510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K260283

B Applicant

bioMérieux, Inc

C Proprietary and Established Names

VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LON	Class II	21 CFR 866.1645 - Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System	MI - Microbiology
LTT	Class II	21 CFR 866.1640 - Antimicrobial susceptibility test powder	MI - Microbiology
LTW	Class II	21 CFR 866.1640 - Antimicrobial susceptibility test powder	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantial equivalence determination for the VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL) for susceptibility testing of *Streptococcus pneumoniae*, *Streptococcus* spp. β-Hemolytic Group and *Streptococcus* spp. Viridans Group on the VITEK 2, VITEK 2 Compact, and VITEK COMPACT PRO Antimicrobial Susceptibility Test (AST) Systems.

B Measurand:

Meropenem ≤0.06 - ≥4 µg/mL

C Type of Test:

Automated quantitative or qualitative antimicrobial susceptibility test

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL) is designed for antimicrobial susceptibility testing of *Streptococcus* species and is intended for use with the VITEK 2 Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents.

VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL) is a quantitative test. Testing is indicated for *Streptococcus pneumoniae*, *Streptococcus* spp. β-Hemolytic Group and *Streptococcus* spp. Viridans Group, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC).

VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL) has demonstrated acceptable performance with the following organisms:

Streptococcus pneumoniae

Streptococcus spp. β-Hemolytic Group (*Streptococcus agalactiae*, *Streptococcus canis*, *Streptococcus dysgalactiae* ssp. *equisimilis*, *Streptococcus equisimilis* ssp. *zooepidemicus*, *Streptococcus pyogenes*)

Streptococcus spp. Viridans Group (*Streptococcus anginosus*, *Streptococcus constellatus*, *Streptococcus cristatus*, *Streptococcus gallolyticus* ssp. *gallolyticus*, *Streptococcus gordonii*, *Streptococcus infantarius* ssp. *infantarius*, *Streptococcus mitis*, *Streptococcus oralis*, *Streptococcus parasanguinis*, *Strepotococcus salivarius* ssp. *salivarius*, *Streptococcus sanguinis*, *Streptococcus uberis*, *Streptococcus vestibularis*)

The VITEK 2 *Streptococcus* Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Streptococcus pneumoniae*, beta-hemolytic *Streptococcus*, and Viridans *Streptococcus* to antimicrobial agents when used as instructed.

C Special Conditions for Use Statement(s):

Rx – For Prescription Use Only

If *Streptococcus anginosus* does not provide a result for the VITEK2 AST-ST test cards but growth is observed on the purity plate, do not retest the isolate on the VITEK2 Systems and perform an alternative method of testing prior to report of results.

The ability of the AST card to detect non-susceptible strains with the following combination(s) is unknown because an insufficient number of non-susceptible strains were available at the time of comparative testing:
Meropenem (mem02n): *Streptococcus* spp. β-Hemolytic Group, *Streptococcus* spp. Viridans Group *(except Streptococcus mitis, Streptococcus oralis, Streptococcus parasanguinis)*

Due to the occurrence of minor errors (resulting in a category agreement below 90% for the manual dilution options), perform an alternative method of testing prior to reporting of results generated with the manual dilution options for the following antibiotic/organism combination:
Meropenem (mem02n): *Streptococcus pneumoniae* (if critical to patient care).

D Special Instrument Requirements:

VITEK 2 Systems (i.e., VITEK 2, VITEK 2 Compact, and VITEK COMPACT PRO), Software version 10.1 or newer

IV Device/System Characteristics:

A 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 AST card contains 64 wells. A control well which contains only nutrient medium is resident on all cards. The remaining wells contain premeasured portions of antimicrobials combined with the nutrient media. The isolate to be tested is diluted to a standardized concentration with 0.45% to 0.50% saline before being used to rehydrate the antimicrobial medium within the card.

VITEK 2 AST cards are intended to be used with VITEK 2 System instruments (VITEK 2, VITEK 2 Compact, and VITEK COMPACT PRO). The VITEK 2 System is a fully automated instrument that integrates sample preparation, incubation, and optical measurement for microbial identification and antimicrobial susceptibility testing (AST).

The VITEK 2 System will automatically (or allow operator to manually) dilute the organism suspension to prepare an inoculum for susceptibility cards. Then, the VITEK 2 will fill, seal and place the card into the incubator/reader. The VITEK 2 Compact and VITEK COMPACT PRO have 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. The analysis program determines when a well demonstrates growth based on attenuation of light measured by an optical scanner. The data are used to determine the minimum inhibitory concentration or “MIC” values for the antimicrobial agent. At the completion of the incubation cycle, a report is generated that contains

the MIC value along with the interpretive category result for each antimicrobial contained on the card.

