

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K132507

B. Purpose for Submission:

The addition of Meropenem to the VITEK[®] 2 AST *Streptococcus* card

C. Measurand:

Meropenem $\leq 0.06 - \geq 4$ $\mu\text{g/mL}$

D. Type of Test:

Antimicrobial Susceptibility Test (Quantitative)

E. Applicant:

bioMerieux, Inc.

F. Proprietary and Established Names:

VITEK[®] 2 AST-ST Meropenem

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* Meropenem 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* Meropenem is a quantitative test. Meropenem 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 strains)

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.

2. Indication(s) for use:

VITEK[®] 2 *Streptococcus* Meropenem 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* Meropenem is a quantitative test. Meropenem 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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3. Special conditions for use statement(s):

- For prescription use only
- The ability of the VITEK[®] 2 AST *Streptococcus* Meropenem to detect resistance to meropenem in *S. pneumoniae*, *S. agalactiae* and *S. pyogenes* is unknown because resistant strains 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 a miniaturized, abbreviated and automated version of the doubling dilution technique for determining the minimum inhibitory concentration (MIC). Each VITEK[®] 2 test card contains 64 microwells, containing a premeasured amount of a specific antibiotic in a culture medium base. A control well, containing only culture medium, is included on all cards. A suspension of organism from a pure culture is prepared in a tube containing 0.45-0.5% sterile saline and standardized to a McFarland 0.5 using the DensiCHEK Plus™. The desired test card is placed in the cassette along with an empty transfer tube which is incorporated into the side of the susceptibility card and placed in the organism suspension. The cassette is placed into the VITEK[®] 2 instrument where a diluted susceptibility test suspension is automatically prepared by the Vitek[®] 2 System, using the original organism suspension. The cards are automatically filled with the susceptibility test suspension via vacuum, the tubes are cut, and the cards are sealed prior to proceeding to the Incubator Loading Station. Cards are transferred from the cassette into a carousel for incubation (35.5°C) and reading via optical scanning. Readings are performed every 15 minutes for the duration of the incubation cycle.

The VITEK[®] 2 AST *Streptococcus* Meropenem has the following concentrations in the card: 0.25, 0.5, 1, 2, and 4 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK[®] 2 AST *Streptococcus* Meropenem card is ≤ 0.06 - ≥ 4 µg/mL. The MIC interpretive criteria and equivalent concentrations are listed in Table 1 below.

Table 1. MIC Interpretive Criteria and Equivalent Concentrations

Vitek [®] 2 AST- <i>Streptococcus</i>	Equivalent Standard Method Conc. By Efficacy in µg/mL	MIC Ranges and CLSI/FDA Categories (MIC in µg/mL)		
		S	I	R
Meropenem	0.25, 0.5, 1, 2, 4	<i>Streptococcus agalactiae</i> <i>Streptococcus pyogenes</i>		
		≤ 0.5*	-	-
		<i>Streptococcus pneumoniae</i>		
		≤ 0.25	0.5	≥ 1

*The current absence of data on resistant isolates precludes defining any category other than “Susceptible”. If isolates yield MIC results other than susceptible, they should be submitted to a reference laboratory for additional testing.

J. Substantial Equivalence Information:

1. Predicate device name(s):

VITEK[®] 2 *Streptococcus* Ceftriaxone

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

K122359

3. Comparison with predicate:

Table. 2- Similarities and Differences of the VITEK[®] 2 *Streptococcus* Meropenem and the Predicate

Similarities		
Item	Device	Predicate
Intended Use	Determine quantitative antimicrobial susceptibility to antimicrobial agents	Same
Inoculum	Saline suspension of organism	Same
Instrument	VITEK [®] 2 and VITEK [®] 2 Compact Systems	Same
Test Card	VITEK [®] 2 Test Card format	Same
Differences		
Item	Device	Predicate
Antimicrobial Agent	Meropenem	Ceftriaxone
Test Isolates	<i>S. pneumoniae</i> <i>S. agalactiae</i> <i>S. pyogenes</i>	<i>S. pneumoniae</i> <i>S. agalactiae</i> <i>S. pyogenes</i> Viridans group <i>Streptococcus</i>
Reading Algorithm	Unique to meropenem	Unique to ceftriaxone

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

- Guidance for Industry and FDA – Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; August 28, 2009.
- Clinical and Laboratory Standards Institute (CLSI). Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard – Eighth Edition. CLSI document M07-A8, 2010.
- CLSI. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-First Informational Supplement. CLSI document M100-S21, 2011.

