510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K172731

B. Purpose for Submission:

To obtain a substantial equivalence determination for Amikacin for testing of gram negative bacilli on the VITEK 2 and VITEK 2 Compact Antimicrobial Susceptibility Test (AST) Systems

C. Measurand:

The VITEK 2 AST-Gram Negative card contains the following concentrations of Amikacin: 2, 4, 16, and 48 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The Amikacin MIC reporting range for the card is ≤ 1 – ≥ 64 µg/mL for all organisms except *Acinetobacter* species. The calling range for *Acinetobacter* species is ≤ 2 – ≥ 64 µg/mL.

D. Type of Test:

Automated quantitative or qualitative antimicrobial susceptibility test for Amikacin

E. Applicant:

bioMérieux, Inc.

F. Proprietary and Established Names:

VITEK 2 AST-Gram Negative Amikacin (≤ 1 – ≥ 64 µg/mL)

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.1645: Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System

2. Classification:

   Class II

3. Product code(s):

   LON – Fully automated short-term incubation cycle antimicrobial susceptibility system
   LTW – Susceptibility Test Cards, Antimicrobial
   LTT – Panels, Test, Susceptibility, Antimicrobial

4. Panel:

   Microbiology (83)

H. Intended Use/Indications for Use:

1. Intended Use (s):

   The VITEK 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK 2 Systems for the automated quantitative or qualitative susceptibility testing of isolated colonies for the most clinically significant aerobic gram-negative bacilli, *Staphylococcus* spp., *Enterococcus* spp., *Streptococcus* spp. and clinically significant yeast.

2. Indications for Use:

   VITEK 2 AST-Gram Negative Amikacin 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 Amikacin is a quantitative test. Amikacin 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:
   Pseudomonas species
   Escherichia coli
   Proteus mirabilis
   Klebsiella species
   Enterobacter species
   Serratia species
   Acinetobacter species (excluding *A. baumannii* Complex)

   In vitro data available but clinical significance unknown:
   Citrobacter freundii

   The VITEK 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK 2 Systems for the automated quantitative or qualitative susceptibility testing of isolated colonies for the most clinically significant aerobic gram-negative bacilli, *Staphylococcus* spp., *Enterococcus* spp., *Streptococcus* spp. and clinically significant yeast.

3. Special conditions for use statement(s):

   For Prescription Use Only

   Limitations:

   1. "*Perform an alternative method of testing prior to reporting of results for the following antibiotic/organism combination(s):*
      Amikacin: Acinetobacter baumannii complex"

   2. "*The ability of the AST card to detect resistance with the following combination(s) is unknown because resistant strains were either not available or an insufficient number were encountered at the time of comparative testing:*
      Amikacin: Pseudomonas species, Escherichia coli, Proteus mirabilis, Klebsiella species, Enterobacter species, Serratia species, Citrobacter freundii"

4. Special instrument requirements:

   VITEK 2 and VITEK 2 Compact Systems using VITEK 2 Systems 8.01 software

I. Device Description:

The VITEK 2 AST card utilizes a miniaturized, abbreviated, and automated version of the doubling dilution technique for determining the minimal inhibitory concentration (MIC) on the VITEK 2 and VITEK 2 Compact Systems.

Each VITEK 2 AST card has 64 microwells containing dehydrated media with or without an antimicrobial. A control well that contains only dehydrated culture medium is resident on all cards, with the remaining wells containing premeasured dried amounts of a specific antibiotic combined with culture medium. VITEK 2 AST-GN Amikacin has 2, 4, 16, and 48 µg/mL concentrations included in the test. The dried media in the card is rehydrated with the organism suspension during the vacuum filling process and is then sealed. The VITEK 2 System has two options for preparing the AST card inoculum including an auto-dilution or manual dilution method. The inoculated, sealed card is automatically loaded into the carousel of the instrument and incubated (35.5°C) for the duration of the test. In contrast, the VITEK 2 Compact instrument has a manual inoculation and sealing operation.