VITEK 2 AST-ST Meropenem has the following concentrations in the card: 0.12, 0.25, 0.5, 1, and 2 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK 2 AST-ST Meropenem test is ≤0.06 - ≥4 µg/mL.

B Principle of Operation:

The VITEK 2 AST cards use an abbreviated doubling dilution series of antimicrobial to establish the MIC. Each VITEK 2 AST card contains 64 wells—one "growth" control well contains nutrient medium only, and the remaining wells contain premeasured antimicrobials in nutrient media.

The VITEK 2 System instruments (VITEK 2, VITEK 2 Compact, and VITEK COMPACT PRO) utilize automated growth-based detection using attenuation of light measured by an optical scanner. The optics in the VITEK 2 Systems use visible light to directly measure organism growth within each of the 64 micro-wells. Transmittance optics is based on an initial light reading of a well before significant growth has begun. Every 15 minutes throughout the incubation cycle (defined period of time based on the VITEK 2 card), light transmittance readings of each well determine organism growth by the amount of light that is prevented from passing through the well. At the completion of the incubation period, the MIC values and their associated interpretive category results for each antimicrobial on the test card are displayed in an automatically generated report.

V Substantial Equivalence Information:

A Predicate Device Name(s):

VITEK 2 AST-*Streptococcus* Penicillin (≤0.06 - ≥8 µg/mL)

B Predicate 510(k) Number(s):

K232201

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device: K260283	Predicate: K232201
Device Trade Name	VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL)	VITEK 2 AST-*Streptococcus* Penicillin (≤0.06 - ≥8 µg/mL)
General Device Characteristic Similarities		
Indications For Use	VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL) is designed for antimicrobial susceptibility testing of *Streptococcus* species and is intended for use with the VITEK 2 Systems as	VITEK 2 *Streptococcus* Penicillin 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

	a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL) is a quantitative test. Testing is indicated for *Streptococcus pneumoniae*, *Streptococcus* spp. β-Hemolytic Group and *Streptococcus* spp. Viridans Group, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC). VITEK 2 AST-*Streptococcus* Meropenem (≤0.06 - ≥4 µg/mL) has demonstrated acceptable performance with the following organisms: *Streptococcus pneumoniae* *Streptococcus* spp. β-Hemolytic Group (*Streptococcus agalactiae*, *Streptococcus canis*, *Streptococcus dysgalactiae* ssp. *equisimilis*, *Streptococcus equi* ssp. *zooepidemicus*, *Streptococcus pyogenes*) *Streptococcus* spp. Viridans Group (*Streptococcus anginosus*, *Streptococcus constellatus*, *Streptococcus cristatus*, *Streptococcus gallolyticus* ssp. *gallolyticus*, *Streptococcus gordonii*, *Streptococcus infantarius* ssp. *infantarius*, *Streptococcus mitis*, *Streptococcus oralis*, *Streptococcus parasanguinis*, *Strepotococcus salivarius* ssp. *salivarius*, *Streptococcus sanguinis*, *Streptococcus uberis*, *Streptococcus vestibularis*) The VITEK 2 *Streptococcus* Susceptibility Card is intended	determination of *in vitro* susceptibility to antimicrobial agents. VITEK 2 *Streptococcus* Penicillin is a quantitative test. Penicillin has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial. Active both *in vitro* and in clinical infections: Beta hemolytic streptococci groups C and G *Streptococcus pyogenes* *Streptococcus agalactiae* *Streptococcus* viridans group *Streptococcus pneumoniae* The VITEK 2 Streptococcus Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Streptococcus pneumoniae*, beta-hemolytic *Streptococcus*, and Viridans *Streptococcus* to antimicrobial agents when used as instructed.

	for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Streptococcus pneumoniae*, beta-hemolytic *Streptococcus*, and Viridans *Streptococcus* to antimicrobial agents when used as instructed.	
Test Methodology	Automated quantitative antimicrobial susceptibility test for use with the VITEK 2 Systems to determine the *in vitro* susceptibility of microorganisms	Same
Inoculum	Saline suspension of organism	Same
Test Card	VITEK 2 *Streptococcus* Susceptibility Test Card	Same
General Device Characteristic Differences		
Antimicrobial Agent	Meropenem	Penicillin
Antimicrobial Concentrations	0.12, 0.25, 0.5, 1, 2 µg/mL	0.06, 0.12, 0.5, 2 µg/mL
Instrument	VITEK 2, VITEK 2 Compact, and VITEK COMPACT PRO Systems	VITEK 2 and VITEK 2 Compact Systems
Analysis Algorithm	Growth Pattern Analysis	Discriminant Analysis
Tested Species	*Streptococcus pneumoniae* *Streptococcus* spp. β-Hemolytic Group (*Streptococcus agalactiae*, *Streptococcus canis*, *Streptococcus dysgalactiae* ssp. *equisimilis*, *Streptococcus equisimilis* ssp. *zooepidemicus*, *Streptococcus pyogenes*) *Streptococcus* spp. Viridans Group (*Streptococcus anginosus*, *Streptococcus constellatus*, *Streptococcus cristatus*, *Streptococcus gallolyticus* ssp. *gallolyticus*, *Streptococcus gordonii*, *Streptococcus infantarius* ssp. *infantarius*, *Streptococcus mitis*, *Streptococcus oralis*, *Streptococcus parasanguinis*, *Strepotococcus salivarius* ssp.	Beta hemolytic Streptococci groups C and G *Streptococcus pyogenes* *Streptococcus agalactiae* *Streptococcus* viridans group *Streptococcus pneumoniae*

