

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

K101566

B. Purpose for Submission:

To obtain a substantial equivalence determination for this premarket notification for VITEK 2 Yeast - Caspofungin

C. Measurand:

Caspofungin concentrations on VITEK 2 AST Yeast Caspofungin card: 1, 4, and 8 µg/mL. The MIC result range of the card is $\leq 0.25 - 2$ µg/mL.

D. Type of Test:

Automated quantitative or qualitative antifungal susceptibility test of *Candida* species to Caspofungin

E. Applicant:

BioMerieux, Inc.

F. Proprietary and Established Names:

VITEK[®] 2 Yeast Caspofungin

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
NGZ, LRG	Class II	21 CFR 866.1640	83 - Microbiology

H. Intended Use:

1. Intended use:

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 in the Online

Product Information.

2. Indication(s) for use:

VITEK® 2 Yeast Caspofungin is designed for antifungal susceptibility testing of *Candida* species. VITEK® 2 Yeast Caspofungin 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 antifungal agents. Caspofungin has been shown to be active against most isolates of the following the microorganisms *in vitro* and in clinical infections according to the FDA label for the antifungal:

Candida albicans, *Candida glabrata*, *Candida guilliermondii*, *Candida krusei*, *Candida parapsilosis*, and *Candida tropicalis*

The VITEK® Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK 2 and VITEK 2 Compact 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 agalactiae*, *S. pneumoniae* and clinically significant yeast.

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

For use with the VITEK 2 and VITEK 2 Compact Systems

I. Device Description:

VITEK® 2 Yeast panels are designed for testing *Candida species*. The panels contain concentrations of antifungal drugs equivalent by efficacy to standard method concentrations in µg/mL dried with microbiological media. Isolated colonies of *Candida* species are diluted to a standardized concentration in 0.45% saline before being used to rehydrate the antifungal drug concentration in the card. The VITEK® 2 automatically fills, seals and places the card into the incubator/reader. The VITEK® 2 monitors the growth of each well in the card over a defined period of time (up to 36 hours). The computer determines when a well demonstrates growth based on attenuation of light measured by an optical scanner. At the completion of the incubation cycle a report is generated that contains the MIC value along with the interpretive category result for each antifungal contained on the card. The final concentration in the card of the inoculum is ~ 10⁶ CFU/ml. A final dilution of organism can be performed using a manual procedure or an automated feature but there are no manual readings possible.

J. Substantial Equivalence Information:

1. Predicate device name(s):

VITEK[®]_Yeast Fluconazole

2. Predicate K number(s):

k061945

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative and qualitative susceptibility for colonies of <i>Candida spp.</i>	Same
Inoculation and test organism	Isolated colonies of <i>Candida spp.</i>	Same
Instrument	Test are run on both the VITEK [®] 2 and VITEK [®] 2 Compact Systems	Same
Test Methodology	Automated yeast antifungal susceptibility test for use with the VITEK [®] 2 and VITEK [®] 2 Compact Systems to determine in vitro susceptibility of <i>Candida</i> species.	Same
Incubation	35° C	Same

Differences		
Item	Device	Predicate
Antifungal	The antifungal agent is Caspofungin- Concentrations of antifungal in the test wells of the VITEK [®] AST card and the analysis algorithms are unique for each specific antifungal	The antifungal agent is Fluconazole- Concentrations of antifungal in the test wells of the VITEK [®] AST card and the analysis algorithms are unique for each specific antifungal

K. Standard/Guidance Document Referenced (if applicable):

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”

CLSI standard M27-A3 "Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard".

L. Test Principle:

The principle of the VITEK® 2 AST cards is based on the broth microdilution minimum inhibitory concentration technique. The VITEK® 2 AST card is essentially a miniaturized, abbreviated and automated version of the doubling dilution technique for MICs determined by the microdilution method. The automated growth-based detection uses attenuation of light measured by an optical scanner. Each AST card contains 64 microwells. A control well containing only microbiological culture medium is resident on all cards, with the remaining wells containing premeasured amounts of specific antimicrobials combined with culture medium. The organism suspension to be tested must be diluted to a standardized concentration in 0.45% saline before being used to rehydrate the antimicrobial medium within the card. The card is then filled, sealed, and placed into the instrument incubator/reader, either automatically (as with VITEK® 2 60 or VITEK® 2 XL) or manually (as with VITEK® 2 Compact). The instrument monitors the growth of each well in the card over a defined period of time (up to 18 hours for bacteria or up to 36 hours for yeast). At the completion of the incubation cycle, MIC values (or test results, as appropriate) are determined for each antimicrobial contained on the card.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

For VITEK 2 System, reproducibility was determined through testing ten isolates (6 *Candida parapsilosis*, 3 *C. guilliermondii*, and 1 *C. lusitaniae*) at three external clinical sites in triplicate over 3 days. The testing was performed using both inoculation options: the manual dilution method and the automated dilution method.

