510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K223481

B Applicant

bioMérieux, Inc

C Proprietary and Established Names

VITEK 2 Streptococcus Tetracycline (≤0.25 - ≥16 µg/mL)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LON	Class II	21 CFR 866.1645 - Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To update the VITEK 2 AST-Streptococcus Tetracycline device labeling to include updated FDA-recognized breakpoints for *Streptococcus pneumoniae*, *Streptococcus pyogenes* (Group A Beta-Hemolytic streptococci) and *Streptococcus* spp. β-Hemolytic Group as published in the FDA STIC website.

B Measurand:

Tetracycline ≤0.25 – ≥16 µg/mL

C Type of Test:

Automated quantitative or qualitative antimicrobial susceptibility test for tetracycline

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

VITEK 2 Streptococcus Tetracycline is designed for antimicrobial susceptibility testing of *Streptococcus* species 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 Streptococcus Tetracycline is a quantitative test. Tetracycline has been shown to be active against the microorganisms listed below, according to the FDA label for this antimicrobial.

Active *in vitro* and in clinical infections:
Streptococcus pneumoniae
*Streptococcus pyogenes**

*The VITEK 2 *Streptococcus* Susceptibility Card also reports the susceptibility of the following additional organisms aslisted on the FDA Susceptibility Test Interpretative Criteria website (STIC): *Streptococcus* spp. ß-Hemolytic Group (other than *S. pyogenes*).

The VITEK 2 *Streptococcus* Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Streptococcus pneumoniae*, beta-hemolytic *Streptococcus*, and Viridans *Streptococcus* to antimicrobial agents when used as instructed.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Limitation:
Perform an alternative method of testing prior to reporting of results for the following antibiotic/organism combination(s):
Tetracycline (te01n): *Streptococcus dysgalactiae equisimilis* when the VITEK 2 MIC is 2 µg/mL

D Special Instrument Requirements:

VITEK 2 and VITEK 2 Compact Systems

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 Streptococcus Tetracycline has the following concentrations in the card: 0.125, 0.5, 1 and 4 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK 2 Streptococcus Tetracycline is ≤0.25 - ≥16 µg/mL.

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 Streptococcus Tetracycline

B Predicate 510(k) Number(s):
K111893

C Comparison with Predicate(s):

Device & Predicate Device(s):	**Device:** K223481	**Predicate:** K111893
Device Trade Name	VITEK 2 Streptococcus Tetracycline (≤0.25 - ≥16 µg/mL)	VITEK 2 Streptococcus Tetracycline
General Device Characteristic Similarities		
Intended Use	VITEK 2 Streptococcus Tetracycline is designed for antimicrobial susceptibility testing of *Streptococcus* species	VITEK 2 Streptococcus Tetracycline is designed for antimicrobial susceptibility testing of *Streptococcus* species.

	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 Streptococcus Tetracycline is a quantitative test. Tetracycline has been shown to be active against the microorganisms listed below, according to the FDA label for this antimicrobial. <u>Active *in vitro* and in clinical infections:</u> *Streptococcus pneumoniae* *Streptococcus pyogenes** *The VITEK® 2 *Streptococcus* Susceptibility Card also reports the susceptibility of the following additional organisms aslisted on the FDA Susceptibility Test Interpretative Criteria website (STIC): *Streptococcus* spp. ß-Hemolytic Group (other than *S. pyogenes*). The VITEK 2 *Streptococcus* Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of *Streptococcus pneumoniae*, beta-hemolytic *Streptococcus*, and Viridans *Streptococcus* to antimicrobial agents when used as instructed.	VITEK 2 Streptococcus Tetracycline is a quantitative test intended for use with the VITEK 2 and the VITEK 2 Compact Systems as a laboratory aid in the determination of *in vitro* susceptibility to antimicrobial agents. Tetracycline has an antimicrobial activity against the microorganisms listed below, according to the FDA label for this antimicrobial. <u>Active *in vitro* and in clinical infections:</u> *Streptococcus pneumoniae* *Streptococcus pyogenes* Viridans group streptococci The VITEK 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK 2 System 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
Test Methodology	Automated quantitative antimicrobial susceptibility test for use with the VITEK 2 and VITEK 2 Compact Systems to determine the *in vitro* susceptibility of microorganisms	Same
Inoculum	Saline suspension of organism	Same
Test Card	Streptococcus (AST-ST) Susceptibility Card	Same
Analysis Algorithms	Discriminant Analysis	Same
Instrument	VITEK 2 and VITEK 2 Compact Systems	Same

