in triplicate over three days with the VITEK 2 Streptococcus Levofloxacin card. The testing was performed using both the manual and the automated dilution methods. Testing was conducted on the VITEK 2 instrument.

All reproducibility isolates were inhibited at concentrations in the susceptible range for Levofloxacin and all MIC values were on-scale. Reproducibility was 100% with by both manual dilution and automated dilution.

b. Linearity/assay reportable range:

Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The recommended *Streptococcus pneumonia* QC organism was tested on every test occasion with the reference method and the VITEK 2 System. Ancillary quality control testing was also performed. Two gram-positive organisms were tested throughout comparative testing at each study site by the reference method only. This was done to perform further quality control of the broth microdilution panels using *E. faecalis* ATCC 29212 and *S. aureus* ATCC 29213 which have a QC range of 0.25 -2 µg/mL and 0.06-0.5 µg/mL respectively for Levofloxacin.

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 acceptable QC results.

Quality Control was performed during the studies using both the auto-dilution and the manual method of diluting the organisms on the VITEK 2 System. Results demonstrated that methods were comparable.

Quality Control Results with the VITEK 2 System for Levofloxacin:

Organism	Concentration (µg/mL)	Auto Dilution		Manual Dilution	
		Reference	VITEK 2	Reference	VITEK 2
Streptococcus pneumonia ATCC 49619 Acceptable MIC range: 0.5-2 µg/mL	≤0.125				
	0.25*				
	0.5*	164	208	166	212
	1*	48	4	48	2
	2*				
	4*				
	8*				
	16*				
	≥32				

* VITEK Card Result Range is ≤ 0.25 – ≥ 16

At least one Quality control organism was in control in the reference on all days. Quality Control results for the VITEK 2 System using either inoculation dilution method demonstrated that the VITEK 2 System could produce the expected quality control results.

A similar QC study was conducted to evaluate the VITEK 2 Compact System. Results were compared to the expected FDA/CLSI QC results. All results for the VITEK 2 Compact System were within the expected QC ranges 100% of the time.

Inoculum density control was monitored using the DensiChek2 instrument. This was standardized weekly with all results recorded and in the expected

range.

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:

Performance was established through a clinical study which was conducted at four external study sites. A total of 1338 clinical isolates were tested by VITEK® 2 Streptococcus Levofloxacin with the VITEK® 2 System. The majority of the isolates were recently isolated from clinical specimens and the growth rate was 100%. Two hundred and nine of the 1338 clinical isolates tested were stock isolates (15.6%). A challenge set consisting of 207 isolates was evaluated with VITEK® 2 Streptococcus Levofloxacin panel at one external site.

Testing of clinical isolates was performed using the automated method of inoculation and the challenge organisms were tested with both the manual dilution and automatic dilution. Each isolate was tested by the VITEK 2 Levofloxacin Streptococcus panel and the CLSI broth microdilution reference method. The inoculum was prepared with direct colony suspension. A comparison was provided to the reference method with the following agreement. Thirty-two minor errors were seen.

AutoDilution

Organism Group	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	# vmj	# maj	# min
***Streptococcus* species**												
CLINICAL	**1338**	**1323**	**98.9**	**1152**	**1143**	**99.2**	**1307**	**97.7**	**19**	**0**	**0**	**31**
CHALLENGE	**207**	**207**	**100**	**190**	**190**	**100**	**206**	**99.5**	**0**	**0**	**0**	**1**
COMBINED (CLINICAL AND CHALLENGE)	**1545**	**1530**	**99.0**	**1342**	**1333**	**99.3**	**1513**	**97.9**	**19**	**0**	**0**	**32**

EA-Essential Agreement **CA-**Category Agreement **maj-**major discrepancies **vmj-**very major discrepancies **min-**minor discrepancies

A CA of 97.7%/99.5 % was observed for clinical/challenge isolates, respectively. An EA of 98.9%/100 % was observed for clinical/challenge isolates, respectively. However, a right shift in MIC occurred around the intermediate breakpoint.

No major or very major categorical errors occurred but a total of 32 (2.1%) minor categorical errors were seen. Of note is that all of the minor errors seen shifted the interpretation from "Susceptible" by the reference method to "Intermediate" by VITEK. Those minor errors were as follows: 17 were with *S. pyogenes,* 6 were with *S. agalactiae*, 6 were with *S. mitis/oralis*, 2 were with *S. dysgalactiae* and 1 was with *S. oralis*. No Levofloxacin-resistant *S. pneumoniae* or *S. pyogenes* isolates were tested in this evaluation.

Performance of the VITEK® 2 and the VITEK® 2 Compact was also evaluated with the same 207 challenge organisms using the manual dilution method. Results from those two studies showed CA of 99.5% and 98.1% and EA of 100% and 98.6% respectively for VITEK® 2 and the VITEK® 2 Compact.

All ranges were acceptable as defined in the AST Guidance Document.

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/Reference range:

FDA Interpretive criteria for Levofloxacin when testing *Streptococcus* species, including *S. pneumoniae* are:

S= ≤ 2 µg/mL, I = 4 µg/mL, R= ≥8 µg/mL

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR section 809.10.

O. Conclusion:

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