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

## I Background Information:

### A 510(k) Number

K232963

### B Applicant

bioMérieux, Inc.

### C Proprietary and Established Names

VITEK 2 AST-Yeast Anidulafungin (≤ 0.015 - ≥ 8 µg/mL)

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| NGZ | 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 |
| LTW | Class II | 21 CFR 866.1640 - Antimicrobial susceptibility test powder | MI - Microbiology |
| LRG | Class II | 21 CFR 866.1640 - Antimicrobial susceptibility test powder | MI - Microbiology |
| 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 obtain a substantial equivalence determination for anidulafungin testing of *Candida* species on the VITEK 2 and VITEK 2 Compact Antimicrobial Susceptibility Test Systems.

**B Measurand:**

Anidulafungin (≤ 0.015 - ≥ 8 µg/mL)

**C Type of Test:**

Automated quantitative antifungal susceptibility test

## III Intended Use/Indications for Use:

**A Intended Use(s):**
See Indications for Use below.

**B Indication(s) for Use:**
VITEK 2 AST-Yeast Anidulafungin is designed for antifungal susceptibility testing of Candida 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 antifungal agents. VITEK 2 AST-Yeast Anidulafungin is a quantitative test. Anidulafungin has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antifungal.

Active *in vitro* and in clinical infections:
*Candida albicans*
*Candida glabrata*
*Candida parapsilosis*
*Candida tropicalis*

*In vitro* data are available, but clinical significance is unknown:
*Candida guilliermondii*
*Candida krusei*

The VITEK 2 Fungal Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of clinically significant yeasts to antifungal agents when used as instructed.

**C Special Conditions for Use Statement(s):**
Rx - For Prescription Use Only

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:
• Anidulafungin (ani01n): Candida spp.

**D Special Instrument Requirements:**

For use with the VITEK 2 and VITEK 2 Compact Systems using VITEK 2 Systems 9.04 software (or later)

## 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 0.5% 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 organism 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 AST-YS Anidulafungin has the following concentrations in the card: 0.0625, 0.125, 0.5, 2, and 8 (equivalent standard method concentration by efficacy in µg/mL). The anidulafungin MIC result range for the VITEK 2 card is ≤0.015 – ≥8 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 AST-Yeast Caspofungin (<=0.125 - >=8 µg/mL)

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

K213899

## C Comparison with Predicate(s):

| Device & Predicate Device(s): | Device: K232963 | Predicate: K213899 |
|---|---|---|
| Device Trade Name | VITEK 2 AST-Yeast Anidulafungin (≤ 0.015 - ≥ 8 µg/mL) | VITEK 2 AST-Yeast Caspofungin (≤ 0.125 - ≥ 8 µg/mL) |
| **General Device Characteristic Similarities** | | |
| Indications for Use | VITEK 2 AST-Yeast Anidulafungin is designed for antifungal susceptibility testing of *Candida* 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 antifungal agents. VITEK 2 AST-Yeast Anidulafungin is a quantitative test. Anidulafungin has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antifungal. The VITEK 2 Fungal Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of clinically significant yeasts to antifungal agents when used as instructed. | VITEK 2 AST-Yeast Caspofungin is designed for antifungal susceptibility testing of *Candida* 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 antifungal agents. VITEK 2 AST-Yeast Caspofungin is a quantitative test. Caspofungin has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antifungal. The VITEK 2 Fungal Susceptibility Card is intended for use with the VITEK 2 Systems in clinical laboratories as an *in vitro* test to determine the susceptibility of clinically significant yeasts to antifungal agents when used as instructed. |
| Test Methodology | Automated quantitative antimicrobial susceptibility test for use with the VITEK 2 and VITEK 2 Compact Systems to determine the *in vitro* susceptibility | Same |
| Inoculum | Saline suspension of organism | Same |
| Test Card | VITEK 2 Yeast Susceptibility Test Card | Same |
| Instrument | VITEK 2 and VITEK 2 Compact Systems | Same |
| Analysis Algorithms | Discriminant Analysis | Same |