Growth of the test organism is optically monitored and measured four times per hour throughout the incubation cycle (up to 18 hours for GN cards). Interpretive calls are calculated by the instrument once a predefined growth threshold is obtained. When the test is complete, the VITEK 2 card is automatically ejected from the carousel into a waste container. A report is generated that contains the minimal inhibitory concentration (MIC) value with an interpretation category of susceptible, intermediate, or resistant for each antimicrobial on the card. The MIC result reporting range for Amikacin on the VITEK 2 AST-GN card is $\leq 1 - \geq 64$ µg/mL for *Enterobacteriaceae* and *Pseudomonas* species

and ≤ 2 – ≥ 64 µg/mL for *Acinetobacter* species.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITEK 2 AST-GN Cefepime

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

   K161227

3. Comparison with predicate:

Similarities		
Item	**Device: VITEK 2 AST-GN Amikacin (K172731)**	**Predicate Device: VITEK 2 AST-GN Cefepime (K161227)**
Intended Use	The VITEK 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK 2 Systems for the automated quantitative or qualitative susceptibility testing of isolated colonies for the most clinically significant aerobic gram-negative bacilli, *Staphylococcus* spp., *Enterococcus* spp., *Streptococcus* spp. and clinically significant yeast.	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	VITEK 2 and VITEK 2 Compact Systems	Same
Analysis Algorithm	Growth pattern analysis	Same
Detection Method	Light optics using optical scanner	Same
Report	Automatically generated and contains the MIC value with an interpretive category (S, I, R) for each antimicrobial on the test card	Same

Differences		
Item	**Device: VITEK 2 AST-GN Amikacin (K172731)**	**Predicate Device: VITEK 2 AST-GN Cefepime (K161227)**
Antimicrobial Agent	Amikacin	Cefepime
Antimicrobial Concentrations	2, 4, 16, 48 µg/mL	0.25, 1, 4, 16, 32 µg/mL
Reporting Range	*Enterobacteriaceae*, *Pseudomonas* species ≤ 1 - ≥ 64 µg/mL *Acinetobacter* species ≤ 2 - ≥ 64 µg/mL	*Enterobacteriaceae*, *P. aeruginosa* ≤0.12 - ≥32 µg/mL
Analysis Algorithm	Unique to Amikacin	Unique to Cefepime

K. Standard/Guidance Document Referenced (if applicable)

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

- CLSI M07, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard-Ninth Edition" Vol. 32 No. 2 (January 2012)

- CLSI M100-S24, "Performance Standards for Antimicrobial Susceptibility Testing"; Twenty-fourth Informational Supplement, Vol. 33 No. 1 (January 2014)

L. Test Principle:

The VITEK 2 and VITEK 2 Compact Systems utilize automated growth-based detection using attenuation of light measured by an optical scanner. The optics within the systems use visible light to directly measure organism growth within each of the 64 microwells. Transmittance optics are 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 measures 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   A reproducibility study for the VITEK 2 AST-GN card with Amikacin was conducted at three clinical sites using ten isolates of Gram-negative bacilli consistent with the

Intended Use. Testing was performed on three separate days and in triplicate for a total of 270 data points. The ten isolates tested in the reproducibility study included *Serratia marcescens* (one isolate), *Pseudomonas aeruginosa* (one isolate), *Escherichia coli* (two isolates), *Proteus mirabilis* (one isolate), *Enterobacter aerogenes* (one isolate), *Providencia stuartii* (one isolate), *Klebsiella pneumoniae pneumoniae* (one isolate), and *Enterobacter cloacae* complex (two isolates). Inocula were prepared using both the auto-dilution and manual dilution methods for testing in the VITEK 2 System. Inocula were prepared by the manual dilution method only for use with the VITEK 2 Compact. The mode MIC value was determined and the reproducibility was calculated based on MIC values that fell within +/- one doubling dilution from the mode MIC value. Both intra-site and inter-site reproducibility for Amikacin was calculated. There were no off-scale MIC results for any inoculum preparation method for both the VITEK 2 or VITEK 2 Compact. Reproducibility was calculated per the AST Special Controls Guidance.

An overall reproducibility of 100% was obtained for the VITEK 2 auto-dilution method, the VITEK 2 manual dilution method, and the VITEK 2 Compact manual dilution method.