Antimicrobial Agent	Tetracycline	Same
General Device Characteristic Differences		
Indicated Organisms	Tetracycline has been shown to active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial. Active *in vitro* and in clinical infections: *Streptococcus pneumoniae* *Streptococcus pyogenes** *The VITEK 2 *Streptococcus* Susceptibility Card also reports the susceptibility of the following additional organisms a slisted on the FDA Susceptibility Test Interpretative Criteria website (STIC): *Streptococcus* spp. β-Hemolytic Group (other than *S. pyogenes*)	Tetracycline has been shown to active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial. Active *in vitro* and in clinical infections: *Streptococcus pneumoniae* *Streptococcus pyogenes* Viridans group streptococci
Breakpoints	*Streptococcus pneumoniae* S≤1, I 2, R≥4 *Streptococcus* spp. β-Hemolytic Group (including *S. pyogenes*) S≤1, I 4, R≥8	*Streptococcus* spp. S≤4, I 8, R≥16

VI Standards/Guidance Documents Referenced:

1. MacLowry, J.D. and Marsh, H.H., Semi-automatic Microtechnique for Serial Dilution Antibiotic Sensitivity Testing in the Clinical laboratory, Journal of Laboratory Clinical Medicine, 72:685-687, 1968.

2. Gerlach, E.H., Microdilution 1: A Comparative Study, p. 63-76. Current Techniques for Antibiotic Susceptibility Testing. A. Balows (ed.), Charles C. Thomas, Springfield, IL, 1974.

3. Barry, A.L., The Antimicrobic Susceptibility Test, Principles and Practices, Lea and Febiger, Philadelphia, PA, 1976.

4. CLSI M7-A5, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard - Fifth Edition", (January 2000)

5. CLSI M07, “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard – 11th Edition”, (January 2018)

6. CLSI M100, "Performance Standards for Antimicrobial Susceptibility Testing; Thirty Second Edition", Vol. 32, No. 1 (February 2022)

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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Refer to K111893. Reproducibility testing for the VITEK 2 Streptococcus Tetracycline was performed in support of clearance of K111893 and was determined acceptable.

2. Linearity:

   No 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, Inoculum and Growth failure for the VITEK 2 Streptococcus Tetracycline was performed in support of clearance of K111893 and was determined acceptable. QC testing specific to the changes in breakpoints was not performed in the current submission.

The QC organism recommended by both the FDA and CLSI, namely *Streptococcus pneumoniae* ATCC 49619, was tested against tetracycline during the clinical study a minimum 20 times/site by the automatic and the manual dilution. The QC organism was tested by the VITEK 2 AST card and the reference broth microdilution method. The QC results for both the reference and test panels appeared to be acceptable.

At the time of the original submission (K111893), the QC range for *S. pneumoniae* ATCC 49619 was 0.12 - 0.5µg/mL. The recommended CLSI QC range for this strain changed to include lower concentrations with a range of 0.06 - 0.5 µg/mL. However, the VITEK 2 MIC reporting range is ≤0.25 – ≥16 µg/mL. The VITEK 2 systems do not provide results lower than 0.25 µg/mL. Therefore, QC results for *S. pneumoniae* ATCC 49619 may be off scale. An MIC value of ≤0.25 µg/mL indicated that the quality control test results were acceptable (**Table 1**).

