

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

A. 510(k) Number:

k111893

B. Purpose for Submission:

The addition of Tetracycline to the VITEK ® 2 and VITEK®2 Compact Systems Antimicrobial Susceptibility Test (AST) Systems

C. Measurand

VITEK ® 2 Streptococcus Tetracycline (≤ 0.25 - ≥ 16 $\mu\text{g/mL}$)

D. Type of Test:

Automated quantitative growth based detection algorithm using optics light detection

E. Applicant:

bioMérieux, Inc.

F. Proprietary and Established Names:

Vitek®2 Streptococcus Tetracycline (≤ 0.25 - ≥ 16 $\mu\text{g/mL}$)

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):

VITEK[®] 2 *Streptococcus* Tetracycline is designed for antimicrobial susceptibility testing of *Streptococcus* species. VITEK[®] 2 *Streptococcus* Tetracycline is a quantitative test intended for use with the VITEK[®] 2 and the VITEK[®] 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. Tetracycline has an antimicrobial activity against the microorganisms listed below, according to the FDA label for this antimicrobial.

Streptococcus pneumoniae
Streptococcus pyogenes
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..

2. Indication(s) for use:

VITEK[®] 2 *Streptococcus* Tetracycline is designed for antimicrobial susceptibility testing of *Streptococcus* species. VITEK[®] 2 *Streptococcus* Tetracycline is a quantitative test intended for use with the VITEK[®] 2 and the VITEK[®] 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. Tetracycline has an antimicrobial activity against the microorganisms listed below, according to the FDA label for this antimicrobial.

Active *in vitro* and in clinical infections:

Streptococcus pneumoniae
Streptococcus pyogenes
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 condition for use statement(s):

Prescription Use Only

4. Special instrument Requirements:

VITEK[®] 2 and the VITEK[®] 2 Compact Systems

I. Device Description:

Each VITEK[®] 2 test card contains 64 micro-wells, with a control well which contains only microbiological culture media 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 AST-ST Tetracycline has the following concentrations in the card: 0.125, 0.5, 1, 4µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK 2 card is ≤0.25 – ≥ 16µg/mL.

J. Substantial Equivalence Information:

1. Predicate device name(s)

VITEK[®] 2 Gram Positive Amoxicillin for *Streptococcus pneumoniae*

2. Predicate K number(s):

k063597

3. Comparison with predicate

Similarities		
Item	Device	Predicate
Intended Use	Determine antimicrobial susceptibility to antimicrobial agents	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	Tetracycline	Amoxicillin
Reading algorithm	Unique for Tetracycline	Unique for amoxicillin
Test organism	<i>S. pneumoniae</i> , <i>S. pyogenes</i> , viridans <i>Streptococci</i>	<i>S. pneumoniae</i>

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

Class II Special Controls Guidance Document: “Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”, issued August 28, 2009.

CLSI M7-A8 “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard”

CLSI M100-S19 “Performance Standards for Antimicrobial Susceptibility; Twenty-First Information Supplement”

L. Test Principle:

Each VITEK® 2 test card contains 64 micro-wells. A control well which contains only microbiological culture media is 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 AST-ST Tetracycline has the following concentrations in the card: 0.125, 0.5, 1, 4µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK 2 card is ≤0.25 – ≥ 16µg/mL.

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):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was demonstrated using 10 isolates at three sites on three separate days in triplicates. The study included the Auto-dilution and the Manual dilution with the VITEK®2, and the Manual dilution with the VITEK®2 Compact. All results were >95% reproducible.

b. *Linearity/assay reportable range:*

Not Applicable

c. *Traceability (controls, calibrators, or method):*

The recommended QC isolates were tested on every test occasion with the reference method and the VITEK®2. 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-dilution and the manual method of diluting the organisms. Results demonstrated that methods were comparable with the same mode.

Quality Control Summary (VITEK®2, Auto and Manual dilution)

Organism	Conc. in µg/ml	Auto-dilution		Manual dilution	
		Ref.	Test	Ref.	Test
<i>S. pneumoniae</i>					
ATCC 49619	≤0.0625	1		1	
Expected Range	0.125	163		165	
0.12- 0.5 µg/mL	0.25	50	214	49	215
(Card Range	0.5				
≤0.25- 0.5 µg/mL)					

An additional QC study was performed with the VITEK®2 Compact, the secondary option, at three sites, with the following results.

Quality Control Summary (VITEK®2 Compact, Manual dilution)

Organism	Conc. in µg/ml	Manual-dilution	
		Ref.	Test
<i>S. pneumoniae</i>			
ATCC 49619	0.125		
Expected Range	0.25	17	60
0.12- 0.5 µg/ml	0.5	43	
(Card Range	0.125		
≤0.25- 0.5 µg/mL)			

Inoculum density control was monitored using the DensiChek2 instrument. This 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:

The reference method follows CLSI approved broth microdilution testing conditions:

- Medium: Mueller-Hinton broth supplemented with lysed blood
- Inoculum: Direct colony suspension
- Incubation : 35°C, ambient air, 20- 24 hours

a. *Method comparison with predicate device:*

Clinical study was performed at four external sites using the VITEK2 *Streptococcus* Tetracycline and broth microdilution panels containing Tetracycline. A total of 1338 clinical isolates were tested at four external sites by auto inoculation. All clinical isolates grew in the VITEK®2 AST-ST Tetracycline Test. Two hundred and nine (15.6%: 209/1338) were from stock isolates. For comparison of auto and manual dilution, the challenge set of 197 isolates was included.

**Performance Summary Table (VITEK 2, Auto Dilution), using FDA Breakpoints
(≤ 4 , 8, ≥ 16)**

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Clinical	1338	1290	96.4	191	155	81.2	1296	96.9	475	36	2	4
Challenge	197	196	99.5	32	32	100	195	99.0	69	2	0	0
Combined	1535	1486	96.8	223	187	83.9	1491	97.1	544	38	2	4

**Performance Summary Table (VITEK 2, Auto Dilution), using CLSI Breakpoints
(≤ 2 , 4, ≥ 8)**

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Clinical	1338	1290	96.4	191	155	81.2	1283	95.9	507	42	2	11
Challenge	197	196	99.5	32	32	100	197	100	71	0	0	0
Combined	1535	1486	96.8	223	187	83.9	1480	96.4	578	42	0	11

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 197 organisms was also tested at one site using the manual method of inoculation with the following performance.

**Comparison Challenge Data - Auto vs. Manual dilution (VITEK 2), FDA
Breakpoints(≤ 4 , 8, ≥ 16)**

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Auto	197	196	99.5	32	32	100	195	99.0	69	2	0	0
Manual	197	195	99.0	33	32	97.0	194	98.5	69	3	0	0

**Comparison Challenge Data - Auto vs. Manual dilution (VITEK 2), CLSI
Breakpoints(≤ 2 , 4, ≥ 8)**

	total	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Auto	197	196	99.5	32	32	100	197	100	71	0	0	0
Manual	197	195	99.0	33	32	97.0	197	100	71	0	0	0

The performance of the optional VITEK®2 Compact was evaluated in the QC, challenge, and reproducibility studies with acceptable results with the FDA breakpoints.

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
 ≤ 4 (S), 8(I), ≥ 16 (R)

N. Proposed Labeling:

The labeling is sufficient and 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.