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

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K191766

B Applicant

bioMerieux, Inc.

C Proprietary and Established Names

VITEK 2 AST-Gram Negative Eravacycline (<=0.12 - >=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
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 eravacycline for testing of Gram-negative bacilli on the VITEK 2 and VITEK 2 Compact Antimicrobial Susceptibility Test (AST) Systems

B Measurand:

Eravacycline ≤0.012 – ≥4 µg/mL

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 Eravacycline is designed for antimicrobial susceptibility testing of Gram negative bacilli 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 AST-Gram Negative Eravacycline is a quantitative test.

Eravacycline 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:
Citrobacter freundii
Enterobacter cloacae
Escherichia coli
Klebsiella oxytoca
Klebsiella pneumoniae

In vitro data are available, but clinical significance is unknown:
Citrobacter koseri
Klebsiella (Enterobacter) aerogenes
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.

C Special Conditions for Use Statement(s):

- Rx - For Prescription Use Only
- 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.

  Eravacycline: *C. freundii, C. koseri, E. coli, K. oxytoca*

- The lack of an intermediate category has shown very major discrepancies when compared to the reference method. Testing should be repeated using an alternative method prior to reporting results for the following antibiotic/organism combination(s):

  Eravacycline: *Klebsiella pneumoniae* when the MIC is 0.5 µg/mL

D Special Instrument Requirements:

VITEK 2 and VITEK 2 Compact Systems using VITEK 2 Systems 9.03 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 Eravacycline has the following concentrations in the card: 0.25, 1, 2 and 4 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The eravacycline MIC result range for the VITEK 2 is ≤0.12 to ≥4 µg/mL. For all species, the VITEK 2 system is capable of reporting the following MIC results: ≤0.12, 0.25, 0.5, 1, 2 and ≥4 µg/mL for the AST-Gram Negative Eravacycline 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):

VITEK2 AST-Gram Negative Delafloxacin (<=0.06->=4 ug/mL)

B Predicate 510(k) Number(s):

K183524

C Comparison with Predicate(s):

Device & Predicate Device(s):	**Device** **K191766**	**Predicate** **K183524**
Device Trade Name	Vitek 2 AST-Gram Negative Eravacycline (≤0.12 – ≥4 µg/mL)	Vitek 2 AST-Gram Negative Delafloxacin (≤0.06 – ≥4 µg/mL)
General Device Characteristic Similarities		
Intended 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 VITEK 2 Compact Systems to determine the *in vitro* susceptibility of Gram-negative bacilli	Same
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	Eravacycline	Delafloxacin
Antimicrobial Concentration	0.25, 1, 2 and 4 µg/mL	0.06, 0.25, 0.5, and 2 µg/mL
Reporting Range	≤0.12 – ≥4 µg/mL	≤0.06 – ≥4 µg/mL
Indicated Organisms	*Citrobacter freundii, Enterobacter cloacae, Escherichia coli, Klebsiella oxytoca, Klebsiella pneumoniae,*	*Escherichia coli, Enterobacter cloacae, Klebsiella pneumoniae, Pseudomonas aeruginosa*

Device & Predicate Device(s):	Device K191766	Predicate K183524
	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-A10, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard-Ninth Edition" Vol. 35 No. 2 (January 2015)
- CLSI M100, "Performance Standards for Antimicrobial Susceptibility Testing"; Twenty-ninth Edition (January 2019)

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Reproducibility testing for the VITEK 2 AST-Gram Negative Eravacycline was conducted at three external clinical sites using a panel of ten Gram-negative bacilli consistent with the indications for use (i.e., two *Enterobacter cloacae*, two *Klebsiella pneumoniae pneumoniae* and six *Klebsiella pneumoniae* isolates). 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. The testing resulted in overall reproducibility of 100% (270/270) for each dilution method for testing in the VITEK 2 System (auto-dilution and manual dilution) and 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, namely *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.

Both 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. Obtaining a VITEK result of ≤ 0.125 µg/mL (lowest dilution on the card) for *E. coli* ATCC 25922 and/or ≥ 4 µg/mL (highest dilution on the card) for *P. aeruginosa* ATCC 27853 was considered as an indicator that the quality control test results were acceptable.