| Device & Predicate Device(s): | Device: K232963 | Predicate: K213899 |
|---|---|---|
| **General Device Characteristic Differences** | | |
| Claimed species | Active *in vitro* and in clinical infections:<br>*Candida albicans*<br>*Candida glabrata*<br>*Candida parapsilosis*<br>*Candida tropicalis*<br><br>*In vitro* data are available, but clinical significance is unknown:<br>*Candida guilliermondii*<br>*Candida krusei* | Active *in vitro* and in clinical infections:<br>*Candida albicans*<br>*Candida guilliermondii*<br>*Candida krusei*<br>*Candida parapsilosis*<br>*Candida tropicalis* |
| Antifungal Agent | Anidulafungin | Caspofungin |
| Antimicrobial Concentrations µg/mL | 0.0625, 0.125, 0.5, 2, 8 | 0.125, 0.5, 2, 8 |

## VI Standards/Guidance Documents Referenced:

CLSI M27M44S, "Performance Standards for Antifungal Susceptibility Testing of Yeasts; Third Edition" (August 2022)

CLSI M27, "Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeast; Fourth Edition" (November 2017)

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:
   Reproducibility testing for the VITEK 2 AST-Yeast Anidulafungin was conducted at three sites (two external and one internal site) using a panel of ten *Candida* species consistent with the indications for use (i.e., two isolates of *Candida glabrata*, six isolates of *Candida krusei*, and two isolates of *Candida parapsilosis*). Each isolate was tested in triplicate, using separate inocula, over three days for a total of 270 data points. Inocula were prepared using both the autodilution and manual dilution methods for testing with the VITEK 2 System. In addition, inocula were prepared by the manual dilution method for testing with the VITEK 2 Compact. The mode of MIC values was determined for each isolate and the reproducibility was calculated based on the number of MIC values that fell within ± 2 doubling dilution of the mode.

All MIC results were on-scale; therefore, only best-case results are reported (Table 1). The testing resulted in overall best case reproducibility of 100% (270/270) for autodilution and manual dilution in the VITEK 2 System and 100% (270/270) for the VITEK 2 Compact System (manual dilution only). The reproducibility data was acceptable.

**Table 1**. Reproducibility Performance

| | **VITEK 2** | | | | **VITEK 2 Compact** | |
|---|---|---|---|---|---|---|
| | **Manual Dilution** | | **Auto-Dilution** | | **Manual Dilution** | |
| | **+/- 1 dilution of the mode** | **+/- 2 dilutions of the mode** | **+/- 1 dilution of the mode** | **+/- 2 dilutions of the mode** | **+/- 1 dilution of the mode** | **+/- 2 dilutions of the mode** |
| **Best Case** | 98.2% | 100% | 98.2% | 100% | 98.2% | 100% |

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Not applicable.

4. Assay Reportable Range:

   Not applicable.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   **Inoculum Density Check:** The DensiCHEK Plus was used to standardize the inoculum to a 0.5 McFarland 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 or Device Failure:** The VITEK 2 AST-YS Anidulafungin trial had several device failures including isolated mechanical failures that did not repeat (card recognition, mechanical jam, failure to eject, dispenser/pipettor failure, communication error and an optics failure). These errors did not raise concerns since they were isolated and did not reflect systematic issues. There were zero growth failures.

   **Quality Control Testing**: The CLSI recommended QC strains *Candida krusei* (ATCC 6258) and *Candida parapsilosis* (ATCC 22019) were tested a minimum of 20 times at each site by the reference method, the VITEK 2 instrument platform using both autodilution and manual dilution methods, and the VITEK 2 Compact instrument platform using the manual dilution method. A summary of the QC performance is provided in Table 2.

The quality control results for the VITEK 2 AST-YS Anidulafungin were within the recommended range ≥95% which is acceptable.