When combined across all three sites, reproducibility results were acceptable.

b. Linearity/assay reportable range:

Not applicable

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

Inoculum Density Control
The DensiCHEK™ Plus was used to standardize the inoculum to a 0.5 MacFarland 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
Of 473 clinical isolates that were evaluated, two isolates did not grow in the VITEK 2 Amikacin test using the VITEK 2 System. Complete test results were available for 471 clinical isolates (344 *Enterobacteriaceae,* 49 Non-*Enterobacteriaceae,* and 78 *Pseudomonas* species). The growth failure rate was 0.4% and was acceptable.

All 95 challenge organisms grew in the VITEK 2 GN card with Amikacin using both the auto-dilution and manual dilution methods of the VITEK 2 and Compact Systems. Therefore, 566 isolates had VITEK 2 AST results available.

Quality Control (QC) Testing

Two FDA/CLSI recommended QC organisms were tested throughout the comparative testing at three study sites. The organisms tested were *Escherichia coli* ATCC 25922 and *Pseudomonas aeruginosa* ATCC 27853. These recommended QC organisms were tested a minimum of 20 times/site by both the VITEK 2 AST-GN card with Amikacin and with the CLSI broth microdilution reference method.

Both the auto-dilution and the manual dilution methods were within the expected range >95% of the time. In instances where any organism was out of range for the reference method, all testing data from that particular day was invalid and repeated. The following table (Table 1) provides a summary of QC results.

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

		VITEK 2 Auto-Dilution		VITEK 2 Manual Dilution		VITEK 2 Compact Manual Dilution	
Organism	**Conc. (µg/mL)**	**Test**	**Reference**	**Test**	**Reference**	**Test**	**Reference**
E. coli ATCC 25922 Expected Range 0.5 – 4 µg/mL	≤0.25						
	0.5						
	≤1*		54		28		28
	2	231	265	106	160	109	160
	4	114	26	99	17	96	17
	8						
	16						
	32						
	64						
	≥128						
P. aeruginosa ATCC 27853 Expected Range 1 – 4 µg/mL	≤0.25						
	0.5						
	≤1*		7		6		6
	2	201	305	125	183	114	182
	4	138	28	75	11	85	11
	8	1					
	16						
	32						
	64						
	≥128						

*The lowest dilution of the VITEK 2 Amikacin MIC range is ≤1 µg/mL.

The expected range for *E. coli* ATCC 25922 with Amikacin is 0.5 – 4 µg/mL. Even though the Amikacin concentrations included in the VITEK 2 AST-GN card are 2, 4, 16, and 48 µg/mL, the reporting range is ≤1 – ≥64 µg/mL for *Enterobacteriaceae* and *Pseudomonas* species. All results for *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were on scale (i.e., at 2 or 4 µg/mL) for the VITEK 2 (both automatic and manual dilutions) and VITEK 2 Compact Systems even though both VITEK systems

report the lowest end of the scale as ≤1 µg/mL. Overall, performance of the QC organisms was found to be acceptable.

d. Detection limit:

Not applicable

e. Analytical Specificity:

Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Results obtained with the bioMérieux VITEK 2 AST-Gram Negative card with Amikacin were compared to results obtained with the CLSI broth microdilution reference panel. The following concentrations of Amikacin are contained in the VITEK 2 AST-GN test card: 2, 4, 16, and 48 µg/mL (equivalent standard method concentration by efficacy in µg/mL) and the reporting range is ≤ 1 – ≥ 64 µg/mL (i.e., ≤ 1, 2, 4, 8, 16, 32, ≥ 64). Reference panels containing two-fold serial dilutions ranging from 0.25 to 256 µg/mL were inoculated as outlined in the CLSI document M07-A9.

All test inocula used for the evaluation of VITEK 2 AST-GN Amikacin and the reference method were standardized using the DensiCHEK™ Plus instrument. The cards were inoculated with each test organism by auto-dilution for reading by the VITEK 2 System and by manual dilution for reading on the VITEK 2 System and Compact instrument.