Because the VITEK card reporting range (≤0.125- ≥ 4 µg/mL) does not include the full CLSI/FDA-recommended dilution range for QC testing, the sponsor included a footnote in labeling to indicate that the device does not include the full CLSI/FDA-recommended dilution range for QC testing. The sponsor also included the following footnote in labeling:

> *Although the VITEK 2 AST-GN Eravacycline calling range for Enterobacteriaceae is 0.12 - >4 µg/mL, the VITEK 2 AST-GN Eravacycline QC calling range for P. aeruginosa, ATCC 27853 is 0.12 - >8 µg/mL*

The quality control results are 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: 0.03 – 0.12 µg/mL		≤0.008						
		0.015						
		0.03						
		0.06		116		88		88
	≤ 0.125	0.125	123	7	90	2	90	2
	0.25	0.25						
	0.5	0.5						
	1	1						
	2	2						
	≥ 4	4						
		8						
		≥16						
P. aeruginosa ATCC 27853		≤0.008						
		0.015						
		0.03						
		0.06						

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
Expected Result: 2 - 16 µg/mL	≤ 0.125	0.125						
	0.25	0.25						
	0.5	0.5						
	1	1						
	2	2	57	4	49	3	42	3
	≥ 4	4	67	86	43	61	50	61
		8		34		28		28
		≥16						

[1]Does not include the full CLSI/FDA-recommended dilution range for QC testing. For *E. coli*, an in-range VITEK result will be ≤ the lowest dilution on the card (i.e., ≤ 0.125). For *P. aeruginosa*, an in-range VITEK result could be ≥ the highest dilution on the card (i.e., ≥ 4).

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:
A total of 320 clinical isolates were evaluated. A total of 319 organisms grew in the VITEK 2 AST-Gram Negative Eravacycline test using the auto-dilution method which is acceptable (< 10% growth failure).

A total of 144 challenge isolates were evaluated at one site. All 144 challenge organisms grew in the VITEK 2 AST-Gram Negative Eravacycline test using both the auto-dilution and manual dilution methods for the VITEK 2 and manual dilution method for the VITEK 2 Compact.

A total of 463 VITEK 2 AST-Gram Negative Eravacycline test results are available.

6. Detection Limit:

Not applicable

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

Testing of eravacycline on the VITEK 2 AST-Gram Negative card was performed at three external sites and one internal site. There were 320 clinical isolates and 144 challenge isolates tested for a total of 464 isolates. Results obtained with the VITEK 2 AST-Gram Negative card with eravacycline were compared to results obtained with the CLSI broth microdilution reference panel. The MIC result range for the VITEK 2 AST-Gram Negative Eravacycline is ≤0.12 – ≥4 μg/mL for all species. The reference panel contained two-fold serial dilutions with a range of ≤0.008 to ≥32 μg/mL. The testing conditions for the reference method consisted of the following:
• Medium – Cation Adjusted Mueller Hinton broth
• Inoculum – Direct colony suspension
• Incubation – 35°C; 16-20 hours

The VITEK 2 AST 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 320 clinical *Enterobacteriaceae* isolates were evaluated: 52.8% were considered contemporary isolates (isolated from clinical specimen and tested within 7 days) and 47.2% were stock isolates. One isolate did not grow in the VITEK 2 AST-Gram Negative Eravacycline test so complete test results are available for 319 clinical isolates: 312 isolates from indicated species (12 *C. freundii*, 7 *C. koseri*, 39 *K. aerogenes*, 19 *E. cloacae*, 22 *E. cloacae* complex, 121 *E. coli*, 23 *K. oxytoca*, 4 *K. pneumoniae pneumoniae* and 65 *K. pneumoniae*) and 7 isolates from non-indicated species (1 *C. braakii*, 2 *E. vulneris*, 1 *L. amnigena* 2, 2 *P. dispersa* and 1 *R. ornithinolytica*). The clinical isolates were tested with the auto-dilution option of the VITEK 2.

A total of 144 challenge isolates (1 *C. freundii*, 7 *K. aerogenes*, 13 *E. cloacae*, 12 *E. coli*, 1 *K. oxytoca*, 15 *K. pneumoniae pneumoniae*, and 95 *K. pneumoniae*) were evaluated at one site. The challenge set was tested with the auto-dilution and manual dilution options of the VITEK 2 and with the manual dilution method on the VITEK 2 Compact.

At the time of comparative testing, non-susceptible isolates were not available for *Citrobacter freundii, Citrobacter koseri, Escherichia coli,* and *Klebsiella oxytoca*. Thus, the following statement is included in the *Limitations* section of 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.*
>
> *Eravacycline: C. freundii, C. koseri, E. coli, K. oxytoca*

To address testing of non-indicated species, the following statement is included in the *Precautions* section of the device labeling:

> *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.