**Table 2.** Quality Control Results for VITEK 2 AST-Yeast Anidulafungin

| Organism | VITEK 2 Result Range | BMD Result Range (µg/mL) | VITEK 2 Auto Dilution | BMD | VITEK 2 Manual Dilution | BMD | VITEK 2 Compact Manual Dilution | BMD |
|---|---|---|---|---|---|---|---|---|
| *C. krusei* ATCC 6258 Expected Range: 0.0313 – 0.12 µg/mL | | ≤0.0078 | | | | | | |
| | ≤0.0156 | 0.0156 | | | | | | |
| | 0.0313 | 0.0313 | 8 | 2 | | | | |
| | 0.0625 | 0.0625 | 34 | 76 | 7 | 32 | 11 | 32 |
| | 0.125 | 0.125 | 96 | 56 | 62 | 34 | 59 | 34 |
| | 0.25 | 0.25 | | 4 | | 4 | | 4 |
| | 0.5 | 0.5 | | | 1 | | | |
| | 1 | 1 | | | | | | |
| | 2 | 2 | | | | | | |
| | 4 | 4 | | | | | | |
| | ≥8 | 8 | | | | | | |
| | | ≥16 | | | | | | |
| *C. parapsilosis* ATCC 22019 Expected Range: 0.25 – 2 µg/mL | | ≤0.0078 | | 1 | | | | |
| | ≤0.0156 | 0.0156 | | | | | | |
| | 0.0313 | 0.0313 | | | | | | |
| | 0.0625 | 0.0625 | | | | | | |
| | 0.125 | 0.125 | | | | | | |
| | 0.25 | 0.25 | | | | | | |
| | 0.5 | 0.5 | 24 | 20 | 4 | 5 | 4 | 5 |
| | 1 | 1 | 86 | 98 | 43 | 50 | 37 | 50 |
| | 2 | 2 | 28 | 19 | 22 | 15 | 29 | 15 |
| | 4 | 4 | | | | | | |
| | ≥8 | 8 | | | 1 | | | |
| | | ≥16 | | | | | | |

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   Not applicable.

## B Comparison Studies:

1. Method Comparison with Predicate Device:

   Testing of anidulafungin was performed at three external sites and one internal site. Results obtained with VITEK 2 AST-Yeast Anidulafungin were compared to results obtained with the CLSI broth microdilution reference panel. The MIC result range for the VITEK 2 AST-Yeast Anidulafungin is ≤ 0.015 - ≥ 8 µg/mL for all species. The testing conditions for the reference method consisted of the following:

   - Medium: RPMI 1640

- Inoculum: Direct colony suspension
- Incubation: 35ºC; 24 hours (up to 48 hours for isolates that are not growing well)

The VITEK 2 cards were inoculated with test organisms using the autodilution method (VITEK 2) and using the manual dilution method (VITEK 2 and VITEK 2 Compact). All test inocula used for the VITEK 2 AST cards and the reference method were standardized using the DensiCHEK instruments. A total of 485 clinical isolates were evaluated using autodilution and VITEK 2. The majority of the isolates were recently isolated from clinical specimens and 177 of the 485 clinical isolates tested were from stock isolates (36.5%). The clinical isolates included: 185 *C. albicans* isolates, 78 *C. glabrata* isolates, 62 *C. parapsilosis* isolates, 74 *C. tropicalis* isolates, 19 *C. guilliermondii* isolates and 67 *C. krusei* isolates.

A total of 80 challenge isolates including 21 *C. albicans* isolates, 38 *C. glabrata* isolates, 10 *C. parapsilosis* isolates, 7 *C. tropicalis* isolates, 2 *C. guilliermondii* isolates and 2 *C. krusei* isolates were evaluated at two external sites and one internal site.

**Clinical and Challenge Data – VITEK 2 Autodilution**
The results obtained using the autodilution method of the VITEK 2 from the 565 total isolates (485 clinical isolates and 80 challenge isolates) are summarized in Table 3.

