SPECIAL 510(K): DEVICE MODIFICATION
OIR DECISION SUMMARY

510(k) Number: K181368

This 510(k) submission contains information/data on modifications made to the applicant's own class II or class I devices requiring 510(k). The following items are present and acceptable

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1. The name and 510(k) number of the applicant's previously cleared device. (For a preamendments device, a statement to this effect has been provided.)

   Trade Name: VITEK 2 AST-YS Micafungin (≤0.06 - ≥8µg/mL)

   510(k) #: K151923

2. Applicant's statement that the **INDICATION/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).

   Indications for Use: The indications for use for both devices are identical. Please refer to the K151923 for the INDICATION/INTENDED USE

   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 applicant'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 applicant has provided the design control information as specified in the New 510(k) Paradigm and on this basis, the device is determined to be substantially equivalent to the previously cleared device.

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**.

   This change is for revising QC organism *Candida parapsilosis* ATCC 22019 expected range from 0.5-2 µg/mL (FDA/CLSI @24h) to 0.25-1 µg/mL (bMx-US) and removal of the following footnote from the package insert under QC table: "**FDA/CLSI@24H = FDA/CLSI Broth Microdilution expected QC range at 24h" and replace with the footnote "**bMx-US = bioMerieux QC range for US".

   bioMerieux performed studies to establish a new quality control ranges for use specifically with their device. The methods used to provide data to support this change were in confomity to those outlined in CLSI M23 (Development of In Vitro Susceptibility Testing and Quality Control Parameters, M23, 5th Ed, Jan 2018).

4. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device is shown in Table 1 below:

Table 1. Comparison with the Predicate

Similarities		
Item	Device VITEK 2 AST-Yeast Micafungin modified (K181368)	Predicate: VITEK2 AST-YS Micafungin (K151923)
Indication for Use	VITEK 2 Yeast Micafungin is designed for antifungal susceptibility testing of Candida species. Vitek 2 Yeast Micafungin is a quantitative test 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 Yeast Micafungin has been shown to be active against most isolates of the microorganisms listed below, according to the FDA label for this antifungal. Active in vitro and clinical infections: *Candida albicans* *Candida glabrate* *Candida guilliermondii* *Candida krusei* *Candida parapsilosis* *Candida tropicalis* 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.	Same
Test Method	Automated yeast antifungal susceptibility test for use with the VITEK 2 and VITEK 2 Compact Systems (VITEK 2 Systems) to determine the in vitro susceptibility of Candida species.	Same
Inoculum	Saline suspension of organism	Same
Test Card	VITEK 2 Antifungal Susceptibility Test Card	Same
Analysis algorithm	Discriminate Analysis	Same
Antifungal Concentrations & Result Range	0.06, 0.25, 1, 4 µg/mL ≤0.06 - ≥8 µg/mL	Same
Antimicrobial Agent	Micafungin	Same

Differences		
Item	Device VITEK 2 AST-Yeast Micafungin modified (K181368)	Predicate: VITEK2 AST-YS Micafungin (K151923)
C. parapsilosis ATCC 22019 expected QC range	0.25-1 µg/mL	0.5-2 µg/mL
Dilution	Manual[1]	Manual and automated
Instruments	VITEK 2 System[#]	VITEK 2 System and VITEK 2 Compact

[1]Equivalence between the manual and automated methods was demonstrated in K151923
[#]Equivalence between the VITEK 2 System and the VITEK 2 Compact was demonstrated in K151923

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 was evaluated in K151923. Please refer to K151923 for results obtained with the bioMerieux VITEK 2 AST-Yeast with Micafungin when compared to results obtained with the CLSI reference frozen both microdilution panel read and interpreted after 24 hours.

This Special 510(k) application included data to support:

1. Revising quality control Micafungin MIC range for *Candida parapsilosis* ATCC 22019 from 0.5-2 µg/mL to 0.25-1 µg/mL for use specifically with the VITEK 2 System and VITEK 2 Compact (bMx-US)
2. Replace the following footnote from under the QC table in the labeling:
   "***FDA/CLSI@24H=FDA/CLSI Broth Microdilution expected QC range at 24hrs"*
   with the following revised footnote:
   "***bMx-US=bioMerieux QC range for US*".

Quality Control (QC) Performance Study:

In compliance with the CLSI M23-A4 guideline, a Tier 2 QC study was designed to establish a new Micafungin MIC QC range for *Candida parapsilosis* for use specifically with the VITEK 2 System and VITEK 2 Compact. The M23 Micafungin Study was conducted at seven sites (six external clinical sites and one internal site). Table 2 below outline the study design. Table 3 outline the FDA/CLSI M27-S4 QC range for Micafungin and the newly proposed bioMerieux QC range for *C. parapsilosis* with Micafungin.

Table 2. Tier 2 Study: Requirements to Establish Quality Control Expected Range

Category	MIC Study
Laboratories*	7
Media Lots	3
Replicates (individual inoculum, max 4 per day)**	10
Total data points	210 (7 x 3 x10)

*All laboratories test all media lots and replicates

**A single replicate per day provides the best opportunity to detect day-to-day variability. A minimum of three days testing is recommended for broth dilution.

