

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

A. 510(k) Number:

K061945.

B. Purpose for Submission:

For testing *Candida species* for fluconazole antifungal susceptibility testing.

C. Measurand:

Fluconazole at 1-64 µg/mL

D. Type of Test:

Growth based quantitative and qualitative susceptibility test

E. Applicant:

bioMerieux, Inc.

F. Proprietary and Established Names:

Vitek®2 Yeast Fluconazole.

G. Regulatory Information:

1. Regulation section:
866.1645 Fully automated short-term incubation cycle antimicrobial susceptibility Test
866.1640 Antimicrobial Susceptibility Test
2. Classification:
Class II
3. Product code:
NGZ Susceptibility testing -antifungal

4. Panel:

Microbiology (83)

H. Intended Use:

1. Intended use(s):

Fluconazole at 1-64 µg/mL is intended for antifungal susceptibility testing of *Candida species* on the Vitek® 2 Fungal Susceptibility Card 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:

Fluconazole at 1-64 µg/mL is indicated for the testing of *Candida species*.

3. Special conditions for use statement(s):

Prescription use only.

4. Special instrument requirements:

Not Applicable

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):

Sensititre® YeastOne

2. Predicate K number(s):

K991810

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative and qualitative susceptibility for colonies of <i>Candida spp.</i>	Same
Incubation	35° C	Same
Inoculation	Isolated colonies of <i>Candida spp.</i>	Same
Differences		
Item	Device	Predicate
Technology	Automated growth based detection using attenuation of light measured by optical scanner.	Broth micro dilution – growth based with colorimetric growth indicator for manual readings
Format	VITEK® 2 AST test card with dried antifungals	Micro tray with dried antifungals
Medium	VITEK® 2 Yeast Base Broth	Sensititre® yeast susceptibility inoculum broth
Time to results	10 to 36 hours	24-25 hours

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-A2 “Reference Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts; Approved Standard”.

L. Test Principle:

Automated growth based detection using attenuation of light measured by an optical scanner.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was conducted at three sites on ten yeast isolates with testing performed over three days in triplicate. The testing was performed using both the manual dilution mode and the automated dilution mode. The reproducibility was >95% with +/- one dilution observations.

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 on the 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 Fluconazole cards and the acceptable range. Quality control was performed on the Vitek®2 on the Vitek®2 Yeast Fluconazole card using both the manual dilution and the automated method.

ORGANISM	Conc in ug/ml	Reference		Conc in ug/ml	Auto dilution VITEK® 2	Manual dilution VITEK® 2
		24 h	48 h			
	0.5					
<i>C. krussi</i> ATCC 6258 Range 24-h-8-64 ug/ml 48h-16-128 µg/mL	1			≤ 1		
	2			2		
	4			4		
	8	29		8	2	3
	16	105		16	50	67
	32	10	74	32	30	3
	≥ 64	2	82	≥ 64		1
<i>C. parapsilosis</i> ATCC 22019 Range 0.5-4 ug/ml	0.5					
	1	37	42	≤ 1	4	34
	2	116	121	2	76	39
	4			4		
	8			8		
	16			16		
	32			32		

At least one Quality control organism was in control in the reference on all days. Quality Control results for the Vitek®2 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:

Performance was established on the VITEK® 2 System for *Candida spp.* at multiple clinical laboratories. The CLSI reference method as described in the CLSI document M27 “Method for Broth Dilution Antifungal Susceptibility Testing of Yeasts” was compared to the Vitek® 2 result. A total of 346 isolates of *Candida species* were tested on the Vitek®2 using the automated inoculation dilution feature. For the evaluation, the 46 *C. krusei* tested were not used in the analysis since these are reported as resistant to fluconazole regardless of the MIC achieved. An additional 75 challenge isolates of *Candida spp.* were tested using the automated inoculum dilution method and added to the data for analysis.

EA was calculated when the results for the reference method and the Vitek® 2 were within +/- two doubling dilutions of the antifungal drug. Purity checks were performed daily during the clinical study. Clinical results on the Vitek®2 were read when the instrument determined the positive control was growing sufficiently to obtain a reading. In this study this occurred as early as 10 hours and a maximum time of 31 hours with an average of 13.5 hours. The following table presents the performance of the Vitek®2 as compared to the reference method when read after both 24 hour and 48 hour readings.

	total	+/- 2 dilutions		+/- 1 dilution		%CA	#R	min	maj	vmj
		# EA	% EA	# EA	% EA					
Fluconazole										
Candida spp. 24 h	375	366	97.6	360	96.0	96.8	12	12	0	0
Candida spp. 48h	375	364	97.1	342	91.2	86.7	14	49	0	1

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates

maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies

An evaluation was also performed using the +/- one dilution for EA to the reference method. The CA would be the same for either method of comparison. The 24 hour reading of the reference method agreed very well with the Vitek®2 results with either the +/- 1 dilution or the +/- 2 dilutions evaluation. There was only one additional vmj with the 48 reference readings but as shown the number of minor errors did increase.

The challenge data was also performed using the manual method of inoculation preparation. The comparison between the data generated with the challenge, reproducibility and quality control using both inoculation methods was very good with no apparent trending. The no growth rate was $\leq 5\%$.

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:

The expected range for Quality Control testing and the interpretive criteria are the same as what is currently recommended and is included in the package insert.

Fluconazole – interpretive criteria for *Candida species*.

Susceptible $\leq 8 \mu\text{g/mL}$; S- Dose Dependent 16-32 $\mu\text{g/mL}$; Resistant $\geq 64 \mu\text{g/mL}$

Fluconazole for *C. krusei* will be reported as resistant with the following comment generated automatically

“Fluconazole is considered resistant to *Candida krusei*”

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.