

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

A. 510(k) Number:

K082534

B. Purpose for Submission:

AST test for *Candida albicans*, *C. glabrata*, *C. krusei*, *C. parapsilosis* and *C. tropicalis*.

C. Measurand:

Voriconazole 0.002 – 32µg/mL

D. Type of Test:

Quantitative AST growth based detection

E. Applicant:

AB bioMerieux (former AB BIODISK)

F. Proprietary and Established Names:

Etest® for Antimicrobial Susceptibility Testing

G. Regulatory Information:

1. Regulation section:
866.1640 Antimicrobial Susceptibility Test
2. Classification:
II
3. Product code:
NGZ
4. Panel:
83 Microbiology

H. Intended Use:

1. Intended use(s):
Etest® is an agar-based gradient technique for quantitative antifungal susceptibility testing of *Candida*. It uses a predefined concentration gradient of the specific antifungal agent to determine the Minimum Inhibitory Concentration (MIC) in ug/mL inhibiting the growth of the test organism under defined conditions.

2. Indication(s) for use:
This submission is for Etest® Voriconazole for MIC determination across 0.002 – 32 µg/mL with *Candida albicans*, *Candida glabrata*, *Candida krusei*, *Candida parapsilosis*, and *Candida tropicalis*.
3. Special conditions for use statement(s):
For prescription use
4. Special instrument requirements:
Manual readings only

I. Device Description:

Etest® consists of a thin, inert and non-porous plastic strip, 5mm wide and 60 mm long. One side of the strip carries a two-letter code designating the identity of the antifungal agent and is calibrated with MIC values in terms of ug/mL, a predefined and exponential gradient of the dried and established antifungal agent which covers a continuous concentration range across two-fold dilutions.

J. Substantial Equivalence Information:

1. Predicate device name(s):
Etest
2. Predicate 510(k) number(s):
K040560
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative susceptibility to antifungal agents for <i>Candida</i> species	Same
Incubation	35°	Same
Inoculation	Isolated colonies of <i>Candida</i> species	Same
Result	MIC	Same

Differences		
Item	Device	Predicate
Antibiotic	Voriconazole	Fluconazole Itraconazole Flucytosine

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”; Reference Method for Broth Dilution Antifungal Susceptibility of Yeasts: Third Informational Supplement (M27-S3)

L. Test Principle:

The Etest® gradient technology is based on a combination of the concepts of dilution and diffusion test methods for susceptibility testing. Etest® is processed like disc diffusion test (i.e. 0.5 McFarland suspension inoculum), but directly quantifies antimicrobial susceptibility in terms of discrete MIC values. When the Etest® strip containing the antibiotic is applied to an inoculated agar plate, the antifungal agent is immediately released from the plastic surface into the agar. A predefined, continuous gradient of antifungal concentrations is created and maintained directly underneath the strip. After incubation whereby growth becomes visible, a symmetrical inhibition ellipse centered along the strip will be seen. The inhibition zone edge intersects the strip of the MIC value in µg/mL of the agent.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Precision/Reproducibility was determined by testing 26 *Candida* species one time at each of three sites. The mode was determined and then the reproducibility was calculated based on plus or minus one well of the mode. The reproducibility for 24 hours and 48 hours was >95% (77/78).

b. *Linearity/assay reportable range:*

Not applicable

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

Quality control was performed each day of testing on both the reference method and the test method at four testing sites.

Voriconazole Quality Control

Organism	Concentration (µg/mL)	Reference	Etest®	
		48 hr	24 hr	48 hr
<i>C. krusei</i> ATCC 6258 FDA/CLSI (48 hrs) 0.12-1 µg/mL	0.064			
	0.125		9	
	0.25	42	46	25
	0.5	23	21	54
	1			1

A 0.5 McFarland ($1-5 \times 10^6$ yeast cells per mL) is used to determine the correct inoculum. Colony counts were performed periodically at each site to demonstrate that the inoculum procedure results were in the expected CFU/ml.

Candida krusei ATCC 6258

The reference method and Etest were both within range. The mode is the same as that of the 48 hours reference method at 24 hours but one dilution higher at 48 hours.

The no growth rate was <10%.

- 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:*

Clinical laboratory studies were performed at three or more clinical laboratories and compared to the CLSI broth micro-dilution method as described in M27 A2. Seventy four challenge strains were tested at one site and were included in the evaluation. Both tests were incubated in ambient air at 35°C. The reference method was read at 48 hours and the Etest® was read at 24 hours and confirmed at 48 hours. A two concentration allowance was used for this comparison due to the difficulty in reading the Essential Agreement (EA) for both the reference method and the Etest®. Category Agreement (CA) was determined based on the interpretation of each test.

Summary Table for Etest® 24 hr vs. Reference 48 hrs ($\leq 1, 2, \geq 4$)

	Total	EA #	% EA (\pm two 2-fold dil)	CA	% CA	NS	min	maj	vmj
Clinical	633	615	97.2	616	98.2	23	11	0	0
Challenge	74	73	98.6	69	98.6	5	1	0	0
Combined	707	688	97.3	685	98.3	28	12	0	0

Summary Table for Etest® 48 hr vs Reference 48 hrs ($\leq 1, 2, \geq 4$)

	Total	EA #	% EA (\pm two 2-fold dil)	CA	% CA	NS	min	maj	vmj
Clinical	633	613	96.8	608	97.1	23	15	3	0
Challenge	74	74	100	70	100	5	0	0	0
Combined	707	687	97.2	678	97.4	28	15	3	0

EA-Essential Agreement
CA- Category Agreement
NS- Non-susceptible

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

The three maj errors at 48 hours were due to *C. glabrata*, resulting in a maj error rate of 2.5% (Etest: 1; reference: 0.25, 0.5, to 1) and a combined overall EA of 93.2%, 91.8% CA. The overall maj error rate was 0.5% (3/610) which was acceptable. There were no maj or vmj at 24 hours.

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:
 $\leq 1, 2, \geq 4$ $\mu\text{g/mL}$

N. Proposed Labeling:

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

O. Conclusion:

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