510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K211630

B Applicant

bioMerieux, Inc

C Proprietary and Established Names

VITEK 2 AST-Gram Negative Piperacillin / Tazobactam (<=4 - =>128 µg/mL)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
LON	Class II	21 CFR 866.1645 - Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System	MI - Microbiology
LTW	Class II	21 CFR 866.1640 - Antimicrobial susceptibility test powder	MI - Microbiology
LTT	Class II	21 CFR 866.1640 - Antimicrobial susceptibility test powder	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To update the VITEK 2 Gram Negative Piperacillin/Tazobactam device labeling to include updated FDA-recognized breakpoints for *Pseudomonas aeruginosa* as published in the FDA STIC website.

Breakpoints for *Enterobacterales and Acinobacter* (also indicated for use with this devices) remain unchanged.

Previously obtained QC and reproducibility data is applicable to this reevaluation.

B Measurand:

Piperacillin/Tazobactam (≤ 4 - ≥ 128 µg/ml)

C Type of Test:

Automated quantitative or qualitative antimicrobial susceptibility test.

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

VITEK® 2 Gram Negative Piperacillin/tazobactam 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 Gram Negative Piperacillin/tazobactam is a quantitative test. Piperacillin/tazobactam 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:
Acinetobacter baumanii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa (given in combination with an aminoglycoside to which the isolate is susceptible).

In vitro data available but clinical significance is unknown:
Citrobacter koseri, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Providencia rettgeri, Salmonella enterica.

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., *S. pneumoniae*, and clinically significant yeast.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Limitations:
"Due to categorical agreement below 90% caused by the occurrence of minor errors and to avoid the potential occurrence of false results, perform an alternative method of testing prior to reporting of results for the following antibiotic/organism combination:
- *Piperacillin/Tazobactam (tzp03n): Pseudomonas aeruginosa when the VITEK2 MIC is 32 µg/mL or 64 µg/mL".*

Footnotes:
"*Piperacillin-tazobactam MIC values for Morganella morganii, Providencia rettgeri and Pseudomonas aeruginosa tended to be at least one doubling dilution higher than the reference method and may contribute to the occurrence of major errors. Piperacillin-tazobactam MIC values for Salmonella enterica tended to be at least one doubling dilution lower than the reference method and may contribute to the occurrence of very major errors*".

"*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*".

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

"*E.coli ATCC 35218 was not tested with piperacillin >64 to confirm the integrity of the respective QC strain per CLSI M100 Ed 31 recommendations*".

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 test card contains 64 microwells. A control well containing only culture medium is included on all cards, with the remaining wells containing premeasured amounts of a specific antimicrobial agent in a culture medium base. A suspension of organism from a pure culture is prepared in a tube containing 0.45-0.5% sterile saline and standardized to a McFarland 0.5 using the DensiCHEK Plus. The VITEK 2 System automatically fills, seals and places the card into the incubator/reader; manual methods can also be used for the inoculation of test cards for use in the VITEK 2 System. The VITEK 2 Compact has a manual filling and sealing operation. The VITEK 2 Systems monitor the growth of each well in the card over a defined period of time (up to 18 hours). 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-GN Piperacillin/Tazobactam has the following concentrations in the card: 2/4, 8/4, 24/4, 32/8 and 48/8µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result reporting range for the card is ≤4 - ≥ 128 µg/mL. For all species, the MIC results range indicates that the VITEK 2 system is capable of producing the following MIC results ≤4, 8, 16, 32, 64 and ≥ 128 µg/mL for AST GN piperacillin/tazobactam test. This

means the VITEK 2 systems does not provide results lower than 4 µg/mL, or greater than 128 µg/mL for the AST-GN Piperacillin/Tazobactam 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 used in the systems use visible light to directly measure organism growth within each of the 64 micro-wells. Transmittance optics are based on an initial light reading of a well before significant growth has begun. Periodic light transmittance samplings of the same well measure organism growth by how much light is prevented from going through the well. The VITEK 2 System monitors the growth of each well in the card over a defined period of time. An interpretive call is made between 4 and 16 hours for a "rapid" read but may be extended to 18 hours in some instances. At the completion of the incubation cycle, a report is automatically generated that contains the MIC value along with the interpretive category result for each antibiotic on the card.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Vitek 2 Ast-gn Piperacillin/tazobactam

B Predicate 510(k) Number(s):

K113200

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device K211630	Predicate K113200
Device Trade Name	VITEK 2 AST-GN Piperacillin/Tazobactam ≤4-≥128 µg/mL.	VITEK 2 AST-GN Piperacillin/Tazobactam
General Device Characteristic Similarities		
Intended Use/Indications For Use	VITEK® 2 Gram Negative Piperacillin/tazobactam 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 Gram Negative Piperacillin/tazobactam is a qualitative test. Piperacillin/tazobactam has been shown to be active against the microorganisms	Same.