**Table 3.** Performance of *Candida* spp. for the Automatic Dilution and the VITEK 2 AST-YS Anidulafungin

| | Total | #EA | %EA | Eval EA Total | Eval EA # | Eval EA % | #CA | %CA | #R | #S | min | maj | vmj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Candida albicans* ≤0.25 (S), 0.5 (I), ≥1 (R)** | | | | | | | | | | | | | |
| **Clinical** | 185 | 185 | 100.0 | 6 | 6 | 100.0 | 185 | 100.0 | 0 | 185 | 0 | 0 | 0 |
| **Challenge** | 21 | 21 | 100.0 | 0 | 0 | - | 21 | 100.0 | 0 | 21 | 0 | 0 | 0 |
| **Combined** | 206 | 206 | **100.0** | 6 | 6 | 100.0 | 206 | **100.0** | 0 | 206 | 0 | 0 | 0 |
| ***Candida glabrata* ≤0.12 (S), 0.25 (I), ≥0.5 (R)** | | | | | | | | | | | | | |
| **Clinical** | 78 | 75 | 96.2 | 78 | 75 | 96.2 | 76 | 97.4 | 2 | 75 | 1 | 1 | 0 |
| **Challenge** | 38 | 38 | 100.0 | 38 | 38 | 100.0 | 38 | 100.0 | 2 | 36 | 0 | 0 | 0 |
| **Combined** | 116 | 113 | **97.4** | 116 | 113 | 97.4 | 114 | **98.3** | 4 | 111 | 1 | 1 | 0 |
| ***Candida parapsilosis* ≤2 (S), 4 (I), ≥8 (R)** | | | | | | | | | | | | | |
| **Clinical** | 62 | 62 | 100.0 | 59 | 59 | 100.0 | 54 | 87.1 | 0 | 53 | 7 | 1 | 0 |
| **Challenge** | 10 | 10 | 100.0 | 10 | 10 | 100.0 | 8 | 80.0 | 0 | 9 | 2 | 0 | 0 |
| **Combined** | 72 | 72 | **100.0** | 69 | 69 | 100.0 | 62 | **86.1** | 0 | 62 | 9 | 1 | 0 |
| ***Candida tropicalis* ≤0.25 (S), 0.5 (I), ≥1 (R)** | | | | | | | | | | | | | |
| **Clinical** | 74 | 72 | 97.3 | 26 | 25 | 96.2 | 71 | 95.9 | 3 | 70 | 2 | 0 | 1 |
| **Challenge** | 7 | 7 | 100.0 | 2 | 2 | 100.0 | 7 | 100.0 | 0 | 7 | 0 | 0 | 0 |
| **Combined** | 81 | 79 | **97.5** | 28 | 27 | 96.4 | 78 | **96.3** | 3 | 77 | 2 | 0 | 1 |
| ***Candida guilliermondii* ≤2 (S), 4 (I), ≥8 (R)** | | | | | | | | | | | | | |
| **Clinical** | 19 | 17 | 89.5 | 19 | 17 | 89.5 | 17 | 89.5 | 0 | 18 | 2 | 0 | 0 |
| **Challenge** | 2 | 2 | 100.0 | 2 | 2 | 100.0 | 2 | 100.0 | 0 | 2 | 0 | 0 | 0 |
| **Combined** | 21 | 19 | **90.5** | 21 | 19 | 90.5 | 19 | **90.5** | 0 | 20 | 2 | 0 | 0 |
| ***Candida krusei* ≤0.25 (S), 0.5 (I), ≥1 (R)** | | | | | | | | | | | | | |
| **Clinical** | 67 | 66 | 98.5 | 67 | 66 | 98.5 | 67 | 100.0 | 0 | 67 | 0 | 0 | 0 |

| | Total | #EA | %EA | Eval EA Total | Eval EA # | Eval EA % | #CA | %CA | #R | #S | min | maj | vmj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Challenge** | 2 | 2 | 100.0 | 2 | 2 | 100.0 | 2 | 100.0 | 0 | 2 | 0 | 0 | 0 |
| **Combined** | 69 | 68 | **98.6** | 69 | 68 | 98.6 | 69 | **100.0** | 0 | 69 | 0 | 0 | 0 |