	salivarius, *Streptococcus sanguinis*, *Streptococcus uberis*, *Streptococcus vestibularis*)	

Predetermined Change Control Plan (PCCP):

To support the implementation of changes to FDA-recognized susceptibility test interpretive criteria (i.e., breakpoints), this submission included a predetermined change control plan (PCCP) with a breakpoint change protocol that was reviewed and accepted by FDA in submission K250274 cleared on April 30, 2025. This protocol addresses future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm). The protocol outlined the specific procedures and acceptance criteria that bioMérieux, Inc. intends to use to evaluate the VITEK 2 AST-*Streptococcus* Meropenem when revised breakpoints for meropenem are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, bioMérieux, Inc. will update the VITEK 2 AST-*Streptococcus* Meropenem label to include (1) the new breakpoints, (2) an updated performance section after re-evaluation of data in this premarket notification with the new breakpoints, and (3) any new limitations as determined by their evaluation.

VI Standards/Guidance Documents Referenced:

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

CLSI M07 12th Edition, Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically (May 2024)

CLSI M100 35th ed. Performance Standards for Antimicrobial Susceptibility Testing (January 2025)

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Reproducibility testing for the VITEK 2 AST-*Streptococcus* Meropenem was conducted at three external sites using a panel of sixteen isolates (7 *S. pneumoniae*, 3 *S. mitis*, 3 *S. agalactiae,* 3 *S. pyogenes*) consistent with the indications for use. Each isolate was tested in triplicate, using separate inocula, over three days for a total of 432 data points. The inocula were prepared using both the auto-dilution and manual dilution methods for testing with the

VITEK 2. In addition, inocula were prepared by the manual dilution method for testing with the VITEK 2 Compact and VITEK COMPACT PRO.

The COMPACT PRO did not obtain premarket clearance until after the closure of the clinical trial sites; therefore, reproducibility for the COMPACT PRO was assessed at one internal site with three instruments and three operators. Additionally, due to the similarities between the two Compact systems, the VITEK 2 Compact reproducibility performance was leveraged to support the VITEK COMPACT PRO. Taken together, this was considered acceptable. The mode of MIC values was determined for each isolate, and the reproducibility was calculated based on the number of MIC values that fell within ± one doubling dilution of the mode MIC value. All data points for *S. pneumoniae* and *S. mitis* (10 isolates) were on-scale and within ± one doubling dilution agreement as compared to the mode MIC. The data was analyzed taking into consideration best-case and worst-case scenarios as described in the Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems. The reproducibility performance is shown in **Table 1**.

Table 1. Reproducibility Performance of VITEK 2 AST-*Streptococcus* Meropenem*

	VITEK 2		**VITEK 2 Compact**	**VITEK COMPACT PRO**
	Auto-Dilution	**Manual Dilution**	**Manual Dilution**	**Manual Dilution**
Best-Case	100%	100%	100%	99.6%
Worst-Case	100%	100%	100%	99.6%

**Streptococcus pneumoniae* and *Streptococcus* spp. Viridans Group

The MIC results for *Streptococcus* spp. β-Hemolytic Group (6 isolates) were off-scale, which is consistent with current epidemiology. The VITEK 2 AST-*Streptococcus* Meropenem reporting range includes sufficient serial two-fold dilutions below the "susceptible-only" breakpoint (meropenem has only a "susceptible" category for *Streptococcus* spp. β-Hemolytic Group). Taken together, reproducibilty results were 100% across all VITEK 2 instruments and dilution methods and is acceptable.

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Not applicable.