	listed below, according to the FDA label for this antimicrobial. Active in vitro and in clinical infections: *Acinetobacter baumanii*, *Escherichia coli*, *Klebsiella pneumonia, Pseudomonas aeruginosa* (given in combination with an aminoglycoside to which the isolate is susceptible) In vitro data available but clinical significance is unknown: *Citrobacter koseri, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia stuartii, Providencia rettgeri, Salmonella enterica.* 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., S. pneumoniae, and clinically significant yeast.	
Test Method	Automated 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	Saline suspension of organism	Same.
Test Card	VITEK 2 AST-GN Piperacillin/tazobactam	Same.
Instrument	VITEK 2 and VITEK 2 COMPACT Systems	Same.
Analysis Algorithm	Discriminate Analysis Algorithm	Same.
Antimicrobial Concentrations & Result Range	Piperacillin/tazobactam: 2/4, 8/4, 24/4, 32/4, 32/8 and 48/8 ug/mL for a calling	Same.

	range of ≤4-≥128 µg/mL.	
General Device Characteristic Differences		
Breakpoints for *P. aeruginosa*	S≤16, I=32-64, R≥128	S≤64, I=(-), R≥128

VI Standards/Guidance Documents Referenced:

Data that was reanalyzed to support this submission was previously obtained from a previously completed clinical studies. The clinical study was reviewed and cleared in K113200. The CLSI Standards listed below were effective during the original clearance:

- CLSI M7-A8, "*Methods For Dilution Antimicrobial Susceptibility Tests For Bacteria That Grow Aerobically Approved Standard* –.Eighth Edition" Vol. 29, No. 2 (January 2009).
- M100 S18., "Clinical and Laboratory Standards Institute (CLSI). *Performance Standards for Antimicrobial Susceptibility Testing*. CLSI supplement
- *CLSI M100-S21, "Performance Standard for Antimicrobial Susceptibility Testing: Twenty-First Informational Supplement" Vol. 31, No. 1 (January 2011).*
- Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems, 2009.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Refer to K113200. Reproducibility testing for the VITEK 2 AST Piperacillin was performed in support of clearance of K113200 and was determined acceptable.

2. Linearity:

   Not appliable.

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 AST Piperacillin-Tazobactam was performed in support of clearance of K113200 and was determined acceptable. QC specific to the change in breakpoints was not performed as QC ranges used in K113200 have not changed.

QC organisms recommended by both the FDA and CLSI, namely *E. coli* ATCC 25922, *E. coli* ATCC 35218 and *P. aeruginosa* ATCC 27853 were tested against Piperacillin-Tazobactam during the clinical study a minimum 20 times/site by the automatic and the manual dilution. The organisms were tested by the VITEK 2 AST cards and the reference broth method. The overall QC results for both the reference and test panels appeared to be acceptable, however the limited range chosen for the VITEK 2 Piperacillin-Tazobactam card ≤4 - ≥128 µg/mL resulted in off-scale MIC values for all QC organisms. An MIC value of ≤4 µg/mL indicated that the quality control test results were acceptable.

bioMerieux included the following footnote in the current submission under the Quality Control Table in the device labeling for all QC organisms:

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

CLSI M100 Ed31 recommends testing of the integrity QC strain namely *E. coli* ATCC 35218. However, this integrity QC strain was not tested in K113200 because CLSI M100 Ed21 had no requirement to test the integrity of the QC. This was addressed in the labeling by adding the following footnote:

"*E.coli ATCC 35218 was not tested with piperacillin >64 to confirm the integrity of the respective QC strain per CLSI M100 Ed 31 recommendations*".

The QC data is acceptable for the purpose of the re-evaluation of the performance of *P. aeruginosa* 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 AST-GN tzp03n (≤4-≥128 ug/mL) was originally cleared in premarket submission K113200 and included indications for *Enterobacterales*, *P. aeruginosa* and *Acinetobacter baumanii* tested with VITEK 2 and auto dilution and VITEK 2 Compact with manual dilution.

The performance of the VITEK 2 AST card with *P. aeruginosa* using revised interpretive criteria (S ≤16, I=32-64, R≥128) currently recognized by FDA was evaluated using data obtained in support of premarket submission K113200. Since there was no change in the design or the dilution range of the VITEK 2 AST card, the performance evaluation was achieved via re-analysis of the MIC data point of the original 510(k) submission (K113200) by using the newly updated interpretive criteria for Piperacillin Tazobactam and *P. aeruginosa*.

