510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K201675

B Applicant

bioMérieux, Inc.

C Proprietary and Established Names

VITEK 2 AST-Gram Negative Meropenem (≤ 0.25 - ≥ 16 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
LTW	Class II	21 CFR 866.1640 - Antimicrobial susceptibility test powder	MI - Microbiology
LTT	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 meropenem for testing of Gram-negative bacilli on the VITEK 2 and VITEK 2 Compact Antimicrobial Susceptibility Test Systems

B Measurand:

Meropenem ≤0.25 - ≥16 µg/mL

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

C Type of Test:
Automated quantitative or qualitative antimicrobial susceptibility test

III Intended Use/Indications for Use:

A Intended Use(s):
The VITEK 2 Gram-negative Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an in vitro test to determine the susceptibility of clinically significant aerobic Gram-negative bacilli to antimicrobial agents when used as instructed.

B Indication(s) for Use:
VITEK 2 AST-Gram Negative Meropenem is designed for antimicrobial susceptibility testing of Gram negative bacilli and is intended for use with the VITEK 2 and VITEK 2 Compact Systsems as a laboratory aid in the determination of in vitro susceptibility to antimicrobial agents. VITEK 2 AST-Gram Negative 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 an in clinical infections:

Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis
Pseudomonas aeruginosa

In vitro data are available, but clinical significance is unknown:
Citrobacter freundii
Citrobacter koseri
Enterobacter cloacae
Hafnia alvei
Klebsiella oxytoca
Morganella morganii
Serratia marcescens

The VITEK 2 Gram Negative Susceptibility Card Meropenem also reports susceptiblity for the following additional organisms as listed on the FDA Susceptibility Test Interpretive Criteria Website:

Acinetobacter spp.

The VITEK 2 Gram-Negative Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an in vitro test to determine the susceptibility of clinically signifiant aerobic Gram-negative bacilli to antimicrobial agents when used as instructed.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Limitations:

Perform an alternative method of testing prior to reporting for the following meropenem/organism combinations:

- *Proteus vulgaris*
- *When the VITEK 2 MIC is greater than or equal to 16 µg/mL for Enterobacter cloacae*
- *Morganella morganii (when tested with VITEK 2 COMPACT if critical to patient care*

Perform an alternate method of testing prior to reporting results when a resistant result is obtained:

- *Klebsiella oxytoca, Proteus mirabilis*

The ability of the VITE 2 AST-Gram Negative Meropenem to detect resistance to meropenem is unknown for the following species because an insufficient number of resistant strains were available at the time of comparative testing:

- *Citrobacter koseri and Hafnia alvei*

D Special Instrument Requirements:

VITEK 2 and VITEK 2 Compact Systems using VITEK 2 Systems 9.02 software

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(s) which contain 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. The VITEK 2 System will automatically (or allow operator to manually) dilute the bacterial 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 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. The analysis program determines when a well demonstrates growth based on attenuation of light measured by an optical scanner. This data is 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-Gram Negative Meropenem has the following concentrations in the card: 0.5, 2, 6 and 12 µg/mL (equivalent standard method concentration by efficacy in µg/mL. The MIC result range for the VITEK 2 AST-GN Meropenem test is ≤0.25 to ≥16 µg/mL. For all species, the

MIC result range indicates that the VITEK 2 system is capable of producing the following MIC results: ≤0.25, 0.5, 1, 2, 4, 8 and ≥16 µg/mL for the AST-GN Meropenem test.

