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

A. 510(k) Number:

k113305

B. Purpose for Submission:

To obtain a substantial equivalence determination for the addition of the VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole (SXT) to the VITEK® 2 and VITEK® 2 Compact Antimicrobial Susceptibility Test (AST) Systems.

C. Measurand:

Trimethoprim/Sulfamethoxazole concentrations of 8/152, 16/304 and 64/1216 µg/mL

D. Type of Test:

A minimum inhibitory concentration (MIC) assay, determined using qualitative growth based detection algorithm using predetermined growth threshold.

E. Applicant:

bioMerieux, Inc.

F. Proprietary and Established Names:

VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole

G. Regulatory Information:

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

H. Intended Use:

1. Intended use:

   VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole is designed for antimicrobial susceptibility testing of Streptococcus species. VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole is a qualitative 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. Trimethoprim/Sulfamethoxazole has been shown to be active against the microorganisms listed below according to the FDA label for the antimicrobial.

Active in vitro and in clinical infections:

Streptococcus pneumoniae

2. Indication(s) for use:

VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole is designed for antimicrobial susceptibility testing of Streptococcus species. VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole is a qualitative 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. Trimethoprim/Sulfamethoxazole has been shown to be active against the microorganisms listed below according to the FDA label for the antimicrobial.

Active in vitro and in clinical infections:

Streptococcus pneumoniae

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 agalactiae, S. pneumoniae* and clinically significant yeast.

3. Special conditions for use statement(s):

Prescription use only.

4. Special instrument requirements:

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

I. Device Description:

VITEK 2 AST card containing the test is inoculated with a standardized suspension of the organism to be tested. The VITEK 2 System automatically fills, seals, and places the card into the incubator/reader while the VITEK 2 Compact System has manual filling, sealing and loading operation. The incubated card is optically monitored by the VITEK 2 Systems for growth within each well in the card throughout the incubation cycle. At the completion of incubation, results are automatically calculated once a predetermined growth threshold is reached. A report is then generated that

contains the MIC value and the interpretive category result (S, I, R) for each antibiotic contained on the card.

The MIC ranges, interpretive criteria and equivalent concentrations for testing *S. pneumoniae* are as follows:

VITEK 2 AST-ST†	Equivalent Standard Method Concentration by Efficacy in µg/mL	MIC Ranges and FDA/CLSI Categories MIC* in µg/mL:		
		S	I	R
Trimethoprim/ Sulfamethoxazole	8/152, 16/304, and 64/1216 µg/mL	≤0.5/9.5	1/19-2/38	≥4/76

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

† VITEK reports MIC values as a combined concentration of Trimethoprim plus Sulfamethoxazole based on a ratio of 1:19.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITEK 2 Gram Positive Amoxicillin for *S. pneumoniae*

2. Predicate K number(s):

   k063597

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Determining quantitative and qualitative susceptibility to antimicrobial agents	Same
Inoculation and test organism	Isolated colonies of *Streptococcus pneumoniae*	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
Antibiotic	Trimethoprim/Sulfamethoxazole -specific concentrations	Amoxicillin-specific concentrations
Reading algorithm	Results generated using the discriminant analysis algorithm that is unique to Trimethoprim/Sulfamethoxazole	Results generated using the discriminant analysis algorithm that is unique to Amoxicillin
Test Method	Automated qualitative antimicrobial susceptibility test to determine the in vitro susceptibility of *Streptococcus pneumoniae*	Automated quantitative antimicrobial susceptibility test to determine the in vitro susceptibility of *Streptococcus* species

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 -7th Edition, Document M7-A8.

Performance Standards for Antimicrobial Susceptibility Testing – 18th 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 Trimethoprim/Sulfamethoxazole card has the following Trimethoprim/Sulfamethoxazole concentrations of 8/152, 16/304 and 64/1216

µg/mL. The MIC result range for the VITEK 2 card is ≤ 10 (0.5/9.5)– ≥320 (16/304) µg/mL.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Reproducibility was conducted at three study sites. Ten isolates of *Streptococcus pneumoniae* were tested at each site and testing was performed in triplicate over three days with The VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole. The testing was performed using both the manual dilution method and the automated dilution mode. Testing was conducted on the VITEK 2 instrument.