Clinical and Challenge Data –VITEK 2 Auto-Dilution

The results obtained using the auto-dilution method of the VITEK 2 from the 463 total isolates (319 clinical isolates and 144 challenge isolates) are summarized in **Table 2.**

Table 2. Performance of All *Enterobacteriaceae* Isolates: VITEK 2 *Auto-Dilution*

Organism Type	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#NS	min	maj	vmj
Clinical	319	307	96.2	103	91	88.3	316	99.1	20	n/a	2	1
Challenge	144	142	98.6	120	118	98.3	143	99.3	40	n/a	0	1
Combined	**463**	**449**	**97.0**	**223**	**209**	**93.7**	**459**	**99.1**	**60**	**n/a**	**2**	**2**

EA – Essential Agreement
CA – Category Agreement
EVAL – Evaluable isolates
NS – Non-susceptible isolates

min – minor errors
maj – major errors
vmj – very major errors

n/a – Not applicable due to only a susceptible interpretive criterion for eravacycline

When using the auto-dilution method of the VITEK 2, the overall performance with all *Enterobacteriaceae* is acceptable with an EA of 97.0% and a CA of 99.1%. As summarized in **Table 4**, there were two very major errors (2/60 = 3.3%) and two major errors (2/403 = 0.5%). Due to the lack of an intermediate interpretive criteria (Eravacycline has only a "susceptible" category), further analysis of the errors is performed and adjustments are made by considering the MIC values where the errors occurred. One of the very major errors had an MIC value that was one doubling dilution from the reference and thus in essential agreement. Therefore, the adjusted very major error is one (1/60 = 1.7%) which is acceptable. The other very major error and both major errors resulted when VITEK 2 AST-Gram Negative Eravacycline was test with *K. pneumoniae*.

Challenge Data –VITEK 2 and VITEK 2 Compact Manual Dilution

The 144 challenge isolates were also evaluated at one site with the manual dilution options of the VITEK 2 and VITEK 2 Compact systems (summarized in **Table 3**).

Table 3. Performance of Challenge Isolates: VITEK 2 and VITEK 2 Compact *Manual Dilution*

System	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#NS	min	maj	vmj
VITEK 2	144	142	98.6	119	117	98.3	139	96.5	40	n/a	3	2
VITEK 2 Compact	144	141	97.9	108	105	97.2	140	97.2	40	n/a	1	3

The overall performance of VITEK 2 when using the manual dilution method with all *Enterobacteriaceae* challenge isolates is acceptable with an EA of 98.6% and a CA of 96.5%. As summarized in **Table 4**, there were two very major errors (2/40 = 5%) and three major errors (3/104 = 2.9%). Both very major errors had MIC values that were one doubling dilution from the reference and thus in essential agreement. Therefore, the adjusted very major error is zero which is acceptable.

The overall performance of VITEK 2 Compact when using the manual dilution method with all *Enterobacteriaceae* challenge isolates is acceptable with an EA of 97.9% and a CA of 97.2%. As summarized in **Table 4**, there were three very major errors (3/40 = 7.5%) and one major error (1/104 = 1.0%). Two of the very major errors had MIC values that were one doubling dilution from the reference and thus in essential agreement. Therefore, the adjusted very major error is one (1/40 = 2.5%), which is unacceptable but addressed as a limitation in the package insert.

K. pneumoniae reported a high number of major and very major errors due to the lack of an intermediate or resistant interpretive category for eravacycline. These error rates are reported in the package insert, however, the error rates are adjusted by taking into consideration the essential agreement with the reference method of MIC values resulting in the errors. The original and adjusted error rates are shown in **Table 4**.

Table 4. Original and Adjusted Major and Very Major Error Rates for Eravacycline

System / Dilution Method	Organism Type	Species	No. Major Errors/Total (%)		No. Very Major Errors/Total (%)	
			Original	Adjusted	Original	Adjusted
VITEK 2: Auto-dilution	Clinical and Challenge	**All *Enterobacteriaceae***	**2/403 (0.5)**	**1/403 (0.2)**	**2/60 (3.3)**	**1/60 (1.7)**
		E. cloacae	0	0	1/7 (14.3)	0
		K. pneumoniae	2/117 (1.7)	1/117 (0.9)	1/49 (2.0)	1/49 (2.0)
VITEK 2: Manual dilution	Challenge	**All *Enterobacteriaceae***	**3/104 (2.9)**	**0**	**2/40 (5.0)**	**0**
		K. pneumoniae	3/70 (4.3)	0	2/31 (6.5)	0
VITEK 2 Compact: Manual dilution	Challenge	**All *Enterobacteriaceae***	**1/104 (1.0)**	**0**	**3/40 (7.5)**	**1/40 (2.5)**
		K. pneumoniae	1/70 (1.4)	0	3/31 (9.7)	1/31 (3.2)

