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

A. 510(k) Number:

K163083

B. Purpose for Submission:

To obtain a substantial equivalence determination for Tobramycin 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 Tobramycin: 8, 16, and 64 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The Tobramycin MIC reporting range for the card is ≤ 1 – ≥ 16 µg/mL.

D. Type of Test:

Automated quantitative or qualitative antimicrobial susceptibility test for Tobramycin

E. Applicant:

bioMérieux, Inc.

F. Proprietary and Established Names:

VITEK® 2 AST-Gram Negative Tobramycin (≤ 1 – ≥ 16 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 Tobramycin 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 Tobramycin is a quantitative[1] test. Tobramycin 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 species
Enterobacter species
Escherichia coli
Klebsiella species
Morganella morganii
Pseudomonas aeruginosa
Proteus mirabilis
Proteus vulgaris
Providencia species
Serratia species

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

[1] FDA review of K163083 was based on a quantitative assessment claim as demonstrated in Table 2 (page 10/13) of this document. Due to an administrative error, the reference to "qualitative" was erroneously included in the original Decision Summary and has now been removed to correctly state "quantitative".

yeast.

3. Special conditions for use statement(s):

   For Prescription Use Only

   Limitations:

   "Perform an alternative method of testing prior to reporting of results for the following antibiotic/organisms combination(s):
   Tobramycin: Providencia stuartii"

   "The ability of the VITEK® 2 AST card to detect resistance with the following combination(s) is unknown because resistant strains were not available at the time of comparative testing:
   Tobramycin: Citrobacter koseri, Morganella morganii, and Proteus vulgaris"

   "The ability of the VITEK® 2 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:
   Tobramycin: Enterobacter aerogenes, Enterobacter cloacae, and Proteus mirabilis"

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 Tobramycin has 8, 16, and 64 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 Tobramycin on the VITEK® 2 AST-GN card is ≤ 1 – ≥ 16 µg/mL.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITEK® 2 AST-GN Piperacillin-Tazobactam

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

   K113200

3. Comparison with predicate:

Similarities		
Item	**Device: VITEK® 2 AST-GN Tobramycin (K163083)**	**Predicate Device: VITEK® 2 AST-GN Piperacillin-Tazobactam (K113200)**
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	Same

Similarities		
Item	**Device: VITEK® 2 AST-GN Tobramycin (K163083)**	**Predicate Device: VITEK® 2 AST-GN Piperacillin-Tazobactam (K113200)**
	the MIC value with an interpretive category (S, I, R) for each antimicrobial on the test card	
Differences		
Item	**Device: VITEK® 2 AST-GN Tobramycin (K163083)**	**Predicate Device: VITEK® 2 AST-GN Piperacillin-Tazobactam (K113200)**
Antimicrobial Agent	Tobramycin	Piperacillin-tazobactam
Antimicrobial Concentrations	8, 16, 64 µg/mL	2/4, 8/4, 24/4, 32/4, 32/8, 48/8 µg/mL
Reporting Range	≤ 1 - ≥ 16 µg/mL	≤ 4 - ≥ 128 µg/mL
Analysis Algorithm	Unique to Tobramycin	Unique to Piperacillin-tazobactam

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-A9, "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. <u>Analytical performance:</u>

   a. Precision/Reproducibility:

A reproducibility study for the VITEK® 2 AST-GN card with Tobramycin 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 isolates tested in the reproducibility study included *Serratia marcescens* (three isolates), *Escherichia coli* (two isolates), *Klebsiella pneumoniae pneumoniae* (three isolates), and *Citrobacter braakii* (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 Tobramycin was calculated. There were some off-scale MIC results; accordingly, reproducibility was calculated for best- and worst-case scenarios per the AST Special Controls Guidance.

For the VITEK® 2 auto-dilution method, overall reproducibility was 100% and 97.78% for best- and worst-case scenarios, respectively. There were a total of 6 off-scale MIC results.

For the VITEK® 2 manual dilution method, overall reproducibility was 100% and 95.2% for best- and worst-case scenarios, respectively.

For the VITEK® 2 Compact manual dilution method, overall reproducibility was 100% and 95.9% for best- and worst-case scenarios, respectively. There were a total of 11 off-scale MIC results.

The combined reproducibility results for all three sites 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 the 961 clinical isolates that were evaluated (810 *Enterobacteriaceae* and 147 *P.*

aeruginosa), three isolates did not grow in the VITEK® 2 Tobramycin test using the VITEK® 2 System. Complete test results were available for 957 isolates out of 961 clinical isolates. The growth failure rate was 0.3% and was acceptable.

All 76 challenge organisms grew in the VITEK® 2 GN card with Tobramycin using both the auto-dilution and manual dilution methods of the VITEK® 2 and Compact Systems. Therefore, 1033 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 Tobramycin 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 0.25 - 1µg/mL	≤0.0625						
	0.125						
	0.25						
	0.5		166		83		83
	≤1*	225	59	112	29	112	29
	2						
	4						
	8						
	16						
	32						
	≥64						
P. aeruginosa ATCC 27853 Expected Range 0.25 - 1µg/mL	≤0.0625						
	0.125						
	0.25		141		67		67
	0.5		71		33		33
	≤1*	216	8	103	7	103	7
	2						
	4						
	8	4		4		4	
	16						
	32						

	≥64						

*The lowest dilution of the VITEK® 2 Tobramycin MIC range is ≤1 µg/mL. Obtaining this value was considered as an indicator that the quality control test results were acceptable.