For the reproducibility calculations, off-scale values are handled in two ways; "best case" and "worst case" scenarios. Best case calculation for reproducibility assumes the off-scale result is within one well from the mode MIC value. Worst case calculation for reproducibility assuming the off-scale result is greater than one well from the mode MIC value. There were no off-scale results in this study. So, only one value for overall reproducibility is reported for each reading method.

Results were reported and analyzed for each method separately. For Automated dilution, the reproducibility values were 97.8%, 93.7% for best case and worst case scenarios, respectively. For Manual dilution, the reproducibility values were 100%, 95.6% for best case and worst case scenarios, respectively.

For the VITEK 2 Compact System, reproducibility was also evaluated using the same protocol and set of isolates used for the VITEK 2 System. Only manual dilution data

is available for VITEK 2 Compact System since the automatic dilution is not an option on this instrument. A reproducibility of 100% was obtained for best case and worst case scenarios since there were no off-scale results.

b. *Linearity/assay reportable range:*

Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

Quality Control testing was performed on each day of clinical testing using two quality control ATCC strains recommended in the CLSI standard M27. The following table represents the frequency of the results in both the reference method and the VITEK 2 Yeast Caspofungin cards and the acceptable range.

Quality control was performed using the VITEK 2 Yeast Caspofungin card and testing was done by both the manual dilution and the automated dilution method (for VITEK 2 System) and by the manual dilution method only (for VITEK 2 Compact System). Testing was performed a minimum of twenty times by automatic and manual dilution.

As shown in the tables below, some of the QC results obtained with the reference method for *C. parapsilosis* were one doubling dilution above the acceptable range. However, all VITEK QC results were within acceptable range. QC results obtained with the reference method for *C. krusei* were acceptable and the VITEK QC values were within acceptable range by both manual dilution and Auto Dilution for both strains.

Quality Control Results with the VITEK 2 System

Organism	Concentration (µg/mL)	Reference (24 hours)	VITEK (24 hours)	
		Auto Dilution, Manual Dilution	Auto Dilution	Manual Dilution
<i>Candida krusei</i> ATCC 6258	≤0.0156			
	0.03			
	0.06			
	0.125			
	0.125-1 µg/mL (24 hours)	9, 8	103	104
	0.25	61, 59		
	0.5	43, 37		
	1			
	2			
	4			
	8			
	≥16			

<i>Candida parapsilosis</i> ATCC 22019 0.25-1 µ/mL (24 hours)	≤0.03			
	0.06			
	0.12			
	0.25	2, 2	52	63
	0.5	14, 14	55	39
	1	85, 80	2	
	2	8, 6		
	4			
	8			
	≥16			

Quality Control Results with the VITEK 2 Compact System

Organism	Concentration (µg/mL)	Reference (24 hours) 24 hours	VITEK (24 hours) Manual Dilution
<i>Candida krusei</i> ATCC 6258 0.125-1 µg/mL (24 hours)	≤0.0156		
	0.03		
	0.06		
	0.125		
	0.25	1	60
	0.5	25	
	1	34	
	2		
	4		
	8		
≥16			
<i>Candida parapsilosis</i> ATCC 22019 0.25-1 µ/mL (24 hours)	≤0.03		
	0.06		
	0.12		
	0.25		26
	0.5	3	33
	1	45	1
	2	12	
	4		
	8		
	≥16		

At least one Quality control organism with the reference test was on-scale on all days. Quality Control results for the VITEK 2 system using either inoculation dilution method demonstrated that the VITEK 2 system could produce the expected quality control results.

The DensiCheck instrument was used to standardize the inoculum with instrument standardization weekly with acceptable performance at all times. Verification of the DensiCheck instrument was performed prior to the study on five instruments.

d. *Detection limit:*

Not applicable.

e. *Analytical specificity:*

Not applicable

f. *Assay cut-off:*

Not applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The performance of the VITEK 2 System was established through a clinical study which was conducted at three sites (2 external, 1 internal). Testing was done on 755 fresh clinical isolates and 98 challenge isolates. Challenge isolates were also tested on the VITEK 2 Compact.