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

Essential agreement (EA) was calculated for when the VITEK 2 system results were within +/- two doubling dilutions of the reference method results. Evaluable results are those that are on-scale for both the reference method and VITEK 2 system or results in which an off-scale result is clearly more than two doubling dilutions from the on-scale result. Category agreement was calculated for when the VITEK 2 system result interpretations agreed exactly with the reference method result qualitative interpretations.

For *C. albicans* evaluated using VITEK 2 and autodilution, the overall EA and CA were both acceptable at 100% (Table 3). For *C. glabrata* evaluated using VITEK 2 and autodilution, the overall EA and CA were acceptable at 97.4% and 98.3%, respectively (Table 3), with one minor error (0.9% of 116 isolates) and one major error (0.9% of 111 isolates). For *C. guilliermondii* evaluated using VITEK 2 and autodilution, the overall EA and CA were both acceptable at 90.5% (Table 3), with two minor errors (10% of 20 isolates). For *C. krusei* evaluated using VITEK 2 and autodilution, the overall EA and CA were acceptable at 98.6% and 100%, respectively (Table 3), with no errors.

For *C. parapsilosis* evaluated using VITEK 2 and autodilution, the overall EA was acceptable at 100% (Table 3); however, the CA was 86.1% with nine of ten errors being minor errors (12.5%) and one major error (1.6%). According to the "Class II Special Control Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA, August 2009" (AST guidance), a CA of < 90% may be acceptable if the EA of the evaluable test results is very good and the majority of the discrepancies as minor discrepancies; therefore, the CA performance was considered acceptable.

For *C. tropicalis* evaluated using VITEK 2 and autodilution, the overall EA and CA were acceptable at 97.5% and 96.3%, respectively (Table 3), with two minor errors (2.5% of 81 isolates). There was one very major error (33.3% of 3 isolates), which is considered a random error due to the limited number of resistant isolates evaluated. To address the high very major error rate, the following statement is included as a footnote to the performance table in the device labeling:

> When evaluating VITEK 2 AST-YS Anidulafungin autodilution performance, there was a single very major error (VMJ) that resulted in an unacceptable VMJ rate of 33.3% (1/3) with *C. tropicalis*.

**Challenge Data –VITEK 2 and VITEK 2 Compact Manual Dilution**
The 80 challenge isolates were also evaluated with the manual dilution option of the VITEK 2 and VITEK 2 Compact systems (summarized in Table 4).

**Table 4.** Performance of *Candida* spp. for the Manual Dilution with the VITEK 2 and the VITEK 2 Compact Systems AST-YS Anidulafungin