Table 1. Quality Control Results for VITEK 2 (Auto-Dilution and Manual 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
S. pneumoniae ATCC 49619		≤0.016						
		0.03						
		0.06		1		1		0
Expected Result: 0.06 - 0.5 µg/mL		0.12		165		167		19
	≤0.25	0.25	222	56	223	55	68	49
	0.5	0.5	0	0	0	0	0	0
	1	1						
	2	2						
	4	4						
	8	8						
	≥16	16						
		≥32						

[1]VITEK 2 Card range is ≤0.25 - ≥16. The lowest dilution of the VITEK 2 Streptococcus Tetracycline MIC range is ≤0.25 µg/mL. Obtaining this value was considered an indicator that the quality control test results were acceptable.

bioMérieux included the following footnote under the Quality Control table in the device labeling:

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

The QC data is acceptable for the purpose of the re-evaluation of the performance of *Streptococcus spp.* when the new breakpoints are applied.

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The VITEK 2 Streptococcus Tetracycline (≤0.25 - ≥16 µg/mL) which was originally cleared in K11893, included indications for *Streptococcus pneumoniae*, *Streptococcus pyogenes* (Group A Beta-Hemolytic streptococci) and *Streptococcus* spp. (Viridans Group) tested with the VITEK 2 auto dilution and the VITEK 2 manual dilution and compared to the CLSI broth microdilution reference method.

The performance of the VITEK 2 AST-ST Tetracycline card with *Streptococcoccus pnuemoniae, Streptococcus pyogenes* (Group A Beta-hemolytic streptococci) *and Streptococcus* spp. (Beta-Hemolytic Group) using revised interpretive criteria currently recognized by FDA was evaluated in the current submission using data obtained in support of K111893. *Streptococcus* spp. (Viridans Group) is no longer recognized by FDA STIC webpage and these data were removed from analysis.

Since there was no change in the design or the dilution range of the VITEK 2 AST-ST card, the performance evaluation was achieved via re-analysis of the MIC data of the original 510(k) submission (K111893). An additional 63 beta-hemolytic *Streptococcus* spp. (not including *S. pyogenes*) challenge organisms were tested and performance was assessed in this submission to determine performance for this indication. For this review, the current Tetracycline interpretive criteria are applied to *Streptococcus pneumoniae* and *Streptococcus* spp. β-Hemolytic Group according to the FDA STIC webpage.

A total of 1127 (clinical and challenge) *Streptococcus* spp. isolates were tested using the VITEK 2 with automatic dilution. The isolates included 964 clinical isolates and 163 challenge isolates.

Results of the re-analyzed 1127 *Streptococcus* spp. clinical and challenge isolates (including 289 *Streptococcus pneumoniae*, 308 *Streptococcus pyogenes* (Group A Beta-Hemolytic streptococci) and 530 *Streptococcus* spp. Beta-Hemolytic Group (other than *S. pyogenes*) are summarized in **Table 2.**

The previously-collected data for the 163 challenge isolates tested at a single site with the VITEK 2 and the VITEK 2 Compact Systems using the manual dilution was also analyzed using the current breakpoints for *Streptococcus pneumoniae*, *S. pyogenes* and *Streptococcus* spp. Beta-Hemolytic Group (other than *S. pyogenes*). The results of the analysis are outlined in **Table 3.**

Table 2. Re-analysis of the Performance of *Streptococcus* spp. for the Auto Dilution and the VITEK 2 AST-ST Tetracycline

	Total	#EA	%EA	Eval EA Total	Eval EA #	Eval EA %	#CA	%CA	#R	#S	min	maj	vmj
***S. pneumoniae* ≤1 (S), 2 (I), ≥4 (R)**													
Clinical	239	234	97.9	6	1	16.7	238	99.6	66	173	1	0	0
Challenge	50	50	100.0	0	0	0.0	50	100.0	17	33	0	0	0
Combined	289	284	**98.3**	6	1	16.7	288	**99.7**	83	206	1	0	0
***S. pyogenes* (Group A Beta-Hemolytic *Streptococcus* spp.) ≤2 (S), 4 (I), ≥8 (R)**													
Clinical	258	257	99.6	3	2	66.7	258	100.0	22	236	0	0	0
Challenge	50	50	100.0	1	1	100.0	50	100.0	6	44	0	0	0
Combined	308	307	**99.7**	4	3	75.0	308	**100.0**	28	280	0	0	0
***Streptococcus* spp. (Beta-Hemolytic Group other than *S. pyogenes*)[a,b] ≤2 (S), 4 (I), ≥8 (R)**													
Clinical	467	455	97.4	44	32	72.7	446	95.5	295	156	18	1	2
Challenge[c]	63	63	100	3	3	100	63	100	53	10	0	0	0
Combined	530	518	**97.7**	47	35	74.5	509	**96.0**	348	166	18	1	2

