510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K200590

B Applicant

bioMérieux, Inc

C Proprietary and Established Names

VITEK 2 AST-Gram Positive Delafloxacin (≤0.015 – ≥1 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 delafloxacin testing of Gram-positive organisms on the VITEK 2 and VITEK 2 Compact Antimicrobial Susceptibility Test (AST) Systems

B Measurand:

Delafloxacin ≤0.015 – ≥1 µg/mL

C Type of Test:

Automated quantitative or qualitative antimicrobial susceptibility test for delafloxacin

III Intended Use/Indications for Use:

A Intended Use(s):

The VITEK 2 Gram-positive Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Staphylococcus* spp., *Enterococcus* spp., and *S. agalactiae* to antimicrobial agents when used as instructed.

B Indication(s) for Use:

VITEK 2 AST-Gram Positive Delafloxacin is designed for antimicrobial susceptibility testing of Gram positive microorganisms 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 Positive Delafloxacin is a quantitative test. Delafloxacin 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:

Acute Bacterial Skin and Skin Structure Infections (ABSSSI):
Staphylococcus aureus (including methicillin-resistant and methicillin-susceptible isolates)
Streptococcus agalactiae
Enterococcus faecalis

Community-Acquired Bacterial Pneumonia (CABP):
Staphylococcus aureus (methicillin-susceptible isolates only)

The VITEK 2 Gram-positive Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Staphylococcus* spp., *Enterococcus* spp., and *S. agalactiae* to antimicrobial agents when used as instructed.

C Special Conditions for Use Statement(s):

- Rx - For Prescription Use Only
- Perform an alternative method of testing prior to the reporting of results for the following antibiotic/organism combination(s):
  Delafloxacin: *Staphylococcus haemolyticus*
- The ability of the AST card to detect resistance with the following combination(s) is unknown because an insufficient number of resistant strains were available at the time of comparative testing:
  Delafloxacin: *Streptococcus agalactiae*

D Special Instrument Requirements:

VITEK 2 and VITEK 2 Compact Systems using VITEK 2 Systems 9.04 software or later versions

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 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 anti-microbial 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-GP Delafloxacin has the following concentrations in the card: 0.008, 0.03, 0.06, and 0.25 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The delafloxacin MIC result range for the VITEK 2 is ≤0.015 – ≥1 µg/mL. For all species, the VITEK 2 system is capable of reporting the following MIC results: ≤0.015, 0.03, 0.06, 0.125, 0.25, 0.5 and ≥1 µg/mL for the AST-GP Dalbavancin 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 Positive Dalbavancin (≤ 0.015 – ≥ 1 µg/mL)

B Predicate 510(k) Number(s):

K190616

C Comparison with Predicate(s):

Table 1: Comparison with Predicate Device

Device & Predicate Device(s):	Device: K200590	Predicate: K190616
Device Trade Name	VITEK 2 AST-GP Delafloxacin (≤0.015 – ≥1 µg/mL)	VITEK 2 AST-GP Dalbavancin (≤0.015 – ≥1 µg/mL)
General Device Characteristic Similarities		
Intended Use	The VITEK 2 Gram-Positive 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-positive microorganisms 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-positive microorganisms	Same
Inoculum	Standardized saline suspension of test organism	Same
Test Card	VITEK 2 Gram Positive Susceptibility Test Card	Same
Instrument	VITEK 2 and VITEK 2 Compact Systems	Same
Analysis Algorithm	Growth pattern analysis	Same
Reporting Range	≤0.015 to ≥1 µg/mL	Same
General Device Characteristic Differences		
Antimicrobial Agent	Delafloxacin (DFX)	Dalbavancin (DAL)
Antimicrobial Concentration	0.008, 0.03, 0.06, 0.25 µg/mL	0.0625, 0.125, 0.25, 0.5 µg/mL

VI Standards/Guidance Documents Referenced:

- CLSI M07, 11th ed., "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard, January 2018".
- CLSI M100, 29th ed., "Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Ninth Informational Supplement, January 2019".

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Reproducibility testing for the VITEK 2 AST-GP card with Delafloxacin was conducted at three clinical sites using a panel of ten Gram-positive microorganisms consistent with the indications for use and included five *Enterococcus faecalis* and five *Staphylococcus aureus* 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 MIC value. 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.