The VITEK 2 Amikacin susceptibility test was evaluated by six independent clinical sites located in different geographic regions of the United States. A total of 473 clinical isolates were tested on the VITEK 2 Amikacin test; however, only 471 isolates grew (344 *Enterobacteriaceae*, 49 non-*Enterobacteriaceae*, and 78 *Pseudomonas* species). Every clinical isolate was tested once by auto-dilution on the VITEK 2 System and the reference method using the same initial standardized suspension. The majority of clinical isolates were isolated from fresh clinical specimens (318 isolates; 67.2%) and 155 were stock isolates (32.8%).

A total of 95 challenge organisms (75 *Enterobacteriaceae,* 2 non-*Enterobacteriaceae* (*Acinetobacter* spp.), and 18 *Pseudomonas* spp.) were evaluated at one external site. The challenge set was tested with both the auto-dilution and manual dilution options

of the VITEK 2 System and with the manual dilution method on the VITEK 2 Compact System.

The study evaluated 471 clinical isolates and 95 challenge isolates for a combined data set of 566 isolates with AST results (419 *Enterobacteriaceae*, 25 *Acinetobacter* species, 26 other non-*Enterobacteriaceae*, 96 *Pseudomonas* species). The combined performance (clinical and challenge isolates) of the VITEK 2 Amikacin test as compared to the reference method is shown in Table 2 for 566 isolates.

Of the 566 total organisms evaluated in the comparative analysis, 79 clinical organisms were not indicated in the FDA drug label for Amikacin (~14%). When the non-indicated organisms were removed from the clinical performance evaluation, the EA and CA were slightly higher at 95.9% and 99.0%, respectively compared to 94.9% EA and 98.4% CA with the non-indicated organisms included. Because overall performance of the VITEK 2 AST-GN card with Amikacin was not affected, incorporation of the 79 non-indicated organisms was acceptable.

Table 2. Performance‡ of Clinical and Challenge Isolates, VITEK 2 Auto-Dilution Method

Organism Group	EA Total	EA N	EA %	Eval EA Total	Eval EA N	Eval EA %	CA N	CA %	#R	Min	Maj	Vmj
Enterobacteriaceae												
Clinical	344	326	94.8	243	225	92.6	344	100.0	0	0	0	0
Challenge	75	74	98.7	46	45	97.8	73	97.3	1	2	0	0
Combined	**419**	**400**	**95.5**	**289**	**270**	**93.4**	**417**	**99.5**	**1**	**2**	**0**	**0**
***Acinetobacter* species**												
Clinical	23	22	95.7	6	5	83.3	23	100.0	5	0	0	0
Challenge	2	2	100.0	0	0	-	2	100.0	0	0	0	0
Combined	**25**	**24**	**96.0**	**6**	**5**	**83.3**	**25**	**100.0**	**5**	**0**	**0**	**0**
Other Non-*Enterobacteriaceae* (excluding *Acinetobacter* species)												
Clinical	26	23	88.5	6	4	66.7	22	84.6	16	2	2	0
Challenge	-	-	-	-	-	-	-	-	-	-	-	-
Combined	**26**	**23**	**88.5**	**6**	**4**	**66.7**	**22**	**84.6**	**16**	**2**	**2**	**0**
***Pseudomonas* species**												
Clinical	78	72	92.3	70	64	91.4	76	97.4	0	2	0	0
Challenge	18	18	100.0	13	13	100.0	17	94.4	3	1	0	0
Combined	**96**	**90**	**93.8**	**83**	**77**	**92.8**	**93**	**96.9**	**3**	**3**	**0**	**0**
***Enterobacteriaceae, Acinetobacter* species, Other Non-*Enterobacteriaceae, Pseudomonas* species**												
Clinical	471	443	94.1	325	298	91.7	465	98.7	21	4	2	0
Challenge	95	94	98.9	59	58	98.3	92	96.8	4	3	0	0
Combined	**566**	**537**	**94.9**	**384**	**356**	**92.7**	**557**	**98.4**	**25**	**7**	**2**	**0**

‡**EA** – Essential Agreement (+/- 1doubling dilution)
CA – Category Agreement
EVAL – Evaluable isolates
R – Resistant isolates
Min – Minor discrepancies
Maj – Major discrepancies
Vmj – Very major discrepancies

Essential agreement (EA) was calculated when the VITEK 2 System results were within +/- one doubling dilution of the reference method results. Category agreement (CA) was calculated when the VITEK 2 System result interpretations agreed exactly with the reference method result interpretations. Evaluable results were defined as when both the reference method results and the VITEK 2 System results were on-scale. Evaluable results were also defined as when the reference method results were on-scale and off-scale VITEK 2 System results clearly did not agree within the accepted +/- one doubling dilution.