B Principle of Operation:

The VITEK 2 and VITEK 2 Compact Systems utilize automated growth-based detection using attenuation of light measured by an optical scanner. The optics in the 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-Gram Negative Eravacycline (≤ 0.12 - ≥ 4µg/mL)

B Predicate 510(k) Number(s):

K191766

C Comparison with Predicate(s):

Device & Predicate Device(s):	**Device K201675**	**Predicate K191766**
Device Trade Name	VITEK 2 AST-Gram Negative Meropenem (≤0.26 - ≥16 µg/mL	VITEK 2 AST-Gram Negative Eravacycline (≤0.12 – ≥4 µg/mL)
General Device Characteristic Similarities		
Intended Use/Indications For Use	The VITEK 2 Gram-Negative Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of clinically significant aerobic Gram-negative bacilli to antimicrobial agents when used as instructed.	Same
Test Method	Automated quantitative antimicrobial susceptibility test for use with the VITEK 2 and	Same

Device & Predicate Device(s):	Device K201675	Predicate K191766
	VITEK 2 Compact Systems to determine the *in vitro* susceptibility of Gram-negative bacilli	
Inoculum	Standardized saline suspension of test organism	Same
Test Card	VITEK 2 Gram Negative Susceptibility Test Card	Same
Instrument	the VITEK 2 and VITEK 2 Compact Systems	Same
Analysis Algorithm	Growth pattern analysis	Same
General Device Characteristic Differences		
Antimicrobial Agent	Meropenem	Eravacycline
Antimicrobial Concentration	≤0.25 - ≥16 µg/mL	0.25, 1, 2 and 4 µg/mL
Reporting Range	≤0.25, 0.5, 1, 2, 4, 8 and ≥16 µg/mL	≤0.12 – ≥4 µg/mL
Indicated Organisms	*Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Pseudomonas aeruginosa, Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae, Hafnia alvei, Klebsiella oxytoca, Morganella morganii, Serratia marcescens* *Acinetobacter spp.*	*Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae, Citrobacter koseri, Klebsiella (Enterobacter) aerogenes*

VI Standards/Guidance Documents Referenced:

- FDA Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA (Issued August 28, 2009)
- CLSI M07-A09, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard-Ninth Edition" Vol. 32 No. 2 (January 2009)
- CLSI M100, "Performance Standards for Antimicrobial Susceptibility Testing"; Twenty-fourth Edition (January 2014)

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Reproducibility testing for the VITEK 2 AST-Gram Negative Meropenem was conducted at three external clinical sites using a panel of ten gram-negative bacilli consistent with the indications for use (i.e., one *Enterobacter cloacae*, and nine *Pseudomonas aeruginosa* isolates). The majority of isolates evaluated in the reproducibility study were *P. aeruginosa* as members of this species were more likely to provide on-scale MICs than isolates belonging to the *Enterobacterales*. Each isolate was tested in triplicate over three days for a total of 270 data points. Inocula were prepared using both the auto-dilution and manual dilution methods for testing in the VITEK 2 System. In addition, inocula were prepared by the manual dilution method for use with the VITEK 2 Compact. 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 ±1 doubling dilution of the mode.

   All MIC values were on-scale and within one doubling dilution of the mode MIC and therefore only best case results are reported. The testing resulted in overall reproducibility of 100% (270/270) for the auto dilution and manual dilution methods for testing in the VITEK 2 System (auto-dilution and manual dilution) and 98.9% (267/270) for the VITEK 2 Compact System (manual dilution only).

   The results are acceptable.

2. Linearity:

   Not applicable

3. Analytical Specificity/Interference:

   Not applicable

4. Assay Reportable Range:

   Not applicable

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

Quality Control (QC) Testing
The CLSI recommended QC strains for meropenem, *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853, were tested a sufficient number of times (i.e., at least 20/site) at each testing site using both the VITEK 2 card and broth microdilution (BMD) reference methods. 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.

Testing with *E. coli* ATCC 25922 provided off-scale results with the VITEK 2 card and the BMD reference. The acceptable range for this strain is lower than the lowest dilution on the BMD panel as well as the reported values for meropenem. In the device labeling the sponsor indicated the expected QC range (0.008 – 0.06 µg/mL) and included the following footnote to the device labeling QC table:

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

Results obtained using the auto-dilution and the manual dilution methods for VITEK 2 and the manual dilution for VITEK 2 Compact QC results are summarized in **Table 1** below. Since The expected range for P. aeruginosa ATCC27853 is contained withing the meropenem concentration range included on the VITEK card, the quality control results were determined to be acceptable.