   All MIC values were on-scale and within one doubling dilution of the mode MIC. The testing resulted in overall reproducibility of 100% for each dilution method and instrument, which is 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 *Enterococcus faecalis* ATCC 29212 and *Staphylococcus aureus* ATCC 29213, 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. The results are summarized in **Table 2** below.

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

Organism	VITEK 2 Result Range[1]	DFX MIC (µg/mL)	VITEK 2 Auto-Dilution	BMD	VITEK 2 Manual Dilution	BMD	VITEK 2 Compact Manual Dilution	BMD
Enterococcus faecalis ATCC 29212 Expected Result: 0.016 – 0.12 µg/mL		≤0.002						
		0.004						
		0.008						
	*	0.015	3		2		2	
	*	0.03		5		5		5
	*	0.06	204	198	160	153	160	153
	*	0.125		4		4		4
	*	0.25						
	*	0.5						
	*	1						
		≥2						
Staphylococcus aureus ATCC 29213 Expected Result: 0.001-0.008 µg/mL		≤0.002		44		32		32
		0.004		166		133		133
		0.008						
	*	0.015	207		163		163	
	*	0.03						
	*	0.06	3		2		2	
	*	0.12						
	*	0.25						
	*	0.5						
	*	1						
		≥2						

DFX: delafloxacin; BMD: broth microdilution

*denotes the on-scale MIC result range of the AST-GP Delafloxacin test

[1]Does not include the full CLSI/FDA-recommended dilution range for QC testing of *S. aureus* ATCC 29213. An in-range VITEK result will be ≤ the lowest dilution on the card (i.e., ≤ 0.015).

The VITEK 2 AST-GP Delafloxacin reporting range (≤0.015 to ≥1 µg/mL) does not include the CLSI/FDA-recommended dilution range for QC testing of *S. aureus* ATCC 29213 (0.001-0.008 µg/mL). As such, an in-range VITEK result will be ≤ the lowest dilution on the card (i.e., ≤ 0.015 µg/mL). This is addressed in the following footnote to the *S. aureus* QC result range within the Quality Control table in the device labeling:

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

Acceptance of QC results for the VITEK 2 AST-GP Delafloxacin was based on the *Enterococcus faecalis* ATCC 29212 strain since it provided results confirming the range. Both the auto-dilution and the manual dilution methods for VITEK 2 and the manual dilution for VITEK 2 Compact QC results were within the expected range >95% of the time, which is acceptable.

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 676 clinical isolates were evaluated at three clinical sites. All 676 organisms grew in the VITEK 2 AST-GP Delafloxacin test using the auto-dilution method.

A total of 87 challenge isolates were evaluated at one external site. All 87 challenge organisms grew in the VITEK 2 AST-GP Delafloxacin 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 763 VITEK 2 AST- GP Delafloxacin 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 delafloxacin on the VITEK 2 AST-Gram Positive card was performed at four clinical sites. There were 676 clinical isolates and 87 challenge isolates tested for a total of 763 isolates. Results obtained with the VITEK 2 AST-Gram Positive card with delafloxacin were compared to results obtained with the CLSI broth microdilution (BMD) reference panel. The MIC result range for the VITEK 2 AST-Gram Positive Delafloxacin is ≤0.015 to ≥1 µg/mL for all species. The reference panel contained two-fold serial dilutions of delafloxacin with a range of ≤0.002 to ≥4 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 for Staphylococci and Enterococci
     35°C; 20-24 hours for Streptococci

   The VITEK 2 AST cards were inoculated with test organisms using the auto-dilution method (VITEK 2) and 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 676 clinical isolates were evaluated at three sites: 43.2% were considered contemporary isolates (isolated from clinical specimen and tested within 6 months) and 56.8% were stock isolates. Complete test results are available for all 676 clinical isolates from indicated species: 317 *Enterococcus faecalis*, 299 *Staphylococcus aureus* (136 MRSA and 163 MSSA), and 60 *Streptococcus agalactiae*. All clinical isolates were tested with the auto-dilution option of the VITEK 2.