L. Test Principle:

The VITEK[®] 2 System optics use visible light to directly measure organism growth. The 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. An interpretive call is made between 4 and 16 hours for a “rapid” read but may be extended to 18 hours in some instances. The VITEK[®] 2 susceptibility card test is based on the microdilution minimum inhibitory concentration (MIC) technique with concentrations equivalent to standard method concentrations. Several parameters based on the growth characteristics observed are used to provide appropriate input for the MIC calculations. Discriminate analysis is used to develop the algorithm that determines the susceptibility result for all antimicrobials on the VITEK[®] 2 System. The MIC result must be linked to organism identification in order to determine a category interpretation. A category interpretation (SIR) will be reported along with each MIC result.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility studies were performed using 10 isolates of *Streptococcus pneumoniae* at 3 sites on 3 separate days, in triplicate. The studies included both the auto- and manual dilution methods with the VITEK[®] 2 instrument system and the manual dilution method with the VITEK[®] 2 Compact instrument system. Greater than 95% reproducibility was demonstrated with both the VITEK[®] 2 and VITEK[®] 2 Compact Systems. All MIC results were on-scale for both inoculation methods and all reading methods; therefore, best case and worst case scenarios were identical. A summary of the reproducibility study performance is illustrated in Table 3 below.

Table 3. - Summary of Reproducibility Studies

VITEK[®] 2 Instrument Platform	Inoculation Method	Best Case	Worst Case
VITEK [®] 2	Auto-dilution	100%	100%
	Manual	100%	100%
VITEK [®] 2 Compact	Manual	100%	100%

b. *Linearity/assay reportable range:* Not Applicable

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

Quality control testing was conducted during device performance testing at each study site. The recommended quality control (QC) isolate, namely *S. pneumoniae* ATCC 49619, was tested on every test occasion with the reference method and the

VITEK[®] 2 instrument platform, using both auto- and manual dilution methods. QC results for the VITEK[®] 2 AST *Streptococcus* Meropenem were within the expected range > 95% of the time for both dilution methods. Testing was conducted a sufficient number of times to demonstrate that the device can produce QC results in the recommended range. A summary of the QC testing is illustrated in Table 4 below.

Table 4. QC Testing - VITEK[®] 2 *Streptococcus* Meropenem (Auto- and Manual Dilution Methods)

ORGANISM	Conc. (µg/mL)	Vitek [®] 2 Auto-dilution		Vitek [®] 2 Manual dilution	
		Test	Ref.	Test	Ref.
<i>S. pneumoniae</i> ATCC 49619 Expected Range : 0.06 – 0.25 µg/mL	0.03125		3		1
	0.0625*	70	196	32	100
	0.125	133	3	72	3
	0.25		1		
	0.5				

*This value is indicated a ≤ 0.06 for the VITEK[®] 2 System

In those instances where the test result was out-of-range for all replicates of the reference method, all data from that day's testing was considered invalid and the testing for that day was repeated.

Inoculum density control was monitored using the DensiCHEK Plus™ instrument. The DensiCHEK Plus™ was standardized weekly with all results recorded and in 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:*

Clinical study testing was conducted at three external sites using the VITEK[®] 2 AST *Streptococcus* Meropenem card on the VITEK[®] 2 instrument platform and the broth microdilution reference method using Mueller-Hinton broth with lysed horse blood prepared as recommended by the CLSI. Performance testing included a total of 699

clinical isolates, both fresh and stock (28.3%; 198/699). Testing of the clinical isolates was performed using the automated method of dilution of the AST card inoculum. Performance data comparing the VITEK[®]2 AST *Streptococcus* Meropenem card and the reference method are illustrated in Table A below.

