K132573

bioMérieux

510(k) SUMMARY

VITEK® 2 AST-ST Moxifloxacin

510(k) Submission Information:

Submitter's Name:	bioMérieux, Inc.
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Date of Preparation:	September 10, 2013

SEP 1 3 2013

A. 510(k) Number:

K132573

B. Purpose for Submission:

Substantial equivalence determination for the addition of Moxifloxacin to the VITEK® 2 and VITEK® 2 Compact Antimicrobial Susceptibility Test (AST) Systems for the testing of *Streptococcus* species.

C. Measurand:

VITEK® 2 AST-ST Moxifloxacin concentrations of 0.5, 1, 4 and 8 µg/ml. The MIC result range of the card is ≤ 0.06 – ≥ 4 µg/mL.

D. Type of Test:

The minimum inhibitory concentration (MIC) is determined using a quantitative growth based detection algorithm according to a predetermined growth threshold.

E. Applicant:

bioMérieux, Inc.

F. Proprietary and Established Names:

VITEK® 2 *Streptococcus* Moxifloxacin
VITEK® 2 AST-ST Moxifloxacin

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation	Class II	21 CFR 866.1645 Short-Term Antimicrobial Susceptibility Test System	83 Microbiology

H. Intended Use:

1. Intended use:

VITEK® 2 *Streptococcus* Moxifloxacin is designed for antimicrobial susceptibility testing of *Streptococcus* species and is intended for use with the VITEK® 2 and VITEK® 2 Compact Systems as a laboratory aid in determination of *in vitro* susceptibility to antimicrobial agents. VITEK® 2 *Streptococcus* Moxifloxacin is a quantitative test. Moxifloxacin 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 anginosus
Streptococcus constellatus
Streptococcus pneumoniae (including multi-drug resistant isolates [MDRSP]*)
Streptococcus pyogenes

*MDRSP, Multi-drug resistant *Streptococcus pneumoniae* includes isolates previously known as PRSP (Penicillin resistant *S. pneumoniae*), and are isolates resistant to two or more of the following antibiotics: penicillin (MIC) ≥2 mcg/mL), 2nd generation cephalosporins (for example, cefuroxime), macrolides, tetracyclines, and trimethoprim/sulfamethoxazole.

The following *in vitro* data are available, **but their clinical significance is unknown.**

Gram-positive bacteria
Streptococcus agalactiae
Streptococcus viridans group

2. Indication(s) for use:

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

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The following *in vitro* data are available, **but their clinical significance is unknown.**

Gram-positive bacteria
Streptococcus agalactiae
Streptococcus viridans group

The VITEK® 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK® 2 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* spp., and clinically significant yeast.

3. Special conditions for use statement(s):

For prescription use only.

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 test contained on the card.

The VITEK® 2 AST-ST Moxifloxacin for *Streptococcus* species has the following concentrations in the card: 0.5, 1, 4 and 8 µg/ml (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK 2 card is ≤ 0.06 – ≥ 4 µg/mL.

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

VITEK® 2 AST-ST	Equivalent Standard Method Concentration by Efficacy in µg/mL	MIC Ranges and FDA Categories* MIC in µg/mL:		
		S	I	R
Moxifloxacin	0.5, 1, 4, and 8	≤ 1	2	≥ 4

* S = Susceptible; I = Intermediate; R = Resistant

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITEK® 2 AST-ST Cefotaxime

2. Predicate K number(s):

   K121863

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Determining quantitative antimicrobial susceptibility for *Streptococcus* species	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	VITEK® 2 card format with	Same

Similarities		
Item	Device	Predicate
	base broth	
Test Method	Automated quantitative antimicrobial susceptibility test to determine the *in vitro* susceptibility of *Streptococcus* species	Same

Differences		
Item	Device	Predicate
Antibiotic	Moxifloxacin-specific concentrations	Cefotaxime -specific concentrations
Reading algorithm	Unique to Moxifloxacin	Unique to Cefotaxime
Test organisms	*Streptococcus anginosus*, *Streptococcus constellatus*, *Streptococcus pneumoniae* (including multi-drug resistant isolates [MDRSP]), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus viridans* group.	*Streptococcus pneumoniae*, *Streptococcus pyogenes* (Group A beta-hemolytic streptococci), *Streptococcus* spp.

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

Clinical and Laboratory Standards Institute (CLSI) M07-A8: "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, Approved Standard -8th Edition", January, 2009.

CLSI M100-S21, "Performance Standards for Antimicrobial Susceptibility Testing - Twenty-first Informational Supplement", January, 2011.