[a] Including the following tested species: *S. agalactiae* (338), *S.canis* (4), *S. dys dysgalactiae* (1), *S.dys.equisimilis* (185) *and S.equi zooepidemicus* (2).
[b] The interpretive criteria are applied to *Streptococcus* spp. Beta-Hemolytic Group according to the FDA STIC webpage.

[c] Additional testing was conducted to assess performance for Beta-Hemolytic *Streptococcus* spp. (not including *S. pyogenes*) against a challenge set of organisms.

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

When applying the new breakpoints of ≤1 (S), 2 (I), ≥4 (R) for *Streptococcus pneumoniae*, the performance of the combined isolates tested with the VITEK 2 and automatic dilution is acceptable with 98.3% EA and 99.7% CA. There were no very major errors and no major errors. One (1) minor error out of 289 isolates (0.3%) tested was observed (**Table 2**).

When applying the new breakpoints of ≤2 (S), 4 (I), ≥8 (R) for *Streptococcus pyogenes*, the performance of the combined isolates tested with the VITEK 2 and automatic dilution is acceptable with 99.7% EA and 100.0% CA. There were no very major errors, no major errors and no minor errors observed (**Table 2**).

When applying the new breakpoints of ≤2 (S), 4 (I), ≥8 (R) for *Streptococcus* spp. (Beta-Hemolytic Group other than *S. pyogenes*), the performance of the combined isolates tested with the VITEK 2 and automatic dilution is acceptable with 97.7% EA and 96.0% CA. There were two very major errors out of 348 isolates (0.6%) and one major error out of 166 isolates (0.6%). Eighteen (18) minor errors out of 530 isolates (3.4%) tested were observed (**Table 2**). The two very major errors (3.4% of 58 isolates), one major error (0.9% of 113 isolates) and 16 of the minor errors (8.6% of 185 isolates) were due to *S. dysgalactiae* subsp. *equisimilis*; therefore, the following limitation was added to the package insert to address these errors generated with the automatic dilution option:

Perform an alternative method of testing prior to reporting of results for the following antibiotic/organism combination(s):

Tetracycline (te01n): Streptococcus dysgalactiae equisimilis when the VITEK 2 MIC is 2 µg/mL

Table 3. Re-analysis of the Performance of *Streptococcus* spp. for the Manual Dilution with the VITEK 2 and the VITEK 2 Compact Systems AST-ST Tetracycline

VITEK 2 Systems	Total	#EA	%EA	Eval Total	No Eval EA	Eval EA %	#CA	%CA	#R	#S	min	maj	vmj
***S. pneumoniae* ≤1 (S), 2 (I), ≥4 (R)**													
VITEK 2	50	49	**98.0**	1	0	0.0	50	**100.0**	17	33	0	0	0
VITEK 2 Compact	50	48	**96.0**	12	10	83.3	50	**100.0**	17	33	0	0	0
***S. pyogenes* (Group A Beta-Hemolytic *Streptococcus* spp.) ≤2 (S), 4 (I), ≥8 (R)**													
VITEK 2	50	50	**100.0**	1	1	100.0	50	**100.0**	6	44	0	0	0
VITEK 2 Compact	50	50	**100.0**	1	1	100.0	50	**100.0**	6	44	0	0	0
***Streptococcus* spp. (Beta-Hemolytic Group other than *S. pyogenes*)[a,b] ≤2 (S), 4 (I), ≥8 (R)**													
VITEK 2[c]	63	63	**100**	3	3	100	63	**100.0**	53	10	0	0	0
VITEK 2 Compact[c]	63	63	**100**	4	4	100	62	**98.4**	53	10	1	0	0

[a] Including the following tested species: *S. agalactiae* (56), *S.canis* (1), *S. dys. dysgalactiae* (1), *S.dys.equisimilis* (4) *and S.equi zooepidemicus* (1).