Table 1: Quality Control Results for VITEK 2 (Auto-Dilution and Method Dilution Methods) and VITEK 2 Compact (Manual Dilution Method)

Organism	VITEK 2 Result Range[1]	BMD Result Range (µg/mL)	VITEK 2 Auto-Dilution	BMD	VITEK 2 Manual Dilution	BMD	VITEK 2 Compact Manual Dilution	BMD
E. coli ATCC 25922 Expected Result: 0.008 – 0.06 µg/mL		≤0.03		175		110		39
		0.06		1		1		
		0.125						
	≤0.25	0.25	176[1]		110[1]		39[1]	
	0.5	0.5						
	1	1						
	2	2						
	4	4			1			
	8	8						
	≥16	16						
		≥32						
P. aeruginosa ATCC 27853 Expected Result: 0.12 - 1 µg/mL		≤0.03						
		0.06						
	≤ 0.125	0.125		4		3		1
	0.25	0.25	143	120	100	76	13	31
	0.5	0.5	28	41	8	26	24	4
	1	1		7		3		1
	2	2						
	≥ 4	4						
		8						
		≥16						

[1]Does not include the full CLSI/FDA-recommended dilution range for QC testing *E. coli*. For *E. coli*, an in-range VITEK result will be ≤ the lowest dilution on the card (i.e., ≤ 0.25 µg/mL)

Two gram positive quality control organisms were tested throughout comparative testing by reference method only. This was done to perform further quality control of the broth microdilution panels. The organisms tested were *Enterococcus faecalis* ATCC 29212 and

Staphylococcus aureus ATCC 29213. QC results for the broth dilution method were within the expected result range >95% of the time (100% within the expected range).

Inoculum Density Check
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.

Growth Failure Rate
The growth failure rate was acceptable.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:

   Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:
   Testing of meropenem on the VITEK 2 AST-Gram Negative card was performed at three external sites and one internal site. Results obtained with the VITEK 2 AST-Gram Negative card with meropenem were compared to results obtained with the CLSI broth microdilution reference panel. The meropenem concentration range for the VITEK 2 AST-Gram Negative meropenem is ≤0.25 to ≥16 µg/mL for all species. The reference panel contained two-fold serial dilutions with a concentration range of ≤0.03 to ≥64 µg/mL. The testing conditions for the reference method consisted of the following:

   Medium – Cation adjusted Mueller Hinton broth
   Inoculation – Direct colony suspension
   Incubation – 35° C in ambient air for 16-20 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 and VITEK 2 Compact). All test inocula used for the VITEK 2 AST cards and the reference method were standardized using the DensiCHEK Plus Instrument.

   A total of 747 clinical isolates belonging to all genera were evaluated. of these 69.7% of isolates were contemporary (tested within six months of isolation) and 30.3% of isolates were stock isolates.

   A total of 335 *Enterobacterales* clinical isolates were tested from indicated species (16 *C. freundii*, 8 *C. koseri*, 53 *E. cloacae*, 109 *E. coli*, 2 *H. alvei*, 45 *K. oxytoca*, 53 *K. pneumoniae*

(including both *K. pneumoniae* and *K. pneumoniae pneumoniae*), 7 *M. morganii*, 26 *P. mirabilis*, 16 *S. marcescens*. A total of 179 *P. aeruginosa* and 176 isolates of *Acinetobacter* spp. were also evaluated. The *Acinetobacter* spp. tested included the following species: 163 *A. baumannii*, 2 *A. haemolyticus*, 1 *A. junii*, 6 *A. lwoffii*, 4 *Acintetobacter* spp.