Challenge study testing was conducted, at one external site using the VITEK[®]2 AST *Streptococcus* Meropenem card on the VITEK[®]2 instrument platform and the broth microdilution reference method using Mueller-Hinton broth with lysed horse blood prepared as recommended by the CLSI. A challenge set consisting of a total of 100 isolates, including 50 isolates of *S. agalactiae* and 50 isolates of *S. pneumoniae*, was used for the performance testing. Testing of the challenge isolates was performed using both the auto- and manual method of dilution of the AST card inoculum. As illustrated in Tables A and B below, there is very little difference in the challenge testing device performance between the two methods of dilution of the AST card inoculum.

Challenge testing of the VITEK[®]2 AST *Streptococcus* Meropenem card on the VITEK[®]2 Compact instrument platform was also conducted as a secondary procedural option against the broth microdilution reference method. Testing was conducted at one external site, using the same challenge set of 100 isolates. Testing was performed using the manual method of dilution of the AST card inoculum. The performance data is illustrated in Table C below.

S. agalactiae, *S. pyogenes* isolates were analyzed using the FDA breakpoint ($\leq 0.5 = S$). *S. pneumoniae* isolates were analyzed using the FDA breakpoints ($\leq 0.25 = S$; $0.5 = I$; $\geq 1 = R$).

Table A. VITEK ² / <i>Streptococcus</i> Meropenem Auto-dilution	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical												
<i>S. agalactiae</i>	226	225	99.6	0	0	0	226	100	0	0	0	0
<i>S. pneumoniae</i>	241	235	97.5	30	27	90	228	94.6	2	12	1	0
<i>S. pyogenes</i>	232	230	99.1	0	0	0	232	100	0	0	0	0
Total Clinical	699	690	98.7	30	27	90	686	98.1	2	12	1	0
Challenge												
<i>S. agalactiae</i>	50	50	100	0	0	0	50	100	0	0	0	0
<i>S. pneumoniae</i>	50	48	96.0	38	36	94.7	36	72.0	2	14	0	0
Total Challenge	100	98	98.0	38	36	94.7	86	86.0	2	14	0	0
Combined Clinical and Challenge	799	788	98.6	68	63	92.6	772	96.6	4	26	1	0

Table B. VITEK ₂ / Streptococcus Meropenem Manual Dilution	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Challenge												
<i>S. agalactiae</i>	50	50	100	0	0	0	50	100	0	0	0	0
<i>S. pneumoniae</i>	50	49	98.0	37	36	97.3	34	68.0	2	16	0	0
Total Challenge	100	99	99.0	37	36	97.3	84	84.0	2	16	0	0

Table C. VITEK ₂ Compact/ Streptococcus Meropenem Manual Dilution	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Challenge												
<i>S. agalactiae</i>	50	50	100	0	0	0	50	100	0	0	0	0
<i>S. pneumoniae</i>	50	49	98.0	37	36	97.3	35	70	2	15	0	0
Total Challenge	100	99	99.0	37	36	97.3	85	85	2	15	0	0

EA = Essential Agreement

R = Resistant Isolates

maj = major discrepancies

CA = Category Agreement

min = minor discrepancies

vmj = very major discrepancies

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within plus/minus one dilution. Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of VITEK[®]2 AST card within plus or minus one serial two-fold dilution of the antibiotic. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the VITEK[®]2 AST card result.

Relative to all the clinical and challenge testing performed using the VITEK[®]2 AST *Streptococcus* Meropenem card, the overall %EA and %CA in most instances, met the acceptance criteria of greater than or equal to 90%. In each instance where the %CA fell below 90%, the percent essential agreement of evaluable results was very good and all the discrepancies were minor discrepancies. There were no categorical very major errors.

Relative to all the clinical and challenge testing performed using the VITEK[®]2 AST *Streptococcus* Meropenem card, there were no instances of growth failure.

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:

The MIC interpretive criteria are illustrated in Table 5 below.

Table 5. - MIC Interpretive Criteria

Antibiotic	Organism	Interpretive Criteria
Meropenem	<i>Streptococcus pneumoniae</i> (penicillin-susceptible strains)	S ≤ 0.25 I = 0.5 R ≥ 1
	<i>Streptococcus agalactiae</i> <i>Streptococcus pyogenes</i>	S ≤ 0.5*

*The current absence of data on resistant isolates precludes defining any category other than “Susceptible”. If isolates yield MIC results other than susceptible, they should be submitted to a reference laboratory for additional testing.

N. Proposed Labeling:

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

O. Conclusion:

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