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

A. 510(k) Number:

k131779

B. Purpose for Submission:

To obtain clearance for the addition of Tigecycline to the VITEK® 2 and VITEK® 2 Compact Systems Antimicrobial Susceptibility Test (AST) Systems

C. Measurand:

VITEK® 2 *Streptococcus* Tigecycline concentrations (≤ 0.06- ≥ 1µg/mL)

D. Type of Test:

Quantitative growth based detection algorithm using optics light detection

E. Applicant:

bioMérieux, Inc.

F. Proprietary and Established Names:

VITEK 2 AST-ST Tigecycline (≤ 0.06- ≥ 1µg/mL)
VITEK 2 *Streptococcus* Tigecycline

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(s):

VITEK® 2 *Streptococcus* Tigecycline 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* Tigecycline is a qualitative test. Tigecycline 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 (penicillin-susceptible isolates)
Streptococcus anginosus grp. (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*)
Streptococcus agalactiae
Streptococcus pyogenes

2. Indication(s) for use:

VITEK® 2 *Streptococcus* Tigecycline 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* Tigecycline is a qualitative test. Tigecycline 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 (penicillin-susceptible isolates)
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Streptococcus agalactiae
Streptococcus pyogenes

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):

- Prescription Use only

- The ability of the VITEK 2 AST-ST card to detect resistance to Tigecycline in *Streptococcus pneumoniae* (penicillin-susceptible isolates), *S. anginosus*, *S. intermedius*, *S. constellatus*, *S. agalactiae* and *S. pyogenes* is unknown because resistant strains were not available at the time of comparative testing.

4. Special instrument requirements:

VITEK® 2 and the VITEK® 2 Compact Systems

I. Device Description:

Each VITEK® 2 test card contains 64 micro-wells. A control well containing only 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 AST-ST Tigecycline has the following concentrations in the card: 0.125, 0.25, and 0.5 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The Tigecycline MIC result range for the VITEK®2 card is ≤0.06 to ≥ 1µg/mL.

The MIC interpretive criteria and equivalent concentrations are as follows:

VITEK® 2 AST-ST	Equivalent Standard Method Concentration by Efficacy in µg/mL	MICs for FDA Categories* MIC in µg/mL:		
		S***	I	R
Tigecycline	0.125, 0.25, 0.5	*Streptococcus agalactiae*, *Streptococcus pyogenes* and *Streptococcus anginosus* group**		
		≤ 0.25	-	-
		Streptococcus pneumoniae (Penicillin susceptible only)		
		≤ 0.06	-	-

* FDA category interpretation indicated by boldface type
** *Streptococcus anginosus* group including *Streptococcus anginosus*, *Streptococcus constellatus*, and *Streptococcus intermedius*
*** Currently only a "Susceptible" category is defined for Tigecycline

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITEK® 2 AST-ST Linezolid

2. Predicate 510(k) number(s):

   k111599

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Determine antimicrobial susceptibility to antimicrobial agents	
Test Card	VITEK® 2 card format with base broth	same
Instrument	VITEK® 2 and VITEK ®2 Compact System	same

Differences		
Item	Device	Predicate
Antibiotic	Tigecycline	Linezolid
Reading Algorithm	Unique for Tigecycline, Growth Pattern Analysis (GPA) algorithm	Unique for Linezolid, Discriminant Analysis
Test organisms	*Streptococcus pneumoniae* (penicillin-susceptible isolates), *Streptococcus anginosus* grp. (includes *S. anginosus*, *S. intermedius*, *S. constellatus*), *S. agalactiae* and *S. pyogenes*	*Streptococcus agalactiae, S. pneumoniae* (including multi-drug resistant isolates), *S. pyogenes*

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

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

CLSI M7-A8 "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard", January 2009

CLSI M100-S21 "Performance Standards for Antimicrobial Susceptibility; Twenty-First Information Supplement", January 2011

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 is 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 AST-ST Tigecycline has the following concentrations in the card: 0.125, 0.25, and 0.5 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The Tigecycline MIC result range for the VITEK®2 card is ≤0.06 to ≥ 1µg/mL.

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. As this is a qualitative test, results were evaluated for reproducibility based on Category Agreement only. Results were >95% reproducible. Of the ten isolates tested, five had on-scale MIC values.