A total of 187 (clinical and challenge) *P. aeruginosa* isolates were tested by the VITEK 2 piperacillin/Tazobactam and the automatic dilution. Of the 187 isolates, 168 were clinical isolates and 19 were challenge isolates. Results of the re-analyzed 187 (clinical and challenge) isolates with the updated breakpoints are summarized in **Tables 1**.

The 19 challenge set was also tested with the manual dilution method at one site with the VITEK 2 and the VITEK 2 Compact Systems. An additional 106 surveillance isolates referred as "expanded" panel which was part of the new formulation tz03n was also tested with the VITEK 2 using the manual dilution. The expanded surveillance data is combined with the challenge data set and results of the re-analysis is outlined in **Table 2**. Results of the re-analyzed challenge set data tested with the Compact System and the manual dilution are summarized in **Table 3**.

Table 1. Re-analysis of the Performance for *P. aeruginosa* with the VITEK 2 Gram Negative Piperacillin/Tazobactam *(Auto Dilution).*

	Tot	No. EA	EA %	Eval Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	min	maj	vmj
Clinical	168	155	92.3	75	62	82.7	143	85.1	44	23	2	0
Challenge	19	19	100	12	12	100	18	94.7	2	1	0	0
Combined	187	174	**93.0**	87	74	**85.1**	161	**86.1**	46	24	2	0

EA – Essential Agreement (+/- 2 dilutions)
CA – Category Agreement
EVAL – Evaluable isolates
R – Resistant

min – minor discrepancies
maj – major discrepancies
vmj – very major discrepancies

Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of VITEK 2 test card within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on scale for both the VITEK 2 test card and the reference method. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the VITEK 2 test card.

The combined Essential Agreement (EA) for *P. aeruginosa* is >90% and is acceptable as described in the "Class II Special Control Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA, August 2009". The updated breakpoints for *P. aeruginosa* lowered the susceptible breakpoint from ≤64 to ≤16 and also introduced an intermediate category of 32-64. The introduction of an intermediate category mitigated the vmj and maj errors observed in the original submission. However, applying the updated breakpoints, resulted in a decrease in the combined category agreement for *P. aeruginosa* from 93% in K113200 to 86.1% in the current submission due to an increase number of minor errors from Not Applicable (NA) to 24 (12.8% minor error rate). There are only 2 major errors out of 122 susceptible isolates (1.6%) and no very major errors out of 46 resistant isolates. The percent of resistant *P. aeruginosa* isolates didn't change and is still appropriate for evaluation with the new breakpoints.

To address the low category agreement and the increased number of minor errors, the following limitation is added to the package insert:

"Due to categorical agreement below 90% caused by the occurrence of minor errors and to avoid the potential occurrence of false results, perform an alternative method of testing prior to reporting of results for the following antibiotic/organism combination: Piperacillin/Tazobactam (tzp03n): Pseudomonas aeruginosa when the VITEK2 MIC is 32 µg/mL or 64 µg/mL".

Table 2. Re-analysis of the Performance of *P. aeruginosa* Challenge and Expanded Isolates, VITEK 2 (Manual Dilution) Gram Negative Piperacillin/Tazobactam

	Tot	EA	%EA	Eval EA Total	Eval EA	Eval %EA	CA	%CA	#R	min	maj	vmj
Challenge	19	18	94.7	12	11	91.7	18	94.7	2	1	0	0
Expanded	106	98	92.5	21	13	61.9	85	80.2	65	20	1	0
Combined	125	116	**92.8**	33	24	72.7	103	**82.4**	67	21	1	0

The Essential Agreement (EA) for *P. aeruginosa* with the combined (challenge and expanded surveillance) data with the VITEK 2 manual dilution is >90% which is acceptable. However, applying the updated breakpoints resulted in a decrease in the category agreement of 82.4% due to an increase number of minor error of 21 (16.8%). There were no very major errors and only 1 major error (2.4%). The low category agreement and the increased number of minor errors was addressed by including the limitation (listed above) in the device labeling.

Table 3. Re-analysis of the Performance of *P. aeruginosa* Challenge Isolates, VITEK2 Compact, (Manual Dilution) Gram Negative Piperacillin/Tazobactam

	Tot	No. EA	EA %	Eval Tot	No. Eval EA	Eval EA %	No. CA	CA %	No. R	min	maj	vmj
Challenge	19	19	100	13	13	100	18	94.7	2	1	0	0

The performance of *P. aeruginosa* challenge isolates with the VITEK 2 Compact and the manual dilution is acceptable with 100% EA and 94.7% CA. There were no very major, no major errors and only 1 minor error (5.3%) observed.