| VITEK 2 Systems | Total | #EA | %EA | Eval Total | Eval EA # | Eval EA % | #CA | %CA | #R | #S | min | maj | vmj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Candida albicans* ≤0.25 (S), 0.5 (I), ≥1 (R)** | | | | | | | | | | | | | |
| **VITEK 2** | 21 | 21 | **100.0** | 0 | 0 | - | 21 | **100.0** | 0 | 21 | 0 | 0 | 0 |
| **VITEK 2 Compact** | 21 | 21 | 100.0 | 0 | 0 | - | 21 | 100.0 | 0 | 21 | 0 | 0 | 0 |
| ***Candida glabrata* ≤0.12 (S), 0.25 (I), ≥0.5 (R)** | | | | | | | | | | | | | |
| **VITEK 2** | 38 | 38 | **100.0** | 38 | 38 | 100.0 | 38 | **100.0** | 2 | 36 | 0 | 0 | 0 |
| **VITEK 2 Compact** | 38 | 38 | **100.0** | 38 | 38 | 100.0 | 38 | **100.0** | 2 | 36 | 0 | 0 | 0 |
| ***Candida parapsilosis* ≤2 (S), 4 (I), ≥8 (R)** | | | | | | | | | | | | | |
| **VITEK 2** | 10 | 10 | **100.0** | 10 | 10 | 100.0 | 9 | **90.0** | 0 | 9 | 1 | 0 | 0 |
| **VITEK 2 Compact** | 10 | 10 | **100.0** | 10 | 10 | 100.0 | 8 | **80.0** | 0 | 9 | 2 | 0 | 0 |
| ***Candida tropicalis* ≤0.25 (S), 0.5 (I), ≥1 (R)** | | | | | | | | | | | | | |
| **VITEK 2** | 7 | 7 | **100.0** | 3 | 3 | 100.0 | 7 | **100.0** | 0 | 7 | 0 | 0 | 0 |
| **VITEK 2 Compact** | 7 | 7 | **100.0** | 4 | 4 | 100.0 | 7 | **100.0** | 0 | 7 | 0 | 0 | 0 |
| ***Candida guilliermondii* ≤2 (S), 4 (I), ≥8 (R)** | | | | | | | | | | | | | |
| **VITEK 2** | 2 | 2 | **100.0** | 2 | 2 | 100.0 | 2 | **100.0** | 0 | 2 | 0 | 0 | 0 |
| **VITEK 2 Compact** | 2 | 2 | **100.0** | 2 | 2 | 100.0 | 2 | **100.0** | 0 | 2 | 0 | 0 | 0 |
| ***Candida krusei* ≤0.25 (S), 0.5 (I), ≥1 (R)** | | | | | | | | | | | | | |
| **VITEK 2** | 2 | 2 | **100.0** | 2 | 2 | 100.0 | 2 | **100.0** | 0 | 2 | 0 | 0 | 0 |
| **VITEK 2 Compact** | 2 | 2 | **100.0** | 2 | 2 | 100.0 | 2 | **100.0** | 0 | 2 | 0 | 0 | 0 |

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

Essential agreement (EA) was calculated for when the VITEK 2 system results were within +/- two doubling dilutions of the reference method results. Evaluable results are those that are on-scale for both the reference method and VITEK 2 system or results in which an off-scale result is clearly more than two doubling dilutions from the on-scale result. Category agreement was calculated for when the VITEK 2 system result interpretations agreed exactly with the reference method result qualitative interpretations.

The EA and CA for *C. albicans, C. glabrata*, *C. tropicalis*, *C. guilliermondii*, and *C. krusei* challenge set were 100% with the manual dilution option and the VITEK 2 systems, which is acceptable.

For *C. parapsilosis* and the VITEK 2 manual dilution method, the overall EA was acceptable at 100% for both VITEK 2 and VITEK 2 Compact and the overall CA for VITEK 2 was 90% which is acceptable (Table 4); however, the overall CA was 80% for VITEK 2 Compact which was caused by two minor errors out of ten values (20% error rate). The AST guidance indicates a CA of < 90% may be acceptable if the EA of the evaluable test results is very good and the majority of the discrepancies as minor discrepancies; therefore, the CA performance was considered acceptable. There were no major errors or very major errors obtained with any of the indicated organisms tested when applying the current FDA-recognized breakpoints.

As required under 511A(b)(2)(C)(ii)(I) of the Federal Food, Drug and Cosmetic Act, the following statement was added to the package insert 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.*

**Resistant Strains**

For *C. albicans*, *C. parapsilosis, C. guilliermondii* and *C. krusei,* no resistant isolates were available for evaluation during clinical or challenge testing. In addition, for *C. glabrata* and *C. tropicalis* there were limited resistant isolates available for evaluation during clinical or challenge testing. The sponsor included the following limitation in the device labeling:

*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:*
*• Anidulafungin (ani01n): Candida spp.*

**MIC Trends**:

A trending analysis was conducted using the combined data (clinical and challenge) obtained from the VITEK 2 autodilution method for each organism group. This trending calculation takes into account 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.