4. Detection Limit and Assay Reportable Range:

   Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Quality Control (QC) Testing:
The CLSI recommended QC strain, *Streptococcus pneumoniae* ATCC 49619 was tested a sufficient number of times (i.e., at least 20/site) at each testing site using the VITEK 2 AST-*Streptococcus* Meropenem and Broth Microdilution (BMD) reference method. Both the automatic dilution and manual dilution methods were used for the VITEK 2 and the manual dilution method was used for the VITEK 2 Compact and VITEK COMPACT PRO. The results are summarized in **Table 2** below. Both the auto-dilution and manual dilution methods for VITEK 2 and the manual dilution methods for VITEK 2 Compact and VITEK COMPACT PRO QC results were within the expected range >95% of the time.

The Meropenem card (≤0.06 - ≥4 µg/mL) does not cover the expected result range of 0.03-0.25 µg/mL for the QC organism *S. pneumoniae* ATCC 49619 and may produce partially off-scale QC results, which was considered acceptable. To address the potential off-scale QC results when testing *S. pneumoniae* ATCC 49619, the following footnote was included in the labeling:

Does not include the CLSI/FDA recommended dilution range for QC testing with this organism

Table 2. Quality Control Results for VITEK 2 AST-*Streptococcus* Meropenem

Organism	VITEK 2 Result Range (µg/mL)	BMD Result Range (µg/mL)	VITEK 2 Auto Dilution	BMD	VITEK 2 Manual Dilution	BMD	VITEK 2 Compact Manual Dilution	BMD	VITEK COMPACT PRO Manual Dilution	BMD
Streptococcus pneumoniae ATCC 49619* Expected Results: 0.03-0.25 µg/mL		≤0.0078125		1						
		0.015625								
		0.03125		15		5		5		
	≤0.0625	0.0625	163	175	76	85	73	85	1	23
	0.125	0.125	28	3	16	2	19	2	22	
	0.25	0.25								
	0.5	0.5								
	1	1								
	2	2								
	≥4	4								
		8								
		≥16								

*Does not include the CLSI/FDA recommended dilution range for QC testing with this organism

Validation of *Streptococcus pneumoniae* ATCC BAA-3353 as an Additional QC Organism for Meropenem on the VITEK 2 System
A study was conducted to identify and verify a new on-scale QC strain for the VITEK 2 AST-ST Meropenem assay only. To validate the use of *S. pneumoniae* ATCC BAA-3353 as a QC organism with the VITEK 2 System, a minimum of 80 replicates of *S. pneumoniae* ATCC BAA-3353 were tested with at least two lots of the antimicrobial reagents over at least two days. All data points fell between 0.25-1 µg/mL.

When *S. pneumoniae* ATCC BAA-3353 was tested on the VITEK 2 System instruments, 81/81 (100%) of the results fell within the QC range of 0.25-1 µg/mL with VITEK 2/auto-

dilution; 165/165 (100%) of the results were within QC range with the VITEK 2/manual dilution, and 81/81 (100%) of the results were within QC range with the VITEK 2 Compact/manual dilution. Taken together, these data are acceptable to support the use of *S. pneumoniae* ATCC BAA-3353 QC organism when testing meropenem on the VITEK 2 System.

Inoculum Density Control:
The DensiCHEK Plus was used to standardize the inoculum to a 0.5 McFarland standard. The instrument was standardized daily with all results recorded at each site. Calibration values were within the expected range.

Purity Check:
A purity check of all organisms was performed on the dilution tube used to prepare the VITEK 2 card inoculum. Only those cultures that were pure were evaluated in the study.

Device Failure:
During the performance of the comparative study, there were zero (0) device failures with the VITEK 2 System instruments.

Growth Failure Rate:
A total of 795 clinical and challenge isolates were tested by VITEK 2 AST-ST Meropenem. There were 13 growth failures recorded, and 782 isolates have VITEK 2 AST results available. Eleven (11) *Streptococcus anginosus* isolates failed to grow. To address the growth failure rate of *S. anginosus*, the following limitation is included in the device labeling:

> *If Streptococcus anginosus does not provide a result for the VITEK2 AST-ST test cards but growth is observed on the purity plate, do not retest the isolate on the VITEK2 Systems and perform an alternative method of testing prior to report of results.*

6. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Testing of meropenem was performed at four external sites and one internal site. Results obtained with VITEK 2 AST-*Streptococcus* Meropenem were compared to results obtained with the CLSI broth microdilution reference panel. The MIC result range for the VITEK 2 AST-*Streptococcus* Meropenem is ≤0.06 - ≥4 µg/mL for *S. pneumoniae, Streptococcus* spp. β-Hemolytic Group, and *Streptococcus* spp. Viridans Group. The testing conditions for the reference method consisted of the following:

- Medium: 2.5% to 5% LHB-supplemented CAMHB
- Inoculum: Direct colony suspension
- Incubation: 35ºC; 20-24 hours

The VITEK 2 cards were inoculated with test organisms using the auto-dilution method (VITEK 2) and using the manual dilution method (VITEK 2, VITEK 2 Compact, VITEK COMPACT PRO). All test inocula used for the VITEK 2 AST cards and the reference method were standardized using the DensiCHEK instruments.