In total, 856 clinical and challenge isolates were tested by VITEK® 2 Yeast Caspofungin with the VITEK® 2 System. The VITEK® 2 results were compared to the reference values that were determined by the CLSI broth microdilution reference method tested at each study site. Of the total 853 isolates have VITEK® 2 AST results available; three isolates did not grow in the VITEK® 2 card.

Since only susceptible breakpoints have been defined for Caspofungin (i.e. no intermediate and resistant categories), the following limitation will be taken for this product:

“The ability of the AST card to detect resistance with the following combination(s) is unknown because Caspofungin-resistant strains were not available at the time of comparative testing for *Candida albicans*, *C. glabrata*, *C. guilliermondii*, *C. krusei*, *C. parapsilosis*, and *C. tropicalis*.”

Results for the 853 clinical and challenge isolates are summarized in the tables below.

Essential Agreement

Number of Isolates			Major Errors	Very Major Errors	Overall Essential Agreement
Total	S	NS	No. (%)	No. (%)	%

853	850	3	0 (0.0)	2 (66.7)	99.5
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Category Agreement

Number of Isolates			Major Errors	Very Major Errors	Overall Essential Agreement
Total	S	NS	No. (%)	No. (%)	%
853	850	3	0 (0.0)	2 (66.7)	99.8

VITEK® 2 Yeast Caspofungin performance with the VITEK® 2 Compact was evaluated with the same 98 isolate challenge set that was tested with the VITEK® 2 System. The challenge set was evaluated at one external site. Results from the VITEK® 2 Yeast Caspofungin were compared to the expected reference results.

All of the challenge organisms grew in the VITEK® 2 Yeast Caspofungin test. Results for the 98 challenge isolates are summarized in the tables below.

VITEK® 2 Compact: Essential Agreement

Number of Isolates			Major Errors	Very Major Errors	Overall Essential Agreement
Total	S	NS	No. (%)	No. (%)	%
98	97	1	0 (0.0)	0 (0.0)	100.0

VITEK® 2 Compact: Category Agreement

Number of Isolates			Major Errors	Very Major Errors	Overall Category Agreement
Total	S	NS	No. (%)	No. (%)	%
98	97	1	0 (0.0)	0 (0.0)	100.0

Caspofungin - Summary Data for Both Challenge and Clinical Data (24 hours)

Clinical Data

Organism Group	Total Tested	# EA	% EA	Total Evaluable	# EA of Evaluable	% EA of Evaluable	# CA	% CA	# NS	# vmj	# maj	# min
<i>C. albicans</i>	452	451	99.8	2	1	50.0	452	100.0	0	0	0	0
<i>C. dubliniensis</i>	3	3	100.0	0	0		3	100.0	0	0	0	0
<i>C. glabrata</i>	128	126	98.4	4	3	75.0	126	98.4	2	2	0	0
<i>C. guilliermondii</i>	7	7	100.0	3	3	100.0	7	100.0	0	0	0	0
<i>C. haemulonii</i>	1	1	100.0	1	1	100.0	1	100.0	0	0	0	0
<i>C. kefyr</i>	8	8	100.0	0	0		8	100.0	0	0	0	0
<i>C. krusei</i>	24	24	100.0	0	0		24	100.0	0	0	0	0
<i>C. lusitaniae</i>	14	14	100.0	4	4	100.0	14	100.0	0	0	0	0
<i>C. parapsilosis</i>	75	74	98.7	42	42	100.0	75	100.0	0	0	0	0
<i>C. pelliculosa</i>	1	1	100.0	0	0		1	100.0	0	0	0	0
<i>C. rugosa</i>	1	1	100.0	0	0		1	100.0	0	0	0	0
<i>C. tropicalis</i>	41	41	100.0	0	0		41	100.0	0	0	0	0
TOTAL	755	751	99.5	56	54	96.4	753	99.7	2	2	0	0

Challenge Data

<i>C. albicans</i>	28	28	100.0	0	0		28	100.0	0	0	0	0
<i>C. glabrata</i>	50	50	100.0	0	0		50	100.0	1	0	0	0
<i>C. guilliermondii</i>	2	2	100.0	1	1	100.0	2	100.0	0	0	0	0
<i>C. krusei</i>	6	6	100.0	0	0		6	100.0	0	0	0	0
<i>C. parapsilosis</i>	7	7	100.0	5	5	100.0	7	100.0	0	0	0	0
<i>C. tropicalis</i>	5	5	100.0	0	0		5	100.0	0	0	0	0
TOTAL	98	98	100.0	6	6	100.0	98	100.0	1	0	0	0