Organism groups for which 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.

**Table 5.** Trending for *Candida* spp. with Anidulafungin and the VITEK 2 Automatic Dilution

| Organism | Total Evaluable for Trending | ≥ 1 Dilution lower No. (%) | Exact No. (%) | ≥ 1 Dilution Higher No. (%) | Percent Difference (CI) | Trending Noted |
|---|---|---|---|---|---|---|
| *Candida albicans* | 17 | 11 (64.7) | 2 (11.8) | 4 (23.5) | -41.2% (-64.0, -7.8) | Yes |
| *Candida glabrata* | 116 | 18 (15.5) | 40 (34.5) | 58 (50.0) | 34.5% (22.7, 45.0) | Yes |
| *Candida parapsilosis* | 72 | 17 (23.6) | 44 (61.1) | 11 (15.3) | -8.3% (-21.1, 4.7) | No |
| *Candida tropicalis* | 46 | 19 (41.3) | 6 (13.0) | 21 (45.7) | 4.4% (-15.4, 23.6) | No |
| *Candida guilliermondii* | 21 | 7 (33.3) | 11 (52.4) | 3 (14.3) | -19.0% (-42.3, 6.9) | No |
| *Candida krusei* | 69 | 7 (10.1) | 30 (43.5) | 32 (46.4) | 36.2% (21.6, 49.0) | Yes |

A trend toward lower MIC values was observed for *C. albicans* when compared to the CLSI broth microdilution reference method, as summarized in Table 5. The following statement is included as a footnote to the performance table in the device labeling to address the observed trending:

> *VITEK 2 Anidulafungin MIC values for C. albicans tended to be in exact agreement or at least one doubling dilution lower than the reference MIC values.*

A trend toward higher MIC values was observed for *C. glabrata* and *C. krusei* when compared to the CLSI broth microdilution reference method, as summarized in Table 5. The following statement is included as a footnote to the performance table in the device labeling to address the observed trending:

> *Anidulafungin MIC values for C. glabrata and C. krusei tended to be in exact agreement or at least one doubling dilution higher than the reference MIC values*.

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 susceptibility interpretive criteria for Anidulafungin are as listed in Table 6.

**Table 6.** FDA Recognized Interpretive Criteria for Anidulafungin

| Pathogen | Minimum Inhibitory Concentrations (µg/mL) [1] | | |
|---|---|---|---|
| | S | I | R |
| *Candida albicans* | ≤0.25 | 0.5 | ≥1 |
| *Candida glabrata* | ≤0.12 | 0.25 | ≥0.5 |
| *Candida guilliermondii* | ≤2 | 4 | ≥8 |
| *Candida krusei* | ≤0.25 | 0.5 | ≥1 |
| *Candida parapsilosis* | ≤2 | 4 | ≥8 |
| *Candida tropicalis* | ≤0.25 | 0.5 | ≥1 |

S = Susceptible; I = Intermediate; R = Resistant

[1] According to FDA STIC Website
https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm

## VIII Proposed Labeling:

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 incorporated by reference a breakpoint change protocol that was reviewed and accepted by FDA in submission K230864 cleared on July 5, 2023. The referenced 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/development-resources/fda-recognized-antimicrobial-susceptibility-test-interpretive-criteria). The referenced protocol outlined the specific procedures and acceptance criteria that bioMérieux intends to use to evaluate the bioMérieux VITEK 2 AST-Yeast Anidulafungin (≤ 0.015 - ≥ 8 µg/mL) when revised breakpoints for Anidulafungin 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 VITEK 2 AST-Yeast Anidulafungin 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.