In addition to the testing performed using indicated species, isolates from the following non-indicated species were also evaluated as clinical isolates: *C. amalonaticus, C. braakii, C. farmeri, E. tarda, K. aerogenes, E. asburiae, E. hermannii, K. pneumoniae ozaenae, M. morganii, Pantoea agglomerans, P. rettgeri, P. stuartii, Raoutella planticola, S. enteritidis, S. enteritidis enterica, Salmonella spp., S. rubideae, S. boydii, S. dysenteriae, S. flexneri*, and *S. sonnei.* As isolates belonging to non-indicated species numbered approximately 10 percent of the total number of *Enterobacterales* species, the performance with non-indicated species was included in the overall performance calculations for *Enterobacterales*.

A total of 177 challenge isolates of *Enterobacterales* were evaluated using autodilution and VITEK 2 including: 1 *C. freundii*, 18 *E. cloacae*, 26 *E. coli*, 1 *H. alvei*, 17 *K. oxytoca*, 81 *K. pneumoniae* (including *K. pneumoniae* and *K. pneumoniae pneumoniae*), 7 *M. morganii* (including 1 *M. morganii sibonii* and 6 *M. morganii*), 7 *P. mirabilis*, and 19 *S. marcescens*. In addition, 103 challenge isolates of *P. aeruginosa* and 43 challenge isolates of *Acinetobacter* spp. were tested.

For *Enterobacterales* evaluated using VITEK 2 and auto-dilution, the overall EA and CA were acceptable at 94.4% and 97.0%, respectively (Table 2). The overall major error rate was acceptable, however an increased major error rate was observed with *K. oxytoca* (4.1%). In addition, the EA for *E. cloacae* was reduced at 82.0%. Performance with *P. vulgaris* was not acceptable and is not included in the intended use for meropenem. Performance issues with *E. cloacae, K. oxytoca* and *P. vulgaris* are addressed in limitations (see below).

Review of the reference method and VITEK 2 MIC values for meropenem showed that the majority of clinical isolates of *Enterobacterales* provided MICs less than or equal to the lowest dilution on both the reference panel and VITEK 2 panel, resulting in unevaluable MICs for the vast majority to tested isolates. The low overall value for EA of evaluable results was most likely influenced by the low number of isolates with evaluable results (2.5% of the overall number tested). This also affected the number of results available to assess trending (see Trending and Table 4 below).

For *P. aeruginosa* evaluated using VITEK 2 and auto-dilution, EA was acceptable at 94.7% (Table 2). The CA was 89.7% caused by 29 (10.3%) minor errors. Because the EA of evaluable results was acceptable at 88.6%, and all errors observed were minor errors (no major or very major errors), the CA of 89.7% was considered acceptable.

For *Acinetobacter* spp. evaluated using VITEK 2 and auto-dilution, EA and CA were acceptable at 98.3% and 97.2%, respectively (Table 2). There were no major or very major errors.

Table 2. Performance of VITEK 2 AST-Gram Negative Meropenem with VITEK 2 and Auto-Dilution

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Enterobacterales* (Breakpoints ≤1, 2, ≥4)**													
Clinical	392	376	95.9	18	7	38.9	377	96.2	11	366	4	2	0
Challenge	177	161	91.0	24	8	33.3	166	93.8	54	115	9	2	0
Total	569	537	94.4	42	15	35.7	552	97.0	65	490	13	4	0
***P. aeruginosa* (Breakpoints ≤2, 4, ≥8)**													
Clinical	179	170	95.0	108	99	91.7	155	86.6	45	112	24	0	0
Challenge	103	97	94.2	24	18	75.0	98	95.1	76	25	5	0	0
Total	282	267	94.7	132	117	88.6	253	89.7	121	137	29	0	0
***Acinetobacter spp.** (Breakpoints ≤2, 4, ≥8)**													
Clinical	176	173	98.3	30	28	93.3	171	97.2	134	38	5	0	0
Challenge	43	39	90.7	18	14	77.8	40	93.0	26	14	3	0	0
Total	219	212	96.8	48	42	87.5	211	96.3	160	52	8	0	0

* Includes *A. baumannii, A. haemolyticus, A. junii, A. lwoffii, Acinetobacter* spp.