Clinical and Challenge Combined

All organisms	853	849	99.5	62	60	96.8	851	99.8	3	2	0	0
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*NS= Non-Susceptible

Caspofungin - Summary of Essential and Category Agreement Results for Challenge and Clinical Strains

Organism Group	Source	Total Tested	# EA	% EA	Total Evaluable	# EA of Evaluable	% EA of Evaluable	# CA	% CA	# NS*	# vmj	# maj	# min
<i>C. albicans</i>	Clinical	452	451	99.8	2	1	50.0	452	100.0	0	0	0	0
	Challenge	28	28	100.0	0	0	0.0	28	100.0	0	0	0	0
	Both	480	479	99.8	2	1	50.0	480	100.0	0	0	0	0
<i>C. dubliniensis</i>	Clinical	3	3	100.0	0	0	0.0	3	100.0	0	0	0	0
<i>C. glabrata</i>	Clinical	128	126	98.4	4	3	75.0	126	98.4	2	2	0	0
	Challenge	50	50	100.0	0	0	0.0	50	100.0	1	0	0	0
	Both	178	176	98.9	4	3	75.0	176	98.9	3	2	0	0
<i>C. guilliermondii</i>	Clinical	7	7	100.0	3	3	100.0	7	100.0	0	0	0	0
	Challenge	2	2	100.0	1	1	100.0	2	100.0	0	0	0	0
	Both	9	9	100.0	4	4	100.0	9	100.0	0	0	0	0
<i>C. haemulonii</i>	Clinical	1	1	100.0	1	1	100.0	1	100.0	0	0	0	0
<i>C. kefyr</i>	Clinical	8	8	100.0	0	0	0	8	100.0	0	0	0	0
<i>C. krusei</i>	Clinical	24	24	100.0	0	0	0	24	100.0	0	0	0	0
	Challenge	6	6	100.0	0	0	0	6	100.0	0	0	0	0
	Both	30	30	100.0	0	0	0	30	100.0	0	0	0	0
<i>C. lusitaniae</i>	Clinical	14	14	100.0	4	4	100.0	14	100.0	0	0	0	0
<i>C. parapsilosis</i>	Clinical	75	74	98.7	42	42	100.0	75	100.0	0	0	0	0
	Challenge	7	7	100.0	5	5	100.0	7	100.0	0	0	0	0
	Both	82	81	98.8	47	47	100.0	82	100.0	0	0	0	0

<i>C. pelliculosa</i>	Clinical	1	1	100.0	0	0	0	1	100.0	0	0	0	0
<i>C. rugosa</i>	Clinical	1	1	100.0	0	0	0	1	100.0	0	0	0	0
<i>C. tropicalis</i>	Clinical	41	41	100.0	0	0	0	41	100.0	0	0	0	0
	Challenge	5	5	100.0	0	0	0	5	100.0	0	0	0	0
	Both	46	46	100.0	0	0	0	46	100.0	0	0	0	0
All Organisms	Clinical	755	751	99.5	56	54	96.4	753	99.7	2	2	0	0
	Challenge	98	98	100.0	6	6	100.0	98	100.0	1	0	0	0
	Both	853	849	99.5	62	60	96.8	851	99.8	3	2	0	0

*NS= Non-Susceptible

The performance of the VITEK 2 Compact System was evaluated through a challenge study which was conducted at one external site. Testing was done on 98 challenge isolates.

Caspofungin - Summary for Challenge Data in VITEK 2 Compact

Organism Group	Total Tested	# EA	% EA	Total Evaluable	# EA of Evaluable	% EA of Evaluable	# CA	% CA	# NS*	# vmj	# maj	# min
<i>C. albicans</i>	28	28	100.0	0	0	-	28	100.0	0	0	0	0
<i>C. glabrata</i>	50	50	100.0	0	0	-	50	100.0	1	0	0	0
<i>C. guilliermondii</i>	2	2	100.0	2	2	100.0	2	100.0	0	0	0	0
<i>C. krusei</i>	6	6	100.0	0	0	-	6	100.0	0	0	0	0
<i>C. parapsilosis</i>	7	7	100.0	7	7	100.0	7	100.0	0	0	0	0
<i>C. tropicalis</i>	5	5	100.0	0	0	-	5	100.0	0	0	0	0
TOTAL	98	98	100.0	9	9	100.0	98	100.0	1	0	0	0

*NS= Non-Susceptible

b. Matrix comparison:

Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical specificity:

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

Not Applicable

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR section 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.