Table 3. FDA/CLSI M27-S4 QC Ranges (µg/mL) for Micafungin with Broth Microdilution and bioMerieux Proposed QC Range (µg/mL) with VITEK 2 System in the US

Drug	*C. parapsilosis* ATCC 22019		*C. krusei* ATCC 6258	
Micafungin (CLSI QC Range)	24 h	48 h	24 h	48 h
	0.5-2	0.5-4	0.125-0.5	0.125-0.5
Micafungin (bioMerieux VITEK 2 System QC Range)	0.25-1	NA	NA	NA

NA=Not Applicable

QC testing was conducted throughout comparative testing at each of the seven sites using two *Candida* species recommended in the FDA approved pharmaceutical drug label and the CLSI : *Candida krusei* (ATCC 6258) and *Candida parapsilosis* (ATCC 22019). *Candida krusei* (ATCC 6258) was used as a control. The QC organisms were tested using three lots of VITEK 2 AST-YS07 suscetibility cards and the CLSI broth microdilution reference panel read after incubation at 24 and 48 hours at all participating study sites. Using individual inoculum preparations all three lots were tested in conjunction with the reference panel. Ten replicates of each QC strain on each of the three lot were tested at each site. No more than four replicates per day were tested. Reproducibility testing was peformed on the VITEK AST-YS07 card and the reference method.

Colony counts for each QC strain inoculum was performed on each day of testing.

DensiCHEK Plus instrument was used to standardize the inoculum (modification of the M23 testing procedure). The DensiCHEK Plus was FDA cleared for standardizing suspensions for AST testing (K932224).

The QC organisms were tested with the reference method (70 data points), and the VITEK 2 instrument platform using the manual dilution method (210 data points).

The reference method QC results were interpreted after 24 hour and 48h of incubation as recommended by the FDA pharmaceutical drug label and the CLSI M27-S4, (Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeast; Fourth Informational Supplement, Vol. 32 No.17). Results are shown in Table 4.

QC results for the VITEK 2 AST-Yeast Micafungin (manual dilution method) with *C. parapsilos* were within the bioMerieux proposed range ≥ 95% of the time, with the exception of one reference method at 24 hour read with *C. parapsilosis* which had QC results of 98.% (69/70). The range for Micafungin's quality control organism, *C. parapsilosis* ATCC 22019, was estimated utilizing the CLSI Range Finder MIC tool. The *C. parapsilosis* ATCC 22019 Micafungin proposed QC range with the VITEK 2 instrument was determined to be 0.25-1. A summary of the QC performance of *C. parapsilosis* ATCC 22012 is provided in Tables 4-5 below.

Table 4. QC Results VITEK 2 for Micafungin
(Reference Method Interpreted after 24h and 48h of Incubation)

QC Strain	VITEK 2 Manual Dilution (Proposed Ranges 0.25-1.)	Reference Method	
		24h (Range 0.5-2)	48h (Range 0.5-4)
C. parapsilosis ATCC 22012	100% (210/210)	98.6% (69/70)	100% (70/70)

Table 5. QC Results for Micafungin
(Test device for new VITEK 2 QC Range)

QC Strain	**Lots****	**MIC (µg/mL)**	**Test Results**		
			VITEK	**Ref read at 24h***	**Ref read at 48h***
C. parapsilosis ATCC 22019 Newly bMX proposed QC range: 0.25-1 µg/mL Reference Expected QC range 24h read: 0.5-2 µg/mL Reference Expected QC range 48h read: 0.5-4 µg/mL	Lot 1	0.25	2	**1**	
		0.5	68	19	7
		1		49	30
		2		1	33
	Lot 2	0.25			
		0.5	70		
		1			
	Lot 3	0.25			
		0.5	70		
		1			

*The reference method was tested with only with one lot
**Three different lot of VITEK 2 card where tested.

Internal Validation Study

Once the new QC range for *C. prapsilosis* ATCC 22019 was established, an internal validation study was performed to demonstrate that users will be able to obtain results within the new established range. Quality control testing was performed using four different inoculum of *C. parapsilosis* strain each day of testing to obtain 20 results (4 inoculum x 5 days =20 QC results). All the results were within the new QC range (0.25-1) established for *C. parapsilosis* ATCC 22019 and Micafungin test. The results showed 100% of the results (20/20) were within the new range.

Expected values/Reference range:

FDA Interpretive Criteria for Micafungin are the same as in K151923. Please refer to K151923 for FDA/CLSI Interpretive Criteria for Micafungin.

Device Labeling Changes:

The data included in this submission validates the sponsor's proposal to remove the following statements from the device instructions for use:

1. Revise QC organism *C. parapsilosis* ATCC 22019 Micafungin MIC range from 0.5-2 µg/mL to 0.25-1 µg/mL (bMx-US)
2. Remove the following footnote from under the QC table: "**FDA/CLSI@24H=FDA/CLSI Broth Microdilution expected QC range at 24h" and replace with footnote "**bMx-US=bioMerieux QC range for US".

Conclusion

The Labeling supports the finding of substantial equivalence for this device