L. Test Principle:

Automated growth based detection using attenuation of light measured by an optical scanner. The optics used in the VITEK® 2 Systems use visible light to directly measure organism growth. Optical readings are based on an initial read of a well before significant growth has begun. Light transmittance sampling at a defined interval of time for the well measures organism growth by how much light is prevented from going through the well. The VITEK® 2 Systems monitor 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 in some instances may be extended to 18 hours for GN and GP cards, up to 24 hours for some Streptococcus species, or up

36 hours for some yeast species. 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 AST-ST Moxifloxacin for *Streptococcus* species has the following concentrations in the card: 0.5, 1, 4, and 8 µg/ml (equivalent standard method concentration by efficacy in µg/ml). The MIC result range for the VITEK® 2 card is ≤ 0.06 – ≥ 4 µg/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A reproducibility study was conducted at three external clinical sites. Two isolates of *Streptococcus pneumoniae*, two isolates of *Streptococcus agalactiae*, and six isolates of viridans group streptococci (i.e. three *Streptococcus sobrinus*, one *Streptococcus infantarius* ssp. *coli*, and two *Streptococcus downei*) were tested at each site and testing with the VITEK® 2 AST-ST Moxifloxacin card was performed in triplicate over three days, resulting in a total of 270 test results. The study included both auto and manual dilution methods for the VITEK® 2 and manual dilution only for the VITEK® 2 Compact, since the VITEK® 2 Compact system does not have functionality to support automatic dilutions to inoculate the cards.
For the sake of reproducibility calculations, off-scale values are handled in two ways; "best case" and "worst case" scenarios. Best case calculation for reproducibility assumes the off-scale result is within one well from the mode MIC value. Worst case calculation for reproducibility assuming the off-scale result is greater than one well from the mode MIC value.

The overall reproducibility was > 95% with +/- one dilution observation for the VITEK® 2 and the VITEK® 2 Compact system. Results were as follows:

VITEK® System	Inoculation Method	Best Case	Worst Case
VITEK® 2	Auto Dilution	100%	100%
	Manual Dilution	100%	100%
VITEK® 2 Compact	Manual Dilution	99.3%	99.3%

b. Linearity/assay reportable range:

Not applicable

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

The recommended *Streptococcus pneumoniae* QC organism was tested on every test occasion with the reference method and the VITEK® 2 System. 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 and manual methods of diluting the organisms on the VITEK® 2 System. Results demonstrated that both methods were comparable. Quality Control Results with the VITEK® 2 System for AST-ST Moxifloxacin were as follows:

Organism	Moxifloxacin Concentration (µg/mL)	Auto Dilution		Manual Dilution	
		Reference	VITEK® 2	Reference	VITEK® 2
Streptococcus pneumoniae ATCC 49619 Acceptable MIC range: 0.06-0.25 µg/mL					
	0.016				
	0.03	1			
	0.06*	140		58	
	0.12*	62	203	46	104
	0.25*				
	0.5*				
	1*				
	2*				
	4*				
	8				

* VITEK® 2 Card Result Range is ≤ 0.06 – ≥ 4 µg/mL.

Results for VITEK® 2 AST-ST Moxifloxacin were within the expected QC results range > 95% of the time for both the automatic and manual dilution options of the VITEK® 2.

A similar QC study was conducted to evaluate the VITEK® 2 Compact, a secondary option, at three sites and the results were within the expected QC ranges as shown in the table below.

Organism	Moxifloxacin Concentration (µg/mL)	Manual Dilution	
		Reference	VITEK® 2
Streptococcus pneumoniae ATCC 49619 Acceptable MIC range: 0.06-0.25 µg/mL			
	0.016		
	0.03		
	0.06*	59	
	0.12*	44	102
	0.25*		1
	0.5*		
	1*		

	2*		
	4*		
	8		

* VITEK® Card Result Range is ≤ 0.06 – ≥ 4 µg/mL.

Inoculum density control was monitored using the DensiCHEK™ Plus instrument. The DensiCHEK™ Plus controls were standardized daily 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:

The reference method follows the CLSI approved broth microdilution testing conditions.

Medium:	Cation-adjusted Mueller-Hinton broth (CAMHB) supplemented with 5% lysed horse blood
Inoculum:	Direct colony suspension
Incubation:	35°C; ambient air; 20-24 hours

a. Method comparison with predicate device:

Performance was established through a clinical study conducted at three external study sites. A total of 951 clinical isolates were tested by the VITEK® 2 AST-ST Moxifloxacin card on the VITEK® 2 System. The majority of the isolates were recovered from clinical specimens. Two hundred twenty-nine of the 951 clinical isolates (24.1%) were stock isolates. Ten of the isolates failed to grow in the VITEK® 2 card giving a no growth rate of 1.1% (10/951). Therefore, the total number of viable clinical isolates evaluated was 941.