A total of 782 isolates (682 clinical isolates and 100 challenge isolates) were evaluated using auto-dilution and VITEK 2. Of these isolates, 49% were contemporary isolates (tested within six months of isolation) and 51 % were stock isolates (no specific time from isolation). The clinical isolates included: 303 *S. pneumoniae* isolates, 241 *Streptococcus* spp. β-Hemolytic Group isolates (98 *Streptococcus agalactiae*, 27 *Streptococcus canis*, 45 *Streptococcus dysgalactiae* ssp. *equisimilis*, 3 *Streptococcus equi* ssp. *zooepidemicus*, 68 *Streptococcus pyogenes*), and 138 *Streptococcus* spp. Viridans Group isolates (13 *Streptococcus anginosus*, 11 *Streptococcus constellatus*, 1 *Streptococcus cristatus*, 2 *Streptococcus gallolyticus* ssp. *gallolyticus*, 9 *Streptococcus gordonii*, 14 *Streptococcus mitis*, 3 *Streptococcus oralis*, 33 *Streptococcus mitis/oralis,* 30 *Streptococcus parasanguinis*, 10 *Strepotococcus salivarius* ssp. *salivarius*, 5 *Streptococcus sanguinis*, 3 *Streptococcus uberis*, 2 *Streptococcus vestibularis,* 2 *Streptococcus* spp. Viridans Group, not differentiated)

A total of 100 challenge isolates were evaluated at two external sites (VITEK 2 and VITEK 2 Compact) or one internal site (VITEK COMPACT PRO). The challenge isolates included: 38 *S. pneumoniae,* 45 β-Hemolytic Group *Streptococcus* spp. (26 *Streptococcus agalactiae*, 19 *Streptococcus pyogenes*), and 17 *Streptococcus* spp. Viridans Group isolates (1 *Streptococcus gallolyticus* ssp. *gallolyticus*, 1 *Streptococcus gordonii*, 1 *Streptococcus infantarius* ssp. *infantarius*, 9 *Streptococcus mitis*, 2 *Streptococcus mitis/oralis,* 2 *Streptococcus oralis*, 1 *Streptococcus sanguinis*).

Clinical and Challenge Data – VITEK 2 Auto-Dilution

The results obtained using the auto-dilution method of the VITEK 2 from the 782 total isolates (682 clinical isolates and 100 challenge isolates) are summarized in **Table 3**.

Table 3. Performance of All Clinical and Challenge Isolates for Meropenem: VITEK 2 Auto-Dilution

	Total	#EA	%EA	Eval EA Total	Eval EA #	Eval EA%	#CA	%CA	#R/NS	#S	min	maj	vmj
***Streptococcus pneumoniae* ≤0.25 (S), 0.5 (I), ≥1 (R)**													
Clinical	303	297	98.0	66	60	90.9	285	94.1	35	247	17	0	1
Challenge	38	38	100	38	38	100	23	60.5	20	3	15	0	0
Combined	341	335	98.2	104	98	94.2	308	90.3	55	250	32	0	1
***Streptococcus* spp. β-Hemolytic Group ≤0.5 (S)**													
Clinical	241	241	100	0	0	NA	241	100	0	241	NA	0	0
Challenge	45	45	100	0	0	NA	45	100	0	45	NA	0	0
Combined	286	286	100	0	0	NA	286	100	0	286	NA	0	0
***Streptococcus* spp. Viridans Group ≤0.5 (S)**													
Clinical	138	133	96.4	39	34	87.2	135	97.8	7	131	NA	0	3
Challenge	17	16	94.1	14	13	92.7	17	100	5	12	NA	0	0
Combined	155	149	96.1	53	47	88.7	152	98.1	12	143	NA	0	3

EA – Essential Agreement
CA – Category Agreement
Eval – Evaluable isolates
R – Resistant
NS – Nonsusceptible
min – Minor Discrepancies
maj – Major Discrepancies
vmj – Very Major Discrepancies
S – Susceptible
NA – Not applicable

Essential agreement (EA) occurs when the result of the reference method and that of the VITEK 2 AST card are within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on-scale for both the reference method and VITEK 2 AST card or results in which an off-scale result is at least two doubling dilutions from the on-scale result. Category agreement occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the VITEK 2 AST card.