Re-analysis of the Overall Performance of all Organisms:
Even though the purpose of this submission was to update the VITEK 2 Gram Negative Piperacillin/Tazobactam device labeling due to updated FDA-recognized breakpoints for *P. aeruginosa*, the overall performance of all organisms tested by the VITEK 2 automatic dilution method as compared to the reference method was re-analyzed in the current submission. Overall performance was acceptable with 94% EA and 92.3% CA. No change was observed in the EA. Applying the updated breakpoints for *P. aeruginosa* resulted in a change in the overall category agreement from 93.2% in K113200 to 92.3% in the current submission. During this review, it was determined that the expanded surveillance set data was mislabeled as being generated by the auto dilution in K113200, which in fact was generated using the manual dilution. This was clarified in the labeling by including the following footnote:

"*Of 2452 clinical and challenge isolates tested to establish the overall performance, 1348 isolates were tested by the VITEK 2 automatic dilution and 1104 were tested by the VITEK 2 manual dilution method*".

As required under 511A(b)(2)(C)(ii)(I) of the Federal Food, Drug and Cosmetic Act, the following statement is included in the device labeling to address testing of non-indicated species:

> *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, expanded surveillance data and clinical) data obtained in K113200 from the VITEK 2 auto-dilution method for all organism including *P. aeruginosa* to align with current trending analysis. The expanded surveillance data set was tested in K113200 with the VITEK 2 manual dilution and combined with challenge and clinical isolates to obtain on-scale isolates for trending.

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.

Evaluation of the results for *P. aeruginosa, Morganella morganii and Providencia rettgeri* using auto dilution on VITEK 2 showed a trend toward higher MIC values (**Table 4**). Evaluation of the results for *Salmonella enterica* showed a trend toward lower MIC values (**Table 4**).

Table 4. Trending Re-Analysis VITEK 2 Gram Negative Piperacillin/Tazobactam (Challenge, Expanded and Clinical Isolates)**

	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)*	Trending Noted
Acinetobacter baumanii	42	17	11	14	-7.14% (-26.58, 13.08)	No
Citrobacter koseri	14	6	5	3	-21.43% (-49.62, 12.42)	No
Escherichia coli	115	42	25	48	5.22% (-7.31%, 17.52)	No
Klebsiella pneumoniae	116	31	38	47	13.79% (1.63, 25.40)	No
Morganella morganii	14	3	1	10	50. 00% (13.06, 71.82)	**Yes**
Proteus mirabilis	24	7	6	11	16.67% (-10.20, 40.49)	No
Proteus vulgaris gr.	0	NA	NA	NA	NA	NA
Providencia rettgeri	5	0	1	4	80.00% (19.26, 96.38)	**Yes**
Providencia stuartii	21	7	5	9	9.52% (-18.61, 35. 69)	No
Salmonella enterica	5	4	1	0	-80.00% (-96, 38, -19.26)	**Yes**
Enterobacterales	314	100	82	132	10.2 (2.6, 17.6)	No
P. aeruginosa	132	18	27	87	52.3% (41.4, 61.2)	**Yes**
Acinetobacter baumanii	42	17	11	14	-7.14% (-26.58, 13.08)	No
All Organisms	488	135	120	233	20.08% (14.05, 25.91)	No

*A positive percent difference value indicates higher MIC when compared to the reference method; A negative percent difference value indicates lower MIC when compared to the reference method.
**The expanded challenge set was added to obtain on-scale MIC values for trending analysis and was tested using the manual dilution in the original submission K113200.

To address the observed trending, the sponsor included the following footnote to the performance table in the labeling:

"*Piperacillin-tazobactam MIC values for Morganella morganii, Providencia rettgeri and Pseudomonas aeruginosa tended to be at least one doubling dilution higher than the reference method and may contribute to the occurrence of major errors. Piperacillin-tazobactam MIC values for Salmonella enterica tended to be at least one doubling dilution lower than the reference method and may contribute to the occurrence of very major errors".*

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 and CLSI identified susceptibility interpretive criteria for Piperacillin-Tazobactam are listed in **Table 5.**

Table 5: FDA Recognized Interpretative Criteria for Piperacillin-Tazobactam

Pathogen	Minimum Inhibitory Concentrations (mcg/mL)[1]		
	S	I	R
Enterobacteriaceae[2,3]	≤ 16/4	32-64	≥ 128/4
P. aeruginosa	≤ 64	32-64	≥ 128
Acinetobacter spp	≤ 64	32-64	≥ 128

S = Susceptible; I = Intermediate; R = Resistant

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

VIII Proposed Labeling:

The labeling was updated to include the statement required by the 21st Century Cures legislation, the updated breakpoints for *P. aeruginosa* with Piperacillin-Tazobactam. In addition, performance calculated using the currently-recognized breakpoints was included along with a limitation to reflect results obtained from this evaluation. A footnote to the performance table reflected results obtained from trending analysis.

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 System with Piperacillin-Tazobactam when revised breakpoints for Piperacillin-Tazobactam 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 Piperacillin-Tazobactam 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.