A total of 87 challenge isolates were evaluated at one site. They included: 43 *Enterococcus faecalis*, 27 *Staphylococcus aureus* (20 MRSA and 7 MSSA), and 17 *Streptococcus agalactiae*. 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, a sufficient number of resistant isolates was not available for *Streptococcus agalactiae*. The following statement is included in the *Limitations* section of the device labeling:

> *The ability of the AST card to detect resistant strains with the following combination(s) is unknown because an insufficient number of resistant strains were available at the time of comparative testing.*
> *Delafloxacin: Streptococcus agalactiae*

Clinical and Challenge Data –VITEK 2 Auto-Dilution
VITEK 2 AST-GP Delafloxacin performance was determined with 763 isolates (676 clinical isolates and 87 challenge isolates) and evaluated based on susceptibility testing interpretive criteria (breakpoints) established for the following clinical indications: Acute Bacterial and Skin Structure Infections (ABSSSI, **Table 3**) and Community Acquired Bacterial Pneumonia (CABP, **Table 4**).

All results for the 763 isolates tested with the auto-dilution method of the VITEK 2 were evaluated using breakpoints established for ABSSSI (**Table 3**).

Table 3: Performance of All Clinical and Challenge Isolates with ABSSSI Breakpoints for Delafloxacin: VITEK 2 *Auto-Dilution*

Organism Type	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#R	#S	min	maj	vmj
***Enterococcus faecalis* [Breakpoints (µg/mL): ≤0.12 (S), 0.25 (I), ≥0.5 (R)]**													
Clinical	317	299	94.3	256	238	93.0	297	93.7	74	233	17	1	2
Challenge	43	43	100	29	29	100	43	100	24	19	0	0	0
Combined	**360**	**342**	**95.0**	**285**	**267**	**93.7**	**340**	**94.4**	**98**	**252**	**17**	**1**	**2**
***Staphylococcus aureus* (MRSA and MSSA combined) [Breakpoints (µg/mL): ≤0.25 (S), 0.5 (I), ≥1 (R)]**													
Clinical	299	296	99.0	76	73	96.1	277	92.6	29	252	20	2	0
Challenge	27	24	88.9	9	6	66.7	23	85.2	7	15	4	0	0
Combined	**326**	**320**	**98.2**	**85**	**79**	**92.9**	**300**	**92.0**	**36**	**267**	**24**	**2**	**0**

Organism Type	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#R	#S	min	maj	vmj
***Streptococcus agalactiae* [Breakpoints (µg/mL): ≤0.06 (S), 0.12 (I), ≥0.25 (R)]**													
Clinical	60	58	96.7	13	11	84.6	60	100	1	59	0	0	0
Challenge	17	17	100	5	5	100	17	100	1	16	0	0	0
Combined	**77**	**75**	**97.4**	**18**	**16**	**88.9**	**77**	**100**	**2**	**75**	**0**	**0**	**0**

EA – Essential Agreement
CA – Category Agreement
EVAL – Evaluable isolates
R – Resistant isolates
min – minor errors
maj – major errors
vmj – very major errors
S – Susceptible isolates

The overall performance of *Enterococcus faecalis* is acceptable with an EA of 95.0% and a CA of 94.4%. There was one major (1/252 = 0.40%) and two very major errors (2/98 = 2.0%). The overall performance of *Staphylococcus aureus* is acceptable with an EA of 98.2% and a CA of 92.0%. There were two major (2/267 = 0.7%) and no very major errors. The overall performance of *Streptococcus agalactiae* is acceptable with an EA of 97.4% and a CA of 100%. There were no major or very major errors.

