SPECIAL 510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

I Background Information:

A 510(k) Number

K212849

B Applicant

bioMérieux, Inc

C Proprietary and Established Names

VITEK 2 AST-Gram Positive Linezolid (≤0.5 - ≥8 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 Review Summary:

This 510(k) submission contains information/data on modifications made to the submitter's own CLASS II device requiring 510(k). The following items are present and acceptable.

1. The name and 510(k) number of the SUBMITTER'S previously cleared device.

   Trade Name: VITEK 2 AST-GP Linezolid (≤0.5 - ≥8µg/mL)
   510(k) #: K032766

2. Submitter's statement that the **INDICATIONS FOR USE/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available,

advertisements or promotional materials (labeling changes are permitted as long as they do not affect the intended use).

The Intended Use/Instructions for Use have not changed, but language has been harmonized to align with recent VITEK 2 antimicrobials. In addition, The VITEK 2 Compact instrument is now included in the Intended Use since the VITEK 2 Compact performance was similar to VITEK 2 System as demonstrated in K050002.

3. A description of the device **MODIFICATION(S)**, including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed.**

   The change was for reanalysis of MIC results for *Staphylococcus* spp. with linezolid using currently recognized interpretative criteria.

   bioMérieux also tested 11 *S. epidermidis* clinical stock linezolid-resistant isolates and 20 *S. haemolyticus* clinical stock isolates to assess performance. All testing was performed with the auto dilution method at a single external clinical site. The methods used to provide data to support this change were in conformity to those outlined in CLSI M07, Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard – 11th Edition; January 2018.

4. Comparison Information (i.e., similarities and differences) to the submitter's legally marketed predicate device including, labeling, intended use, and physical characteristics.

5. A Design Control Activities Summary which includes:

   a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis.

   b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied.

The device performance for *Streptococcus agalactiae* and *Enterococcus* spp. was evaluated in K032766. Please refer to K032766 for results obtained with the bioMérieux VITEK 2 AST-Gram Positive Linezolid when compared to results obtained with the CLSI reference agar dilution method.

***Staphylococcus* spp. Performance Study:**
A supplemental clinical study was conducted in accordance with the Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA, issued August 28, 2009 (AST Guidance document). Supplemental testing was performed at one external clinical site. All reference method testing follows CLSI approved agar dilution testing conditions, which consisted of:

- Medium: Mueller Hinton agar with the appropriate dilutions of antimicrobial solution added
- Inoculum: Direct colony suspension
- Incubation: 35°C; 16-20 hours

Previously collected clinical and challenge data and newly collected clinical data of 390 isolates of *Staphylococcus* spp. (337 clinical and 53 challenge isolates) were reanalyzed using the current FDA-recognized breakpoints using auto dilution method. Results obtained with the auto dilution method were acceptable (Table 1).

Table 1. *Staphylococcus* spp. of Clinical and Challenge Isolates for Linezolid: VITEK 2 Auto-Dilution

Organism Type	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#R	#S	min	maj	vmj
***Staphylococcus*[1] spp. [Breakpoints (µg/mL): ≤4 (S), - (I), ≥8 (R)]**													
Clinical	337	328	97.3	324	315	97.2	336	99.7	11	326	0	1	0
Challenge	53	51	96.2	53	51	96.2	53	100	0	53	0	0	0
Combined	**390**	**379**	**97.2**	**377**	**366**	**97.1**	**389**	**99.7**	**11**	**379**	**0**	**1**	**0**

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

[1]When evaluating performance of the clinical and challenge isolates, testing with *Staphylococcus haemolyticus* isolates yielded an EA of 82.9% (29/35) and an CA of 97.1% (34/35). There was one major error (2.9%%, 1/35).

For supplemental testing, DensiChek was used for the preparation of inoculum for the VITEK 2 AST cards in the trial and standardized daily. Two quality control organisms, *Enterococcus faecalis* ATCC 29212 and *Staphylococcus aureus* ATCC 29213, were tested throughout comparative testing by both the VITEK 2 AST-GP Linezolid and reference agar dilution methods. The QC organisms were tested a minimum of twenty times by both the VITEK 2 card and reference method. QC results for the VITEK 2 AST-GP Linezolid were within expected results' range >95% of the time for automatic dilution mode of the VITEK 2.