EA – essential agreement
EVAL – evaluable isolates
CA – categorical agreement
R – resistant
S – susceptible
min – minor discrepancies
maj – major discrepancies
vmj – very major discrepancies

Essential agreement (EA) occurs when the result of the reference method and that of the VITEK 2 AST-Gram Negative Meropenem 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 the VITEK 2 AST-Gram Negative Meropenem. Category agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation provided by VITEK 2 AST-Gram Negative Meropenem.

To assess the performance of manual dilution with the VITEK 2 and the VITEK 2 Compact, a total of 233 challenge isolates of *Enterobacterales* were evaluated including the following species: 1 *C. freundii*, 18 *E. cloacae*, 26 *E. coli*, 1 *H. alvei*, 17 *K. oxytoca*, 115 *K. pneumoniae* (including *K. pneumoniae* and *K. pneumoniae pneumoniae*, 14 *M. morganii* (including 12 *M. morganii* and 2 *M. morganii sibonii*, 7 *P. mirabilis* and 34 *S. marcescens*.

For manual dilution, *E. cloacae* and *P. mirabilis* showed decreased EA and CA when read using both VITEK 2 and VITEK 2 Compact at higher MICs. In addition, *M. morganii* showed decreased EA when read using VITEK Compact at higher MICs. Performance issues with *E. cloacae, P. mirabilis* and *M. morganii* are addressed in limitations (see below). Also, as noted above the majority of clinical isolates of *Enterobacterales* showed MICs less than or equal to the lowest dilution on both the reference panel and VITEK 2 panel, resulting in unevaluable MICs for the vast majority to tested isolates. Consequently, a low overall value for EA of evaluable results was most likely influenced by the low number of isolates with evaluable results (3% of the overall number tested).

A total of 103 isolates of *P. aeruginosa* and 43 isolates of *Acinetobacter* spp. were evaluated using manual dilution; results showed acceptable performance for both genera for manual dilution with both VITEK 2 systems (Table 3).

Table 3. Performance for Manual Dilution with VITEK 2 and VITEK 2 Compact

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Enterobacterales* (Breakpoints ≤1, 2, ≥4)**													
VITEK 2 Manual	233	217	93.1	23	7	30.4	220	94.4	54	171	9	4	0
VITEK 2 Compact	233	212	91.0	26	7	26.9	219	94.0	54	171	9	5	0
***P. aeruginosa* (Breakpoints ≤2, 4, ≥8)**													
VITEK 2 Manual	103	99	96.1	25	21	84.0	99	96.1	76	25	4	0	0
VITEK 2 Compact	103	97	94.2	26	20	76.9	97	94.2	76	25	6	0	0
***Acinetobacter* spp. (Breakpoints ≤2, 4, ≥8)**													
VITEK 2 Manual	43	40	93.0	18	15	83.3	40	93.0	26	14	3	0	0
VITEK 2 Compact	43	40	93.0	18	15	83.3	40	93.0	26	14	3	0	0

To address the performance issues noted above for both autodilution and manual dilution, the sponsor included the following limitations in the device labeling:

Perform an alternative method of testing prior to reporting for the following meropenem/organism combinations:

- *Proteus vulgaris*
- *When the VITEK 2 MIC is greater than or equal to 16 µg/mL for Enterobacter cloacae*
- *Morganella morganii (when tested with VITEK 2 COMPACT if critical to patient care*

Perform an alternate method of testing prior to reporting results when a resistant result is obtained:

- *Klebsiella oxytoca, Proteus mirabilis*

Resistant Strains

An insufficient number of resistant strains of *C. koseri* and *H. alvei* were evaluated. The sponsor included the following limitation in the device labeling:

The ability of the VITEK 2 AST-Gram Negative Meropenem to detect resistance to meropenem is unknown for the following species because an insufficient number of resistant strains were available at the time of comparative testing:

- *Citrobacter koseri* and *Hafnia alvei*

Resistance Mechanism Characterization

Isolates with the following resistance mechanisms were evaluated: KPC, KPC-2, KPC-3, NDM, NDM-1, NDM-5, NDM-6, SME, VIM, OXA-48, OXA-181, OXA-232, CTX-M-1, and ACT/MIR.