Testing of the clinical isolates was performed using the automated method of inoculation and the challenge organisms were tested with both the manual and automatic dilution methods. Each isolate was tested by VITEK® 2 AST-ST Moxifloxacin and the CLSI broth microdilution reference method. The inoculum was prepared with direct colony suspensions. A comparison was

provided to the reference method with the agreement shown in the following tables.

There is only one set of Moxifloxacin breakpoints [≤ 1 (S), 2 (I), ≥ 4 (R)] for *Streptococcus pneumoniae* and *Streptococcus* spp. in the FDA drug label. The performance data were analyzed using the FDA breakpoints. A summary of the combined clinical and challenge data for the auto dilution method is shown in the table below.

Auto Dilution (VITEK® 2)

VITEK® 2 Auto	Total	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	# vmj	# maj	# min
CLINICAL	941	878	93.3	917	860	93.8	936	99.5	9	0	0	5
CHALLENGE	159	151	95.0	158	150	94.9	158	99.4	0	0	0	1
COMBINED (CLINICAL AND CHALLENGE)	1100	1029	93.5	1075	1010	94.0	1094	99.5	9	0	0	6

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

Essential agreement (EA) is when the VITEK® 2 panels agree with the broth microdilution reference results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the VITEK® 2 panel result interpretation agrees exactly with the broth microdilution reference panel result interpretation. Evaluable (Eval EA) is when the MIC result is on-scale for both the VITEK® 2 and the reference method and have on-scale EA.

For the combined *Streptococcus* species and *S. pneumoniae*, 6 (0.5%) minor categorical errors were observed, with a total EA of 93.5%, evaluable EA of 94.0%, and a CA of 99.5%. The clinical study demonstrated a trend, which was one doubling dilution higher when compared to the reference method. Of the 1100 Streptococci, 9 isolates of the *Streptococcus viridans* group were resistant with no very major errors. The MDRSP were evaluated in the challenge study. The combined clinical and challenge set included 295 *S. pneumoniae*, 256 *S. pyogenes*, 260 *S. agalactiae* and 269 viridans streptococci group, in addition to 12 *S. anginosus* and 8 *S. constellatus*.

The challenge set of 159 isolates was also tested against a manual dilution method on the VITEK® 2. A summary of VITEK® 2 manual dilution data is shown in the table below.

Manual Dilution (VITEK® 2) - Challenge

VITEK® 2 Manual	Total	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	# vmj	# maj	# min
CHALLENGE	159	152	95.6	158	151	95.6	158	99.4	0	0	0	1

Performance of the VITEK® 2 Compact was evaluated as a secondary procedural option. The evaluation was conducted using the same 159 challenge isolates that were tested on the VITEK® 2 system. VITEK® 2 Compact comparison testing against the reference method is shown in the table below.

Manual Dilution (VITEK® 2 Compact) - Challenge

VITEK® 2 Compact Manual	Total	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	# vmj	# maj	# min
CHALLENGE	159	152	95.6	158	151	95.6	157	98.7	0	0	0	2

The performance of the VITEK® 2 Compact, a secondary option, was evaluated in the reproducibility, QC, and challenge studies with acceptable results.

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:

Streptococcus species and *S. pneumoniae*: ≤ 1 (S), 2 (I), ≥ 4 (R)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

bioMérieux, Inc.
c/o Mr. Nathan Hardesty
Staff Regulatory Affairs Specialist
595 Anglum Road
Hazelwood, MO. 63042

September 13, 2013

Re: k132573
Trade/Device Name: VITEK®2 AST-ST Moxifloxacin (≤ 0.06- ≥4µg/mL)
Regulation Number: 21 CFR §866.1645
Regulation Name: Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System
Regulatory Class: II
Product Code: LON
Dated: August 13, 2013
Received: August 16, 2013

Dear Mr. Hardesty:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Sally A. Hojvat -S

Sally A. Hojvat, M.Sc., Ph.D
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number : k132573

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(≤ 0.06 – ≥ 4 µg/mL)

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Prescription Use ___X___ AND/OR Over-The-Counter Use _____
(Part 21 CFR 801 Subpart D) (21 CFR 807 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of In Vitro Diagnostics and Radiological Health (OIR)

Ribhi Shawar -S