Performance of all clinical and challenge isolates for linezolid using the automatic dilution method were stratified by organism and the results were acceptable (Table 2). Performance of all challenge isolates for linezolid using the manual dilution method stratified by organism remains unchanged from K032766. A trending analysis was conducted using the combined clinical and challenge data for all organisms. Evaluation of the results for *S. haemolyticus* showed a trend toward higher MIC values using the auto-dilution method (Table 3).

Table 2. Performance of All Clinical and Challenge Isolates for Linezolid Stratified by Organism: VITEK 2 Auto-Dilution

Organism Type	EA Tot	EA N	EA %	Eval. EA Tot	Eval. EA N	Eval. EA %	CA N	CA %	#R	#S	min	maj	vmj
***Staphylococcus*[1] spp. [Breakpoints (µg/mL): ≤4 (S), - (I), ≥8 (R)]**													
Clinical	337	328	97.3	324	315	97.2	336	99.7	11	326	0	1	0
Challenge	53	51	96.2	53	51	96.2	53	100	0	53	0	0	0
Combined	**390**	**379**	**97.2**	**377**	**366**	**97.1**	**389**	**99.7**	**11**	**379**	**0**	**1**	**0**
***Enterococcus* spp. [Breakpoints (µg/mL): ≤2 (S), 4 (I), ≥8 (R)]**													
Clinical	368	367	99.7	359	358	99.7	360	97.8	8	354	8	0	0
Challenge	35	35	100	35	35	100	35	100	0	35	0	0	0
Combined	**403**	**402**	**99.8**	**394**	**393**	**99.7**	**395**	**98.0**	**8**	**389**	**8**	**0**	**0**
***Streptococcus agalactiae* [Breakpoints (µg/mL): ≤2 (S), - (I), - (R)]**													
Clinical	54	54	100	53	53	100	54	100	0	54	0	0	0
Challenge	10	10	100	10	10	100	10	100	0	10	0	0	0
Combined	**64**	**64**	**100**	**63**	**63**	**100**	**64**	**100**	**0**	**64**	**0**	**0**	**0**

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[1]When evaluating performance of the clinical and challenge isolates, testing with *Staphylococcus haemolyticus* isolates yielded an EA of 82.9% (29/35) and an CA of 97.1% (34/35). There was one major error (2.9%%, 1/35).

Table 3. Trending by *S. haemolyticus* (clinical and challenge isolates)

VITEK 2 Auto-Dilution						
Organism	**Total Evaluable for Trending**	**≥1 dil. Lower # (%)**	**Exact # (%)**	**≥1 dil. Higher # (%)**	**Percent Difference (95% CI)**	**Trending Noted**
Staphylococcus haemolyticus	35	1 (2.86)	7 (20.00)	27 (77.14)	74.29% (54.35 to 85.33)	Yes[1] High

[1]Trending is addressed in a footnote to the performance table in the device labeling.

To support the implementation of changes to FDA-recognized susceptibility test interpretive criteria (i.e., breakpoints), this submission included a breakpoint change protocol that was reviewed and accepted by FDA. This protocol addresses future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm). The protocol outlined the specific procedures and acceptance criteria that bioMérieux intends to use to evaluate the VITEK 2 AST-GP Linezolid when revised breakpoints for linezolid 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 linezolid 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.

The data included in this submission supported the sponsor's proposal to revise the following from the device instructions for use:

1. Updated performance for *Staphylococcus* spp. using the currently-recognized interpretive criteria for linezolid and *Staphylococcus* spp. (as noted on the FDA Susceptibility Test Interpretive Criteria website (STIC).

2. Added the following footnotes under the table *Performance Characteristics Antimicrobial Susceptibility Testing* in the labeling:
"*VITEK 2 AST-Gram Positive Linezolid MIC values tended to be in exact agreement or at least one doubling dilution higher when testing Staphylococcus haemolyticus compared to the CLSI reference agar dilution method."*

"When evaluating performance of the clinical and challenge isolates, testing with Staphylococcus haemolyticus isolates yielded an EA of 82.9% (29/35) and an CA of 97.1% (34/35). There was one major error (2.9%%, 1/35)."

3. Removed *S. epidermidis* from the limitation regarding lack of resistant isolate availability in the labeling. The modified limitation is shown below:
"*The ability of the AST card to detect resistance with the following combination(s) is unknown because resistant strains were not available at the time of comparative testing:*
    - *[lzn02n]*
    Linezolid: Enterococcus spp., Staphylococcus aureus, Staphylococcus haemolyticus, Streptococcus agalactiae"

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their pre-amendment) device.