To address the high rate of very major errors, the following statement is included as a footnote to the performance table in the package insert:

> *The overall categorical very major error rate for eravacycline when testing Enterobacteriaceae clinical and challenge isolates with the VITEK 2 system was 3.3%. Based on the essential agreement and lack of an intermediate breakpoint for eravacycline, the overall adjusted very major error rate for Enterobacteriaceae clinical and challenge isolates is 1.7% which is acceptable.*

In addition, to address the *K. pneumoniae* very major errors and the reporting of non-susceptible isolates, the following statement is included in the *Limitations* section of the package insert:

> *The lack of an intermediate category has shown very major discrepancies when compared to the reference method. Testing should be repeated using an alternative method prior to reporting results for the following antibiotic/organism combination(s): Eravacycline: Klebsiella pneumoniae when the MIC is 0.5 µg/mL*

Resistance Mechanism Characterization:
Challenge isolates of *Enterobacteriaceae* harboring various molecular mechanisms of resistance noted in the FDA drug label were tested with eravacycline. The following resistance mechanisms were evaluated: *tet(A)* and *tet(B)*.

MIC Trends:
A trending analysis was conducted using the combined data (clinical and challenge) obtained from the VITEK 2 auto-dilution method for each organism species and group. This trending calculation analyzes device MIC values that are determined to be one or more doubling dilutions lower or higher than the reference method. MIC values that are off-scale for both the reference and device are not considered in the trending analysis.

Trending results were stratified by species to determine if species-related trends were observed (**Table 5**). Species for which the difference between the percentage of isolates with higher or lower MIC values was ≥30% with a statistically significant confidence interval were considered to have evidence of trending.

Table 5: Trending by Species (clinical and challenge isolates)

VITEK 2 Auto-Dilution (Challenge and Clinical Isolates)						
Organism	**Total Evaluable for Trending**	**≥1 dil. Lower # (%)**	**Exact # (%)**	**≥1 dil. Higher # (%)**	**Percent Difference (95% CI)**	**Trending Noted**
C. freundii	**8**	**6 (75.0%)**	**1 (12.5%)**	**1 (12.5%)**	**-62.5% (-83.1 to -14.0%)**	**Yes**
C. koseri [1]	1	1 (-100%)	0	0	-100.0% (-100.0 to 12.2%)	No [1]
E. aerogenes	**33**	**20 (60.6%)**	**9 (27.3%)**	**4 (12.1%)**	**-48.5% (-64.6 to -25.7%)**	**Yes**
E. cloacae [2]	**54**	**23 (42.6%)**	**31 (57.4%)**	**0**	**-42.6% (-55.8 to -28.7%)**	**Yes**
E. coli	**41**	**40 (97.6%)**	**1 (2.4%)**	**0**	**-97.56% (-99.6 to -82.3%)**	**Yes**
K. oxytoca	5	3 (60.0%)	0	2 (40.0%)	-20.0% (-59.9 to 32.2%)	No
K. pneumoniae [3]	**157**	**73 (46.5%)**	**77 (49.0%)**	**7 (4.5%)**	**-42.0% (-50.2 to -33.2%)**	**Yes**
***Enterobacteriaceae* (all)**	**299**	**166 (55.5%)**	**119 (39.8%)**	**14 (4.7%)**	**-50.8% (-56.7 to 44.4%)**	**Yes**

[1]There were not enough *C. koseri* isolates to be appropriately evaluated for trending.
[2]*E. cloacae* and *E. cloacae complex* were consolidated into a single group, *E. cloacae*.
[3]*K. pneumoniae* and *K. pneumoniae pneumoniae* were consolidated into a single group, *K. pneumoniae*.

A trend toward lower MIC values was observed for the *Enterobacteriaceae* family, specifically when testing for *C. freundii*, *E. aerogenes*, *E. cloacae*, *E. coli*, and *K. pneumoniae*. The following footnote to the performance table is included in the package insert to address the trending observed for VITEK 2 AST-Gram Negative Eravacycline:

VITEK 2 AST-Gram Negative Eravacycline values tended to be in exact agreement or at least one doubling dilution lower when testing Enterobacteriaceae compared to the CLSI reference broth microdilution.

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:

The FDA-identified susceptibility interpretive criteria for eravacycline are listed in **Table 6**.

Table 6: FDA-Identified Interpretive Criteria for Eravacycline (µg/mL)[a]

Organisms	S	I	R
Enterobacteriaceae	≤0.5	-	-

[a]According to 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 Eravacycline when revised breakpoints for eravacycline 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 eravacycline 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.