***Enterobacteriaceae*:** The overall performance of *Enterobacteriaceae* was acceptable with 95.5% EA and 99.5% CA. There were no major or very major errors.

Non-*Enterobacteriaceae*: The overall performance of non-*Enterobacteriaceae* organisms (*Acinetobacter* species and few non-indicated organisms) was acceptable with 92.2% EA and 92.2% CA. There were two major errors and no very major errors.

***Pseudomonas* species:** The overall performance of *Pseudomonas* species was acceptable with 93.8% EA and 96.9% CA. There were no major or very major errors.

Overall Performance: The overall performance using the auto-dilution method of the VITEK 2 System demonstrated an EA of 94.9% and an overall CA of 98.4%. There were no very major errors, two major errors (0.4% error rate, 2/535 susceptible organisms), and 7 minor errors (1.2% error rate, 7/566 total organisms). Performance for Amikacin on the VITEK 2 card met the acceptance criteria for major error (≤3%).

The performance based on combined clinical and challenge data was acceptable.

Challenge Data – Auto and Manual Dilution
The challenge set of 95 isolates (75 *Enterobacteriaceae,* 2 non-*Enterobacteriaceae*; *Acinetobacter* species, and 18 *Pseudomonas aeruginosa*) was evaluated on the VITEK 2 System using both auto and manual dilution methods and on the VITEK 2 Compact System with the manual dilution method only. All challenge data was generated at one testing site. Overall performance of the challenge data is shown in Table 3.

Table 3. Performance of Challenge Isolates, VITEK 2 and VITEK 2 Compact-Manual Dilution

Organism Group	EA Total	EA N	EA %	Eval EA Total	Eval EA N	Eval EA %	CA N	CA %	#R	Min	Maj	Vmj
VITEK 2 System												
Auto-dilution	95	94	98.9	59	58	98.3	92	96.8	4	3	0	0
Manual dilution	95	94	98.9	62	61	98.4	93	97.9	4	2	0	0
VITEK 2 Compact												
Manual dilution	95	93	97.9	62	60	96.8	92	96.8	4	3	0	0

The performance of the challenge isolates using the VITEK 2 Amikacin test on both the VITEK 2 and VITEK 2 Compact Systems was acceptable.

Resistant Organisms
A total of 25 resistant isolates were identified in the combined clinical (n=21) and challenge (n=4) study of Amikacin for the VITEK 2 auto-dilution method out of 566 organisms (4.4%). However, the following indicated organisms had no resistant isolates and/or an insufficient number of resistant isolates available during

comparative testing: *Pseudomonas* species, *Escherichia coli*, *Proteus mirabilis, Klebsiella* species, *Enterobacter* species, *Serratia* species, and *Citrobacter freundii*. This was addressed with the following limitation in the package insert:

> "*The ability of the AST card to detect resistance with the following combination(s) is unknown because resistant strains were either not available or an insufficient number were encountered at the time of comparative testing:*
>
> *Amikacin: Pseudomonas species, Escherichia coli, Proteus mirabilis, Klebsiella species, Enterobacter species, Serratia species, Citrobacter freundii*"

MIC Trends

Using the combined clinical and challenge data for indicated *Enterobacteriaceae* organisms, an analysis of trending was conducted. This trending calculation takes into account MIC values that are determined to be ≤ 1 or ≥ 1 doubling dilution compared to the reference method irrespective whether the device MIC values are on-scale or not. Results of trending analyses for evaluable isolates are shown in Table 4.1 and Table 4.2 for *Enterobacteriaceae* and *P. aeruginosa*, respectively.