For testing *S. pneumoniae* with the auto-dilution method of the VITEK 2, the EA was acceptable at 98.2% (**Table 3**). The CA was acceptable at 90.3% and there were thirty-two minor errors, zero major errors and one very major error (1.8%).

For *Streptococcus* spp. β-Hemolytic Group evaluated with the auto-dilution method of the VITEK 2, the overall EA was acceptable at 100% (**Table 3**). The overall CA was acceptable at 100% and there were no potential major or very major errors. Due to the lack of a resistant interpretive category, all errors are considered potential. Since only susceptible *Streptococcus* spp. β-Hemolytic Group isolates were evaluated, the following limitation is included in the device labeling:

The ability of the AST card to detect non-susceptible strains with the following combination(s) is unknown because an insufficient number of non-susceptible strains were available at the time of comparative testing:

- *Meropenem (mem02n): Streptococcus spp. β-Hemolytic Group*

For *Streptococcus* spp. Viridans Group evaluated with the auto-dilution method of the VITEK 2, the overall EA was acceptable at 96.1% (**Table 3**). The overall CA was acceptable at 98.1% and there were no potential major errors and three potential very major errors. Errors are considered potential errors since no other category is defined other than "susceptible". When errors cannot be categorized as minor, adjustments are made to categorical errors by considering if the MIC values where the errors occur were in essential agreement with the reference method. All three potential very major errors have an MIC value that were in essential agreement with the reference method MIC value; therefore, the adjusted potential very major error rate is 0%, which is acceptable.

When evaluating by individual species, *S. parasanguinis* had an EA of 87.5% (21/24) and CA of 91.7% (22/24) and no potential major errors and 2 potential very major errors. The two potential very major errors have an MIC value that were in essential agreement with the reference method MIC value; therefore, the adjusted potential very major error rate is 0%, which is acceptable. However, the EA performance was not acceptable. *S. constellatus* had an EA of 66.7% (2/3) and CA of 100% (3/3) with no potential errors, which was not acceptable. *S. gordonii* had an EA of 66.7% (2/3) and CA of 100% (3/3) with no potential errors, which is not acceptable.
A supplemental study was performed to address the unacceptable EA performance of *S. parasanguinis*, S. *constellatus*, and *S. gordonii* with the auto-dilution method of the VITEK 2.

Six additional *S. parasanguinis* clinical isolates were tested in a supplemental study performed at one internal site. The supplemental *S. parasanguinis* testing had an EA of 100% (6/6) and CA of 100% (6/6) with no potential errors, which was acceptable. When the original and supplemental data were combined, *S. parasanguinis* had an EA of 90% (27/30) and CA of 93.3% (28/30) with no potential major errors and no adjusted potential very major errors when evaluated with the auto-dilution method of the VITEK 2, which was acceptable.

Eight additional *S. constellatus* clinical isolates were tested in a supplemental study performed at one internal site. The supplemental *S. constellatus* testing had an EA and CA of 100% (8/8) with no potential errors, which was acceptable. When the original and supplemental data were combined, *S. constellatus* had an EA of 90.9% (10/11) and CA of 100% (11/11) with no potential errors when evaluated with the auto-dilution method of the VITEK 2, which was acceptable.

Seven additional *S. gordonii* clinical isolates were tested in a supplemental study performed at one internal site. The supplemental *S. gordonii* testing had an EA of 100% (7/7) and CA of 100% (7/7) with no potential errors, which was acceptable. When the original and supplemental data were combined, *S. gordonii* had an EA of 90% (9/10) and CA of 100% (10/10) with no potential errors when evaluated with the auto-dilution method of the VITEK 2, which was acceptable.

The original clinical and challenge data for *Streptococcus* spp. Viridans Group were combined with the supplemental testing. The combined results demonstrated an EA of 96.1% (149/155) and CA of 98.1% (152/155) with no potential major errors and no potential adjusted very major errors, which was acceptable.

Since only susceptible *Streptococcus* spp. Viridans Group isolates were evaluated, the following limitation is included in the device labeling:

The ability of the AST card to detect non-susceptible strains with the following combination(s) is unknown because an insufficient number of non-susceptible strains were available at the time of comparative testing:

- *Meropenem (mem02n): Streptococcus spp. Viridans Group (except Streptococcus mitis, Streptococcus oralis, Streptococcus parasanguinis)*

Challenge Data –VITEK 2, VITEK 2 Compact, and VITEK COMPACT PRO Manual Dilution

The 100 challenge isolates were also evaluated at two external sites with the manual dilution option of the VITEK 2 and VITEK 2 Compact systems, and one internal site with the VITEK COMPACT PRO (summarized in **Table 4**).