MIC Trending

A trending analysis was conducted using the combined data (clinical and challenge) obtained from the VITEK 2 auto-dilution method for each organism group. 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. Results that are not clearly at least one dilution lower, at least one dilution higher or in exact agreement with the CLSI reference method are not considered int the trending analysis.

Organism groups 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 showed higher or lower MIC values compared to the reference is addressed in the labeling.

Evaluation of results for the *Enterobacterales* showed that a majority of isolates provided MICs that were not evaluable for trending. Trending, therefore, was calculated using results for all *Enterobacterales* combined (**Table 4**). Results for *Enterobacterales* and *P. aeruginosa* showed higher trending for all inoculation and read methods, while results for *Acinetobacter* spp. showed lower trending for all inoculation and read methods. For the *Enterobacterales*, only 6.5% of trending-evaluable isolates evaluated with autodilution, and no isolates evaluated by manual dilution (VITEK 2 or Compact), gave the exact MIC as that obtained by the reference method (which affected wording of the trending footnote).

Table 4. Trending Observed for *Enterobacterales*, *P. aeruginosa* and *Acinetobacter* spp. with all Dilution and Read Methods

	Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
Enterobacterales	Autodilution	46	12 (26.1)	3 (6.5)	31 (67.4)	41.3 (21.1 to 57.1)	Yes high
	VITEK 2 Manual Dilution	28	7 (25.0)	0	21 (75.0)	50.0 (24.0 to 67.4)	Yes high
	Compact Manual Dilution	30	8 (26.7)	0	22(73.3)	46.7 (21.5 to 64.3)	Yes high
P. aeruginosa	Autodilution	172	32 (18.6)	48 (27.9)	92 (53.5)	34.9 (25.0 to 43.8)	Yes high
	VITEK 2 Manual Dilution	45	3 (6.7)	6 (13.3)	36 (80.0)	73.3 (55.6 to 83.4)	Yes high
	Compact Manual Dilution	46	2 (4.4)	3 (6.5)	41 (89.1)	84.8 (68.1 to 91.7)	Yes high
Acinetobacter spp.	Autodilution	26	15 (57.7)	8 (30.8)	3 (11.5)	-46.2 (-64.5 to -20.6)	Yes low
	VITEK 2 Manual Dilution	18	14 (77.8)	4 (22.2)	0	-77.8 (-91.0 to -48.8)	Yes low
	Compact Manual Dilution	18	13 (72.2)	5 (27.8)	0	-72.2 (-87.5 to -43.2)	Yes low

The following footnote to the performance table was added to the device labeling to address the observed trending:

Meropenem MIC values for Enterobacterales and P. aeruginosa tended to be at least one doubling dilution higher than the reference method and may contribute to the occurrence of major errors for Enterobacterales. Meropenem MIC values for Acinetobacter spp. tended to be at least one doubling dilution lower than the reference method.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable

2. Clinical Specificity:

Not applicable

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

Not applicable

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Table 5: FDA-Recognized Interpretive Criteria for Meropenem

Organisms	Interpretive Criteria (µg/mL) [a]		
	S	I	R
Enterobacteriaceae	≤1	2	≥4
P. aeruginosa	≤2	4	≥8
Acinetobacter spp.	≤2	4	≥8

[a]As noted on the FDA STIC Website.

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.

To support the implementation of changes to FDA-recognized susceptibility test interpretive criteria (i.e., breakpoints), this submission included a breakpoint change protocol that was reviewed and accepted by FDA. 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 intends to use to evaluate the VITEK 2 AST-GN 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 will update the meropenem device 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.