Table 4.1. Trending Analysis of Evaluable *Enterobacteriaceae* Clinical and Challenge Isolate Results, VITEK 2 Auto-Dilution Method

Amikacin ≤1 - ≥ 64µg/mL	# Eval Isolates[a]	Difference in MIC as Compared to the CLSI Reference Method				
		≥ 2 dilution lower	≥ 1 dilution lower	Exact	≥ 1 dilution higher	≥ 2 dilution higher
C. freundii	41	1	5	12 (29.27%)	20	3
		6 (14.63%)[b] 95% CI (6.88% to 28.44%)			23 (56.10%)[b] 95% CI (41.04% to 70.11%)	
E. cloacae complex	14	0	1	2 (14.29%)	10	1
		1 (7.14%)[c] 95% CI (1.27% to 31.47%)			11 (78.57%)[c] 95% CI (52.41% to 92.43%)	
E. coli	103	3	14	47 (45.63%)	39	0
		17 (16.50%)[d] 95% CI (10.57% to 24.85%)			39 (37.86%)[d] 95% CI (29.09% to 47.51%)	
K. pneumoniae pneumoniae	14	0	1	1 (7.14%)	12	0
		1 (7.14%)[e] 95% CI (1.27% to 31.47%)			12 (85.71%)[e] 95% CI (60.06% to 95.99%)	
S. marcescens	13	0	1	3 (23.08%)	9	0
		1 (7.69%)[f] 95% CI (1.37% to 33.31%)			9 (69.23%)[f] 95% CI (42.37% to 87.32%)	

[a] Total number of evaluable results for trending analysis
[b] Difference: 41.46%: 95% CI (21.03% to 57.48%)
[c] Difference: 71.43%: 95% CI (35.70% to 86.48%)
[d] Difference: 21.36%: 95% CI (9.25% to 32.68%)
[e] Difference: 78.57%: 95% CI (43.22% to 90.41%)
[f] Difference: 61.54%: 95% CI (24.42% to 80.70%)

Table 4.2. Trending Analysis of Evaluable *P. aeruginosa* Clinical and Challenge Isolate Results, VITEK 2 Auto-Dilution Method

Amikacin ≤1 - ≥ 64µg/mL	# Eval Isolates[a]	Difference in MIC as Compared to the CLSI Reference Method				
		≥ 2 dilution lower	≥ 1 dilution lower	Exact	≥ 1 dilution higher	≥ 2 dilution higher
P. aeruginosa	85	1	2	27 (31.76%)	50	5
		3 (3.53%)[b] 95% CI (1.21% to 9.87%)			55 (64.71%)[b] 95% CI (54.11% to 74.03%)	

[a] Total number of evaluable results for trending analysis
[b] Difference: 61.18%: 95% CI (48.83% to 70.78%)

A higher MIC reading trend was observed in the overall performance of *C. freundii, E. cloacae* complex*, E. coli, K. pneumoniae pneumoniae, S. marcescens,* and *P. aeruginosa* compared to CLSI broth microdilution, which raises concerns for potential major errors.

To address the high trending and the potential occurrence of major error(s) for Amikacin when testing select clinical and challenge *Enterobacteriaceae* and *Pseudomonas aeruginosa* with the VITEK 2 System, the following statement was added as a footnote in the labeling (Product Information Manual):

> "*VITEK 2 Amikacin MIC values for evaluable C. freundii, E. cloacae* complex*, E. coli, K. pneumoniae pneumoniae, P. aeruginosa, and S. marcescens tended to be in exact agreement or at least one doubling dilution higher compared to the CLSI reference broth microdilution.*"

The analysis of *Acinetobacter* species MIC data demonstrated no notable trending.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

   Not applicable

5. Expected values/Reference range:

Table 5. Interpretive Criteria for Amikacin (FDA Drug Label)

Organism	FDA Interpretive Criteria for Amikacin MIC (µg/mL)		
	S	I	R
Enterobacteriaceae	≤16	32	≥64
Pseudomonas species	≤16	32	≥64
Acinetobacter species	≤16	32	≥64

N. Proposed Labeling:

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

O. Conclusion:

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