Table 4. Performance of Challenge Isolates for Meropenem: VITEK 2, VITEK 2 Compact and VITEK COMPACT PRO Manual Dilution

VITEK 2 Systems	Total	#EA	%EA	Eval EA Total	Eval EA #	Eval EA%	#CA	%CA	#R/NS	#S	min	maj	vmj
***Streptococcus pneumoniae* ≤0.25 (S), 0.5 (I), ≥1 (R)**													
VITEK 2	38	38	100	38	38	100	22	57.9	20	3	16	0	0

VITEK 2 Compact	38	38	100	38	38	100	23	60.5	20	3	15	0	0
VITEK 2 COMPACT PRO	38	38	100	37	37	100	22	57.9	20	3	16	0	0
***Streptococcus* spp. β-Hemolytic Group ≤0.5 (S)**													
VITEK 2	45	45	100	0	0	NA	45	100	0	45	NA	0	0
VITEK 2 Compact	45	45	100	0	0	NA	45	100	0	45	NA	0	0
VITEK 2 COMPACT PRO	45	45	100	0	0	NA	45	100	0	45	NA	0	0
***Streptococcus* spp. Viridans Group ≤0.5 (S)**													
VITEK 2	17	16	94.1	14	13	92.9	17	100	5	12	NA	0	0
VITEK 2 Compact	17	16	94.1	14	13	92.9	17	100	5	12	NA	0	0
VITEK 2 COMPACT PRO	17	16	94.1	15	14	93.3	16	94.1	5	12	NA	1	0

EA – Essential Agreement
CA – Category Agreement
Eval – Evaluable isolates
R – Resistant
NS – Nonsusceptible
min – Minor Discrepancies
maj – Major Discrepancies
vmj – Very Major Discrepancies
S – Susceptible
NA – Not applicable

Essential agreement (EA) occurs when the result of the reference method and that of the VITEK 2 AST card are within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on-scale for both the reference method and VITEK 2 AST card or results in which an off-scale result is at least two doubling dilutions from the on-scale result. Category agreement occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the VITEK 2 AST card.

The overall performance of the VITEK 2 AST-*Streptococcus* Meropenem when testing *S. pneumoniae* with the manual dilution method was not acceptable with an EA of 100%, CA of 57.9% and sixteen (16) minor errors, and no major or very major errors. The overall performance of the VITEK 2 AST-*Streptococcus* Meropenem when testing *S. pneumoniae* with the VITEK 2 Compact was not acceptable with an EA of 100%, CA of 60.5% and fifteen (15) minor errors, and no major or very major errors. The overall performance of the VITEK 2 AST-*Streptococcus* Meropenem when testing *S. pneumoniae* with the COMPACT PRO was not acceptable with an EA of 100%, CA of 57.9% and sixteen (16) minor errors, and no major or very major errors (**Table 4**). To address the observed low CA performance with the manual dilution option of the VITEK 2 instruments, the following limitation was included in the device labeling.

Due to the occurrence of minor errors (resulting in a category agreement below 90% for the manual dilution options), perform an alternative method of testing prior to reporting of results generated with the manual dilution options for the following antibiotic/organism combination:
Meropenem (mem02n): Streptococcus pneumoniae (if critical to patient care).

The overall performance of the VITEK 2 AST-*Streptococcus* Meropenem when testing *Streptococcus* spp. β-Hemolytic Group with the manual dilution method, VITEK 2 Compact

System, and the VITEK COMPACT PRO was acceptable with an EA and CA of 100%, and no potential major or very major errors (**Table 4**). Errors are considered potential errors since no other category is defined other than "susceptible".

The overall performance of the VITEK 2 AST-*Streptococcus* Meropenem when testing *Streptococcus* spp. Viridans Group with the manual dilution method and the VITEK 2 Compact System, the performance was acceptable with an EA of 94.1% and CA of 100%, with no potential major or very major errors. The overall performance of the VITEK 2 AST-*Streptococcus* Meropenem when testing *Streptococcus* spp. Viridans Group with manual dilution method and the VITEK COMPACT PRO was acceptable with an EA and CA of 94.1% with one (1) potential major error (8.3%) and no potential very major error (**Table 4**). When errors cannot be categorized as minor, adjustments are made to categorical errors by considering if the MIC values where the errors occur were in essential agreement with the reference method. The one potential major error had an MIC value that was not in essential agreement with the reference method MIC value; therefore, the adjusted potential major error rate is 8.3%. The one adjusted potential major error was due to a single *S. gallolyticus ssp. gallolyticus* isolate. Due to the limited. *S. gallolyticus ssp. gallolyticus* evaluated, the adjusted potential major error was considered random, and performance is acceptable.

MIC Trending

A trending analysis was conducted using the combined data (clinical and/or challenge) obtained for *Streptococcus* spp. This trending calculation takes into account MIC values that are determined to be one or more doubling dilutions lower or higher than the reference method irrespective of whether the device MIC values are on-scale or not.