A subset of results (from 170 methicillin-susceptible *S. aureus* isolates) obtained using the auto-dilution method of the VITEK 2 were evaluated using the breakpoints established for CABP (**Table 4).**

Table 4: Performance of Clinical and Challenge MSSA Isolates with CABP Breakpoints for Delafloxacin: VITEK 2 *Auto-Dilution*

Organism Type	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#R	#S	min	maj	vmj
Methicillin-susceptible *Staphylococcus aureus* (MSSA) [Breakpoints (µg/mL): ≤0.12 (S), 0.25 (I), ≥0.5 (R)]													
Clinical	163	162	99.4	12	11	91.7	158	98.6	5	150	5	0	0
Challenge	7	7	100	2	2	100	7	100	2	5	0	0	0
Combined	**170**	**169**	**99.4**	**14**	**13**	**92.9**	**165**	**97.1**	**7**	**155**	**5**	**0**	**0**

When using the auto-dilution method of the VITEK 2 and evaluating data with breakpoints established for CABP, the overall performance of methicillin-susceptible *Staphylococcus aureus* is acceptable with an EA of 99.4% and a CA of 97.1%. There were no major or very major errors.

Challenge Data – VITEK 2 and VITEK 2 Compact Manual Dilution

The 87 challenge isolates were also tested at one site with the manual dilution option for the VITEK 2 and VITEK 2 Compact systems and evaluated based on clinical indication: ABSSSI (**Table 5**) and CABP (**Table 6**).

All results for the 87 isolates tested with the manual dilution method of the VITEK 2 and VITEK 2 Compact were evaluated using breakpoints established for ABSSSI (**Table 5).**

Table 5: Performance of Challenge Isolates with ABSSSI Breakpoints for Delafloxacin: VITEK 2 *Manual Dilution*

System	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#R	#S	min	maj	vmj
***Enterococcus faecalis* [Breakpoints (µg/mL): ≤0.12 (S), 0.25 (I), ≥0.5 (R)]**													
VITEK 2	43	43	100	27	27	100	43	100	24	19	0	0	0
VITEK 2 Compact	43	43	100	31	31	100	43	100	24	19	0	0	0
Methicillin- Resistant *Staphylococcus aureus* (MRSA) [Breakpoints (µg/mL): ≤0.25 (S), 0.5 (I), ≥1 (R)]													
VITEK 2	20	17	85.0	7	4	57.1	16	80.0	6	14	4	0	0
VITEK 2 Compact	20	17	85.0	5	2	40.0	16	80.0	6	14	4	0	0
Methicillin- Susceptible *Staphylococcus aureus* (MSSA) [Breakpoints (µg/mL): ≤0.25 (S), 0.5 (I), ≥1 (R)]													
VITEK 2	7	7	100	2	2	100	6	85.7	1	6	1	0	0
VITEK 2 Compact	7	7	100	1	1	100	6	85.7	1	6	1	0	0
***Staphylococcus aureus* (MRSA and MSSA combined) [Breakpoints (µg/mL): ≤0.25 (S), 0.5 (I), ≥1 (R)]**													
VITEK 2	27	24	88.9	7	4	57.1	22	81.5	7	15	5	0	0
VITEK 2 Compact	27	24	88.9	6	3	50.0	22	81.5	7	15	5	0	0
***Streptococcus agalactiae* [Breakpoints (µg/mL): ≤0.06 (S), 0.12 (I), ≥0.25 (R)]**													
VITEK 2	17	16	94.1	6	5	83.3	17	100	1	16	0	0	0
VITEK 2 Compact	17	16	94.1	5	4	80.0	17	100	1	16	0	0	0

The overall performance of *Enterococcus faecalis* is acceptable with an EA of 100% and a CA of 100% with both the VITEK 2 and VITEK 2 Compact systems. There were no major or very major errors. The overall performance of *Streptococcus agalactiae* is acceptable with an EA of 94.1% and a CA of 100% with both the VITEK 2 and VITEK 2 Compact systems. There were no major or very major errors. The overall performance of *Staphylococcus aureus* is not acceptable with an EA of 88.9% and a CA of 81.5% with both the VITEK 2 and VITEK 2 Compact systems. There were no major or very major errors.

When *S. aureus* performance data was stratified by methicillin-resistant and methicillin-susceptible, performance of MSSA is acceptable with an EA of 100% and an CA of 85.7%. Since the EA of test results was very good, the <90% CA is acceptable. Meanwhile, performance of MRSA is unacceptable with an EA of 85.0% and an CA of 80.0% with both the VITEK 2 and VITEK 2 Compact systems. The following footnote statement is included in the device labeling to address performance:

When evaluating performance of the challenge isolates on the manual dilution option for the VITEK 2 and VITEK 2 Compact, testing with MRSA isolates yielded an EA of 85% (17/20) and an CA of 80% (16/20). For challenge isolates on the auto dilution option for the VITEK 2, testing with MRSA isolates yielded an EA of 85% (17/20) and an CA of 85% (17/20). All categorical errors were considered minor.