The study included the Auto-dilution and the Manual dilution with the VITEK 2, and the Manual dilution with the VITEK 2 Compact.

b. Linearity/assay reportable range:

Not Applicable

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

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	
S. pneumoniae ATCC 49619 Expected Range 0.015- 0.125 µg/ml		**Reference**	**VITEK 2**	**Reference**	**VITEK 2**
	≤0.0078	2		1	
	0.015	61		27	
	0.03	129		68	
	0.06	8	201	5	102
	0.125	1		1	

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

Quality Control Summary (VITEK 2 Compact, Manual dilution)

Organism	Conc in µg/ml	Manual-dilution	
S. pneumoniae ATCC 49619 Expected Range 0.015- 0.125 µg/ml		**Reference**	**VITEK 2 Compact**
	≤0.0078	1	
	0.015	25	
	0.03	69	
	0.06	5	101
	0.125	1	

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 the CLSI approved broth microdilution testing conditions for Tigecycline:

- Medium: Mueller-Hinton broth supplemented with lysed blood. The broth was prepared fresh and immediately frozen. For use, it was inoculated no longer than one hour for thawing at room temperature.
- Inoculum: Direct colony suspension
- Incubation : 35°C, ambient air, 20- 24 hours

a. Method comparison with predicate device:

There are less than five discrete dilutions in the VITEK 2 AST-ST Tigecycline card. Therefore, essential agreement (EA) was not established.

A total of 722 clinical and 161challenge organisms were tested at four sites. Six clinical isolates failed to grow in the VITEK 2 card, giving a no growth rate of 0.83% (6/722). There were 202 stock isolates (28.0%, 202/722). The total number of viable clinical isolates was 716. There were a total of 877 results for evaluation. The performance data were analyzed using FDA interpretative criteria. A summary of the

clinical and challenge data for various *Streptococcus* spp. for the auto-dilution method is shown in the table below.

Performance Summary Table (VITEK 2, Auto Dilution)

	CA total	**CA#**	**%CA**	**#R**	**min**	**maj**	**vmj**
S. pneumoniae ≤0.06, -, -							
Clinical	241	241	100	0	NA	0	0
Challenge	50	50	100	0	NA	0	0
Combined	291	291	100	0	NA	0	0
S. agalactiae, S. pyogenes, S. anginosus group ≤0.25, -, -							
Clinical	475	473	99.6	0	NA	2	0
Challenge	111	111	100	0	NA	0	0
Combined	586	584	99.7	0	NA	2	0
Total	**877**	**875**	**99.8**	**0**	**NA**	**2**	**0**

maj-major discrepancies
CA-Category Agreement vmj-very major discrepancies
R-resistant isolates min- minor discrepancies
Category agreement (CA) is when the VITEK® 2 panel result interpretation agrees exactly with the broth microdilution reference panel result interpretation.

S. agalactiae
There were two major discrepancies (Susceptible by reference, non-susceptible by VITEK) for *S. agalactiae*, with an acceptable rate of 0.7% (2/276) when analyzed for this organism separately.

The challenge set of 161 isolates was also tested against a manual dilution method on the VITEK 2. The performance of the VITEK 2 Compact was evaluated as a secondary procedural option. The evaluation was conducted using the same 161 challenge isolates. A summary of VITEK 2 and VITEK 2 Compact manual dilution data is shown in the table below.

Comparison Challenge Data - VITEK 2, and VITEK®2 Compact (Manual dilution)

	CA total	**CA#**	**%CA**	**#R**	**min**	**maj**	**vmj**
VITEK2	161	161	100	0	NA	0	0
VITEK2 Compact	161	161	100	0	NA	0	0

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:

   Susceptibility Test Result Interpretive Criteria for Tigecycline are as follows:

S. pneumoniae	S= ≤0.06, NS=*
S. agalactiae, S. pyogenes, S. anginosus group	S= ≤0.25, NS=*

   *Currently only a "Susceptible" category is defined for Tigecycline. Strains yielding test results suggestive of a "nonsusceptible" category should be retested, and if the result is confirmed, the isolate should be submitted to a reference laboratory for further testing.

N. Proposed Labeling:

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

O. Conclusion:

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