

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

**A. 510(k) Number:**

k121002

**B. Purpose for Submission:**

To obtain clearance for the addition of ceftaroline at concentrations 0.002 – 32 µg/mL to the Etest strip

**C. Measurand:**

Ceftaroline 0.002 – 32µg/mL

**D. Type of Test:**

Quantitative AST growth based detection

**E. Applicant:**

bioMérieux, Inc

**F. Proprietary and Established Names:**

Etest<sup>®</sup> Ceftaroline (0.002 – 32 µg/mL)

**G. Regulatory Information:**

1. Regulation section:

866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

II

3. Product code:

JWY - Manual Antimicrobial Test Systems

4. Panel:

83 Microbiology

## H. Intended Use:

### 1. Intended use(s):

Etest® is a quantitative technique for determining the antimicrobial susceptibility testing of Gram-negative and Gram positive aerobic bacteria such as *Enterobacteriaceae*, *Pseudomonas*, *Staphylococcus* and *Enterococcus* species and fastidious bacteria, such as anaerobes, *N. gonorrhoeae*, *S. pneumoniae*, *Streptococcus* and *Haemophilus* species. The system comprises a predefined antibiotic gradient which is used to determine the Minimum Inhibitory Concentration (MIC), in µg/mL, of different antimicrobial agents against microorganisms as tested on agar media using overnight incubation.

This submission is for the addition of the antimicrobial ceftaroline at concentrations of 0.002 – 32 µg/mL to the Etest® product. Ceftaroline has been shown to be active *in vitro* against most strains of the microorganism listed below, as described in the FDA-approved label for this antimicrobial agent.

#### Active *in vitro* and in clinical infections

##### Skin Infections

*Staphylococcus aureus* (including methicillin-susceptible and -resistant isolates)

### 2. Indication(s) for use:

Etest® is a quantitative technique for determining the antimicrobial susceptibility testing of Gram-negative and Gram positive aerobic bacteria such as *Enterobacteriaceae*, *Pseudomonas*, *Staphylococcus* and *Enterococcus* species and fastidious bacteria, such as anaerobes, *N. gonorrhoeae*, *S. pneumoniae*, *Streptococcus* and *Haemophilus* species. The system comprises a predefined antibiotic gradient which is used to determine the Minimum Inhibitory Concentration (MIC), in µg/mL, of different antimicrobial agents against microorganisms as tested on agar media using overnight incubation.

This submission is for the addition of the antimicrobial ceftaroline at concentrations of 0.002 – 32 µg/mL to the Etest® product. Ceftaroline has been shown to be active *in vitro* against most strains of the microorganism listed below, as described in the FDA-approved label for this antimicrobial agent.

#### Active *in vitro* and in clinical infections

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### 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 antibiotic and is calibrated with MIC values in terms of µg/mL. A predefined exponential gradient of the dried and stabilized antibiotic covers a continuous concentration range across 15 two-fold dilutions of a conventional MIC method.

*Staphylococcus aureus* (skin isolates only)                      S= ≤ 1 µg/mL\*

\* The current absence of resistant isolates precludes defining any results other than “Susceptible.” Isolates yielding MIC results other than “Susceptible” should be submitted to a reference laboratory for further testing.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

Etest® Tobramycin

2. Predicate 510(k) number(s):

k102668

3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Intended Use	Quantitative susceptibility to antimicrobial agents	Same
Incubation	35°	Same
Inoculation	Isolated colonies from culture used	Same
Result	MIC	MIC

<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Antibiotic	Ceftaroline	Tobramycin

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

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

CLSI M7-A8 “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard, January 2009”

CLSI M100-S21 “Performance Standards for Antimicrobial Susceptibility Testing: Twentieth Informational Supplement, January 2011”

**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® directly quantifies antimicrobial susceptibility in terms of discrete MIC values. When the Etest® strip is applied to an inoculated agar plate, the antibiotic is immediately released from the plastic surface into the agar. A predefined, continuous gradient of antibiotic concentrations is created and maintained directly underneath the strip. After incubation whereby bacterial growth becomes visible, a symmetrical inhibition ellipse centered along the strip will be seen. The MIC value in µg/mL is read where the ellipse edge intersects the strip. Since Etest® generates MIC values which fall between two-fold dilutions for interpretation; the MIC value read must be recorded to the next two-fold dilution.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Twenty-five *Staphylococcus aureus* were tested at three external sites to determine site to site reproducibility demonstrating ≥95% reproducibility. Results were within +/- one doubling dilution agreement as compare to the mode for all sites and there were no off-scale results.

b. *Linearity/assay reportable range:*

Not applicable

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

The recommended QC isolates were tested a sufficient number of times with acceptable results with the reference method. The Etest® results demonstrate that the system can produce QC results in the recommended range.

Quality Control Data

<b>ORGANISM</b>	<b>conc.</b>	<b>Reference Frequency</b>	<b>Etest® Frequency</b>
<i>Staphylococcus aureus</i>	0.125	1	4
ATCC 29213	0.25	112	113
Expected Results 0.125- 0.5	0.5	4	

A 0.5 McFarland was 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.

d. *Detection limit:*

Not Applicable

e. *Analytical specificity:*

Not Applicable

f. *Assay cut-off:*

Not Applicable

2. Comparison studies:

Clinical testing was performed at three external sites; there were 355 *S. aureus*, of which 172 were stock (48.5%), and a challenge set of 79 *S. aureus* isolates.

a. *Method comparison with predicate device:*

The CLSI recommended broth dilution reference panel was prepared according to the CLSI recommendation. Etest was set up following Table 1 (Recommended Media, Inoculum and Incubation) of the Generic Package Insert.

All isolates grew in the clinical studies.

The clinical testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. A comparison was provided to the reference method with the following agreement. The ceftaroline range for *S. aureus* in the studies were at 0.125 - 2 µg/mL in this submission.

Summary Table for *S. aureus*

	EA Tot	EA #	EA%	Eval EA tot	Eval EA#	Eval EA%	CA#	CA%	NS	vmj	maj	min
Clinical	355	354	99.7	355	354	99.7	355	100	0	0	0	NA
Challenge	79	79	100	79	79	100	78	98.7	0	0	1	NA
Combined	434	433	99.8	434	433	99.8	433	99.8	0	0	1	NA

EA-Essential Agreement

CA-Category Agreement

NS-not susceptible isolates.

Essential agreement (EA) is when the Etest® results agree with the reference test panel results exactly or within one doubling dilution of the reference method.

Category agreement (CA) is when the Etest® result interpretation agrees exactly with the reference panel result interpretation.

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:

*Staphylococcus aureus* (skin isolates only)

S =  $\leq 1 \mu\text{g/mL}^*$

\* The current absence of resistant isolates precludes defining any results other than “Susceptible.” Isolates yielding MIC results other than “Susceptible” should be submitted to a reference laboratory for further testing.

The Interpretative criteria, QC isolates and the expected ranges are the same as recommended by the CLSI and the FDA. All values will be included in the package insert.

**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.