A subset of results (from 7 methicillin-susceptible *S. aureus* isolates) obtained using the manual dilution method of the VITEK 2 and VITEK 2 Compact systems were evaluated using the breakpoints established for CABP (**Table 6).**

Table 6: Performance of MSSA Challenge Isolates with CABP Breakpoints for Delafloxacin: VITEK 2 *Manual Dilution*

System	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#R	#S	min	maj	vmj
Methicillin-susceptible *Staphylococcus aureus* (MSSA) [Breakpoints (µg/mL): ≤0.12 (S), 0.25 (I), ≥0.5 (R)]													
VITEK 2	7	7	100	2	2	100	7	100	2	5	0	0	0
VITEK 2 Compact	7	7	100	1	1	100	7	100	2	5	0	0	0

The overall performance of methicillin-susceptible *Staphylococcus aureus* is acceptable with an EA of 100% and a CA of 100% with both the VITEK 2 and VITEK 2 Compact systems. There were no major or very major errors.

To address testing and reporting 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.*

Resistance Mechanism Characterization

Three challenge isolates (*S. aureus* and *E. faecalis*) harboring the following molecular mechanism of resistance noted in the FDA drug label were tested with delafloxacin: quinolone resistance determining region (GyrA and ParC).

MIC Trends

A trending analysis was conducted using the combined data (clinical and challenge) obtained from the VITEK 2 auto-dilution method for each indicated organism species (**Table 7**). 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. 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 7. Trending by Species (clinical and challenge isolates)

VITEK 2 Auto-Dilution						
Organism	**Total Evaluable for Trending**	**≥1 dil. Lower # (%)**	**Exact # (%)**	**≥1 dil. Higher # (%)**	**Percent Difference (95% CI)**	**Trending Noted**
Enterococcus faecalis	296	48 (16.22)	176 (59.46)	72 (24.32)	8.11% (1.63 to 14.52)	No
Staphylococcus aureus (MSSA and MRSA)	103	3 (2.91)	56 (54.37)	44 (42.72)	39.81% (29.25 to 49.64)	Yes
Streptococcus agalactiae	24	10 (41.67)	10 (41.67)	4 (16.67)	-25.00 (-46.91 to 0.77)	No

A trend toward higher MIC values was observed for *Staphylococcus aureus*. The following footnote to the performance table is included in the package insert to address the trending observed for VITEK 2 AST-Gram Positive Delafloxacin:

VITEK 2 AST-Gram Positive Delafloxacin MIC values tended to be in exact agreement or at least one doubling dilution higher when testing Staphylococcus aureus compared to the CLSI reference broth microdilution 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:

The FDA-identified susceptibility interpretive criteria for delafloxacin for Acute Bacterial Skin and Skin Structure Infections are listed in **Table 8.** The FDA-identified susceptibility interpretive criteria for delafloxacin for Community Acquired Bacterial Pneumonia are listed in **Table 9**.

Table 8: FDA-Identified Interpretive Criteria for Delafloxacin for Acute Bacterial Skin and Skin Structure Infections (µg/mL) [a]

Organism	Susceptible	Intermediate	Resistant
Enterococcus faecalis	≤0.12	0.25	≥0.5
Staphylococcus aureus (methicillin-resistant and methicillin-susceptible isolates)	≤0.25	0.5	≥1
Streptococcus agalactiae	≤0.06	0.12	≥0.25

[a] According to FDA STIC Website

Table 9: FDA-Identified Interpretive Criteria for Delafloxacin for Community Acquired Bacterial Pneumonia (µg/mL) [a]

Organism	Susceptible	Intermediate	Resistant
Staphylococcus aureus (methicillin-susceptible isolates)	≤0.12	0.25	≥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-GP Delafloxacin when revised breakpoints for delafloxacin 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 delafloxacin 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.