The expected range for *E. coli* ATCC 25922 with Tobramycin is 0.25 – 1µg/mL. Even though the Tobramycin concentrations included in the VITEK® 2 AST-GN card are 8, 16, and 64 µg/mL, the reporting range is ≤1 – ≥16 µg/mL. Therefore, all results for *E. coli* ATCC 25922 were off scale for the VITEK® 2 and VITEK® 2 Compact Systems as both VITEK® systems report the lowest end of the scale as ≤1 µg/mL. *P. aeruginosa* ATCC 27853 was also tested to verify the performance of the device. Many results for this QC strain were also off scale (≤1 µg/mL). Overall, performance of the QC organisms was found to be acceptable.

There was no specific recommendation for any additional QC strains to be tested, but the sponsor's internal QC process assures that the devices are produced and manufactured appropriately. To inform the end-user of this point, the sponsor included the following footnote to the QC table in the device labeling:

> *"The VITEK® 2 Gram Negative Tobramycin does not include the full CLSI/FDA-recommended dilution ranges for QC testing with E. coli ATCC 25922 and P. aeruginosa ATCC 27853".*

In addition, two Gram-positive organisms and one Gram-negative organism were tested as supplemental quality control organisms throughout comparative testing at each study site by the reference method only. This was done to provide further assurance of the performance of the broth microdilution panels. The organisms tested were:

- *Enterococcus faecalis* ATCC 29212
- *Staphylococcus aureus* ATCC 29213
- *Klebsiella pneumoniae* subspecies *pneumoniae* ATCC 700603

Performance of these additional QC organisms was evaluated and deemed 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 Tobramycin were compared to results obtained with the CLSI broth microdilution reference panel. The following concentrations of Tobramycin are contained in the VITEK® 2 AST-GN test card: 8, 16, and 64 µg/mL (equivalent standard method concentration by efficacy in µg/mL) and the reporting range is ≤ 1 – ≥ 16 µg/mL (i.e., ≤ 1, 2, 4, 8, ≥ 16). The reference panel contained two-fold serial dilutions with a range of ≤ 0.0625 to ≥ 128 µg/mL. The testing conditions for the reference method consisted of the following:

- Medium – Mueller Hinton broth with appropriate dilutions of antimicrobial solution added
- Inoculum – Direct colony suspension
- Incubation – 35°C ambient air incubator; 16-20 hours for all organisms

All test inocula used for the evaluation of VITEK® 2 AST-GN Tobramycin 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. Reference broth microdilution panels were inoculated in adherence with CLSI document, M07-A9.

The VITEK® 2 Tobramycin susceptibility test was evaluated by three independent clinical sites located in different geographic regions of the United States. Every clinical isolate was tested one time by auto-dilution on the VITEK® 2 System and the reference method using the same initial standardized suspension. The study evaluated 961 clinical isolates and 76 challenge isolates for a combined data set of 1037 isolates. Of the 1037 clinical and challenge isolates that were tested by the VITEK® 2 card with Tobramycin, 1033 isolates yielded AST results. However, 33 of these isolates were removed from analysis due to inherent forcing rules applied by the VITEK® 2 software for non-indicated *Salmonella* and *Shigella* species. Thus, the combined performance of the VITEK® 2 Tobramycin test as compared to the reference method is shown in Table 2 for 1000 isolates (924 *Enterobacteriaceae* and 76 *P. aeruginosa*).

The majority of clinical isolates were isolated from fresh clinical specimens (825 isolates, 85.8%) and 136 were stock isolates (14.2%).

A total of 76 challenge organisms (51 *Enterobacteriaceae* and 26 *P. aeruginosa*) 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. Overall performance of the challenge organisms is shown in Table 2.

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	777	762	98.1	71	56	78.9	748	96.3	35	28	1	0
Challenge	51	51	100.0	4	4	100.0	50	98.0	20	1	0	0
Combined	828	813	98.2	75	60	80.0	798	96.4	55	29	1	0
Pseudomonas aeruginosa												
Clinical	147	146	99.3	1	0	0.0	146	99.3	6	1	0	0
Challenge	25	25	100.0	1	1	100.0	24	96.0	5	1	0	0
Combined	172	171	99.4	2	1	50.0	170	98.8	11	2	0	0
Enterobacteriaceae, Pseudomonas aeruginosa												
Clinical	924	908	98.3	72	56	77.8	894	96.9	41	29	1	0
Challenge	76	76	100.0	5	5	100.0	74	97.4	25	2	0	0
Combined	1000	984	98.4	77	61	79.2	968	96.8	66	31	1	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 was calculated when the VITEK® 2 System results were within +/- one doubling dilution of the reference method results. Category agreement 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.