   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.

   There were no off-scale MIC values. The overall reproducibility was 100% with +/- one dilution observation for Automatic and Manual Dilution methods.

   A similar reproducibility study was conducted by testing on the VITEK 2 Compact instrument. The VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole card gave a reproducibility of 100% by Manual Dilution. Only Manual Dilution testing was conducted since the VITEK 2 Compact system does not have a functionality to support automatic dilution to inoculate the card.

   b. *Linearity/assay reportable range:*

   Not applicable

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

   One QC isolate of *Streptococcus pneumoniae* 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 and reference testing was performed a minimum of twenty times by each method at each site. There were some instances were either VITEK or reference results were out of range. In such instances where any organism was out of range for the reference method, all data from that day's testing was considered

invalid and that day's testing was repeated.

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

Organism	Concentration (µg/mL)	Auto Dilution		Manual Dilution	
		Reference	VITEK 2	Reference	VITEK 2
Streptococcus pneumoniae ATCC 49619 Acceptable MIC range: 0.12/2.4 to 1/19 µg/mL	≤ 0.06/1.2				
	0.12/2.4	22		22	
	0.25/4.75	150		147	
	0.5/9.5	7		7	
	1/19	2		2	
	≤10 (0.5/9.5)*		181		178
	20 (1/19)*				
	40 (2/38)*				

* VITEK Card Result Range is ≤10 (0.5/9.5) to ≥320 (16/304) µg/mL. VITEK reports MIC values as a combined concentration of Trimethoprim plus Sulfamethoxazole based on a ratio of 1:19.

Quality Control results for the VITEK 2 System using either inoculation dilution method demonstrated that the VITEK 2 System could produce the expected QC ranges with an acceptable rate.

A similar QC study was conducted to evaluate the VITEK 2 Compact System. Results were compared to the expected 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 sites. A total of 306 clinical isolates were tested by the VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole. The vast majority of the isolates were recently isolated from clinical specimens. A challenge set consisting of 50 isolates was also evaluated. Testing was done using the VITEK® 2 Streptococcus Trimethoprim/Sulfamethoxazole and the broth microdilution method using cation-adjusted Mueller Hinton (MH) broth. The MH broth was incubated at 35°C in ambient air for up to 16-20 hours. The inoculum was prepared with direct colony suspension. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. Two methods of inoculation (manual and auto dilution) were evaluated. Clinical testing was performed using the automated method of inoculation and the challenge set was tested using both the manual and the auto dilution method. A comparison was provided to the reference method with the following agreement.

AutoDilution

Organism Group	CA Tot	CA N	CA %	#R	# vmj	# maj	# min
Streptococcus pneumoniae							
CLINICAL	306	292	95.4	83	0	0	14
CHALLENGE	50	50	100	50	0	NA	0
COMBINED (CLINICAL AND CHALLENGE)	356	342	96.1	133	0	0	14

maj-major discrepancies; **vmj**-very major discrepancies; **min**-minor discrepancies

Essential agreement (EA) is when the VITEK 2 panels agree with the reference test panel 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 reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the VITEK 2 and the reference and have on-scale EA.

EA was not evaluated since this is a qualitative test. However, CA of 96.1% was observed for both clinical and challenge isolates, which is an acceptable

performance. Also, another study on the VITEK 2 Compact Systems demonstrated acceptable CA (See below).

A total of 50 Challenge *S. pneumoniae* isolates were also tested in the VITEK 2 Compact using the manual dilution method. A comparison was provided to the reference method with the following agreement.

Manual Dilution

Organism Group	CA Tot	CA N	CA %	#R	# vmj	# maj	# min
***Streptococcus pneumoniae* CHALLENGE**	50	50	100	50	0	NA	0

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 MIC in µg/ml for Trimethoprim/Sulfamethoxazole when testing *Streptococcus pneumoniae* are:
S= ≤ 0.5/9.5 µg/mL
I=1/19 to 2/38
R= ≥ 4/76 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.