Species for which the difference between the percentage of isolates with higher vs. lower readings was ≥30% and for which the confidence interval was determined to be statistically significant were considered to show evidence of trending. Trending that shows higher or lower MIC values compared to the reference is addressed in the labeling.

Table 5. Trending for *Streptococcus* spp. with Meropenem and the VITEK 2 Systems

	Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
VITEK 2/Auto	*S. pneumoniae*	112	52 (46.4)	55	5 (4.5)	-42% (-52%, -31%)	Yes
	S. agalactiae	3	3 (100)	0	0 (0)	-100% (-100%, -21%)	Yes
	S. canis	0	0 (0)	0	0 (0)	0	NA
	S. dysgalactiae ssp. *equisimilis*	0	0 (0)	0	0 (0)	0	NA
	S. equi ssp. *zooepidemicus*	0	0 (0)	0	0 (0)	0	NA
	S. pyogenes	0	0 (0)	0	0 (0)	0	NA
	Streptococcus spp. Viridans Group	68	44 (64.7)	20	4 (5.9)	-59% (-70%, -44%)	Yes
VITEK 2/ Manual	*S. pneumoniae*	38	15 (39.5)	20	3 (7.9)	-32% (-48%, -13%)	Yes
	S. agalactiae	0	0 (0)	0	0 (0)	0	NA

	Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
	S. pyogenes	0	0 (0)	0	0 (0)	0	NA
	Streptococcus spp. Viridans Group	14	8 (57.1)	6	0 (0)	-57% (-79%, -24%)	Yes
VITEK 2 Compact	*S. pneumoniae*	38	15 (39.5)	20	3 (7.9)	-32% (-48%, -13%)	Yes
	S. agalactiae	0	0 (0)	0	0 (0)	0	NA
	S. pyogenes	0	0 (0)	0	0 (0)	0	NA
	Streptococcus spp. Viridans Group	14	5 (35.7)	9	0 (0)	-36% (-61%, -7%)	Yes
VITEK COMPACT PRO	*S. pneumoniae*	38	13 (34.2)	18	7 (18.4)	-16% (-34%, 4%)	No
	S. agalactiae	0	0 (0)	0	0 (0)	0	NA
	S. pyogenes	0	0 (0)	0	0 (0)	0	NA
	Streptococcus spp. Viridans Group	15	4 (26.7)	9	2 (13.3)	-13% (-40%, 16%)	No

NA: Not applicable

A trend toward lower MIC values was observed for *S. pneumoniae* (VITEK 2/auto, VITEK 2/manual, VITEK 2 Compact)*, S. agalactiae* (VITEK 2/auto) and *Streptococcus* spp. Viridans Group (VITEK 2/auto, VITEK 2/manual, VITEK 2 Compact) when compared to the CLSI broth microdilution reference method, as summarized in **Table 5**. The following statement is included as a footnote to the performance table in the device labeling to address the observed trending:

VITEK 2 Meropenem MIC values tended to be in exact agreement or at least one doubling dilution lower when testing Streptococcus pneumoniae, Streptococcus agalactiae and Streptococcus spp. Viridans Group compared to the CLSI reference broth microdilution method.

Testing/Reporting MICs for Species Not Listed in the Indications for Use

For this review, the interpretive criteria are applied to the organisms/organism groups according to the FDA STIC website. As required under 511A(b)(2)(C)(ii)(I) of the Federal Food, Drug and Cosmetic Act, the following statement was added to the package insert to address testing and reporting of species not listed in the Indications for Use:

Per the FDA-Recognized Susceptibility Test Interpretive Criteria website, the safety and efficacy of antimicrobial drugs, for which antimicrobial susceptibility is tested by this AST device, may or may not have been established in adequate and well-controlled clinical trials for treating clinical infections due to microorganisms outside of those found in the indications and usage in the drug label. The clinical significance of susceptibility information in those instances is unknown. The approved labeling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

3. Clinical Cut-Off:

   Not applicable.

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

   Not applicable.

D Expected Values/Reference Range:

Table 6. FDA-Approved or Recognized Interpretive Criteria

Organism	Minimum Inhibitory Concentrations (µg/mL)[a]		
	Susceptible	**Intermediate**	**Resistant**
Streptococcus pneumoniae	≤ 0.25	0.5	≥ 1
Streptococcus spp. β-Hemolytic Group	≤0.5	-	-
Streptococcus spp. Viridans Group	≤0.5	-	-

[a]According to FDA STIC Webpage, FDA-Recognized Antimicrobial Susceptibility Test Interpretive Criteria

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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