The overall performance using the auto-dilution method of the VITEK® 2 System demonstrated an essential agreement of 98.4% and an overall category agreement of 96.8%. There were no very major errors, 1 major error (0.1% error rate, 1/864 susceptible organisms), and 31 minor errors (3.1% error rate).

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

Evaluable *P. aeruginosa* Isolates:
*P. aeruginos*a provided evaluable results for a total of two isolates. Of these two isolates, only one was within essential agreement (EA) for a percent EA of evaluable isolates of 50%. Because of the limited data submitted with evaluable MIC data, the performance of this device with isolates that have MICs near the breakpoints could not be determined and the following footnote was added in the labeling (Product Information Manual):

"*Due to an insufficient number of on-scale isolates available for comparative testing, the performance of VITEK® 2 Gram Negative Tobramycin is unknown for P. aeruginosa isolates with MICs in the range of 4-16 µg/mL. If critical to patient care, isolates with MICs of 4-16 µg/mL should be retested using another method".*

Resistant Organisms:
A total of 66 resistant isolates were identified in the combined clinical and challenge study of Tobramycin for the VITEK® 2 auto-dilution method out of 1000 organisms (6.6%). However, the following organisms had no resistant isolates available during comparative testing: *Citrobacter koseri*, *Morganella morganii*, and *Proteus vulgaris*. This was addressed by adding the following limitation in the package insert:

> "*The ability of the VITEK® 2 AST card to detect resistance with the following combination(s) is unknown because resistant strains were not available at the time of comparative testing:*
>
> *Tobramycin: Citrobacter koseri, Morganella morganii, and Proteus vulgaris"*

In addition, there was an insufficient number of resistant isolates tested during the comparative study for the following organisms: *Enterobacter aerogenes*, *Enterobacter cloacae*, and *Proteus mirabilis*. This was addressed by adding the following limitation in the package insert:

> "*The ability of the VITEK® 2 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:*
>
> *Tobramycin: Enterobacter aerogenes, Enterobacter cloacae, and Proteus mirabilis"*

Challenge Data – Auto and Manual Dilution:
The challenge set of 76 isolates (51 *Enterobacteriaceae* and 25 *Pseudomonas aeruginosa*) was evaluated on the VITEK® 2 System and the VITEK® 2 Compact System with the manual dilution method only.

Overall performance 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	76	76	100.0	5	5	100.0	76	97.4	25	2	0	0
Manual dilution	76	75	98.7	7	6	85.7	76	97.4	25	2	0	0
VITEK® 2 Compact												
Manual dilution	76	76	100.0	6	6	100.0	76	97.4	25	2	0	0

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

MIC Trends:

Using the combined clinical and challenge data for *Enterobacteriaceae,* 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. The data for 122 results constitute the evaluable data for trend analysis which is presented in Table 4.

Table 4. Trending Analysis of Evaluable *Enterobacteriaceae* Clinical and Challenge Isolate Results, VITEK® 2 Auto-Dilution Method

Enterobacteriaceae	# Eval Isolates	≥ 1 dilution lower	Exact	≥ 1 dilution higher
Combined Clinical and Challenge	122	71	28	23
		58.2%*	**23.0%**	**18.9%***
		95% CI: 49.3% to 66.6%	95% CI: 16.4% to 31.2%	95% CI: 12.9% to 26.7%

*Difference: 39.3%
95% CI: 27.5% to 49.6%

Using the combined clinical and challenge data for *P. aeruginosa,* 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. The data for 13 results constitute the evaluable data for trend analysis which is presented in Table 5.

Table 5. Trending Analysis of Evaluable *P. aeruginosa* Clinical and Challenge Isolate Results, VITEK® 2 Auto-Dilution Method

P. aeruginosa	# Eval Isolates	≥ 1 dilution lower	Exact	≥ 1 dilution higher
Combined Clinical and Challenge	13	11	0	2
		84.6%*	**0%**	**15.4%***
		95% CI: 57.8% to 95.7%		95% CI: 4.3% to 42.2%

*Difference: 69.2%
95% CI: 31.3% to 84.9%

A lower MIC reading trend was observed in the overall performance of *Enterobacteriaceae* and *Pseudomonas aeruginosa* compared to CLSI broth microdilution, which raises concerns for potential very major errors.

To address the low trending and the potential occurrence of very major error(s) for Tobramycin when testing clinical and challenge *Enterobacteriaceae* and *P. aeruginosa* isolates with the VITEK® 2 System, the following statement was added as a footnote in the labeling (Product Information Manual):

> "*VITEK® 2 Tobramycin MIC values for evaluable Enterobacteriaceae and P. aeruginosa isolates tended to be one or more doubling dilutions lower compared to reference broth micro-dilution*".

b. Matrix comparison:

Not applicable

3. Clinical studies:

   Not applicable

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

Table 6. Interpretive Criteria for Tobramycin (FDA Drug Label)

Organism	FDA Interpretive Criteria for Tobramycin MIC (µg/mL)		
	S	I	R
Enterobacteriaceae	≤4	8	≥16
Pseudomonas aeruginosa	≤4	8	≥16

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.