[b] The interpretive criteria are applied to *Streptococcus* spp. Beta-Hemolytic Group according to the FDA STIC webpage.
[c] Additional testing was conducted to assess performance for Beta-Hemolytic *Streptococcus* spp. (not including *S. pyogenes*) against a challenge set of organisms.

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

When applying the new breakpoints of ≤1 (S), 2 (I), ≥4 (R), the performance of *Streptococcus pneumoniae* challenge isolates tested with the manual dilution and the VITEK 2 and the VITEK 2 Compact systems is acceptable with % EA and % CA >90%. There were no very major errors, no major errors and no minor errors observed with both the VITEK 2 and the VITEK 2 Compact out of 50 challenge isolates tested (**Table 3**).

When applying the new breakpoints of ≤2 (S), 4 (I), ≥8 (R), the performance of *Streptococcus pyogenes* challenge isolates tested with the manual dilution and the VITEK 2 and the VITEK 2 Compact systems is acceptable with % EA and % CA >90%. There were no very major errors, no major errors and no minor errors observed with both the VITEK 2 and the VITEK 2 Compact out of 50 challenge isolates tested (**Table 3**).

When applying the new breakpoints of ≤2 (S), 4 (I), ≥8 (R) for *Streptococcus* spp. (Beta-Hemolytic Group other than *S. pyogenes*) challenge isolates tested with the manual dilution and the VITEK 2 and VITEK 2 Compact systems is acceptable with % EA and % CA >90%. There were no very major errors and no major errors observed. One (1) minor error out of 63 isolates (1.6%) tested was observed for the VITEK 2 Compact system (**Table 3**).

As required under 511A(2) (2) (B) of the Federal Food, Drug and Cosmetic Act, the following statement was included under Precautions Section in 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.*

Trending

A trending re-analysis was performed using the combined (challenge and clinical) data obtained in K111893 from the VITEK 2 auto-dilution method for all *Streptococcus* spp. to align with current trending analysis.

This trending calculation takes into account the MIC values that are determined to be one or more doubling dilutions lower or higher than the reference method irrespective of whether the device MIC values are on-scale or not. Results that are not clearly at least one dilution lower, at least one dilution higher or in exact agreement with the CLSI reference method are not considered int the trending analysis.

When the difference between the percentage of isolates with higher vs. lower readings was > 30% and for which the confidence interval was determined to be statistically significant were considered to show evidence of trending. Trending that showed higher or lower MIC values compared to the reference is addressed in the labeling.

No trending was observed with *Streptococcus pneumoniae*, *S. pyogenes* (Group A Beta-Hemolytic streptococci) and *Streptococcus* spp. (Beta-Hemolytic Group other than *S. pyogenes*) (Table 4).

Table 4. Trending Re-analysis for *Streptococcus* spp. with Tetracycline and the VITEK 2 Automated Dilution

Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
Streptococcus pneumoniae	12	4 (33.3)	1 (8.3)	7 (58.3)	25.0%	No
Streptococcus pyogenes	6	3 (50.0)	0 (0.0)	3 (50.0)	0%	No
Streptococcus spp. Beta-Hemolytic Group (other than *S. pyogenes*)	50	27 (54.0)	7 (14.0)	16 (32.0)	-22.0%	No

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 recognized susceptibility interpretative for Tetracycline are listed in Table 5.

Table 5. FDA Recognized Interpretative Criteria for Tetracycline

Pathogen	Minimum Inhibitory Concentrations (µg/mL) [1]		
	S	I	R
S. pneumoniae	≤1	2	≥4
Streptococcus spp. β-Hemolytic Group[2]	≤2	4	≥8

S = Susceptible; I = Intermediate; R = Resistant

[1] FDA-Recognized Antimicrobial Susceptibility Test Interpretive Criteria Website https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm

[2]Includes *S. pyogenes* (Group A β-Hemolytic streptococci) and other β-hemolytic streptococci other than *S. pyogenes*.

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device when evaluated with the current FDA-recognized Tetracycline breakpoints.

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 System with Tetracycline when revised breakpoints for Tetracycline 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 Tetracycline 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.