

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

A. 510(k) Number:

k081325

B. Purpose for Submission:

Addition of doripenem to the Etest® strip

C. Measurand:

Doripenem 0.002 – 32 µg/mL

D. Type of Test:

Quantitative Antimicrobial Susceptibility Test (AST) growth based detection

E. Applicant:

AB BIODISK

F. Proprietary and Established Names:

Etest® for Antimicrobial Susceptibility Testing

G. Regulatory Information:

1. Regulation section:

866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

Class II

3. Product code:

JWY - Manual Antimicrobial Test Systems

4. Panel:

Microbiology

H. Intended Use:

1. Intended use(s):

Etest® is a quantitative technique for determining antimicrobial susceptibility testing of both non-fastidious 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 to determine the Minimum Inhibitory Concentration (MIC) in ug/mL of different antimicrobial agents against microorganisms as tested on agar media using overnight incubation.

2. Indication(s) for use:

This submission is for the addition of the antibiotic doripenem at concentrations of 0.002 – 32 µg/mL to the Etest® strip for testing *Acinetobacter baumannii*, *E. coli*, *K. pneumoniae*, *P. mirabilis*, *P. aeruginosa*, *Bacteroides caccae*, *Bacteroides fragilis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, and *Bacteroides vulgatus*.

3. Special conditions for use statement(s):

Prescription use

4. Special instrument requirements:

Manual readings only

There was not sufficient data to evaluate the performance of doripenem with *Peptostreptococcus*. An alternate method should be performed.

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 ug/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.

J. Substantial Equivalence Information:

1. Predicate device name(s):

The Etest®

2. Predicate K number(s):

k913459

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Etest® is a quantitative technique for determining antimicrobial susceptibility testing of both non-fastidious Gram-negative and Gram positive aerobic bacteria such as <i>Enterobacteriaceae</i> , <i>Pseudomonas</i> , <i>Staphylococcus</i> and <i>Enterococcus</i> species and fastidious bacteria, such as anaerobes, <i>N. gonorrhoeae</i> , <i>S. pneumoniae</i> , <i>Streptococcus</i> and <i>Haemophilus</i> species. The system comprises a predefined antibiotic gradient to determine the Minimum Inhibitory Concentration (MIC) in ug/mL of different antimicrobial agents against microorganisms as tested on agar media using overnight incubation.	Same
Inoculation	Isolated colonies from culture used	Same
Result	MIC	Same
Type of Test	Manual read only	Same

Differences		
Item	Device	Predicate
Antibiotic	Doripenem	Various antibiotics

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA”; CLSI M7 (M100-S18) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard; CLSI M11-A6, “Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard – Sixth Edition.”

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 ug/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:*

Reproducibility testing was performed on 26 gram negative isolates, and 23 *Bacteroides* spp. All organisms were tested once at all three sites which demonstrated >95% reproducibility.

b. *Linearity/assay reportable range:*

Not applicable

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

The recommended Quality Control (QC) isolates were tested at the concentrations listed (see tables below). The results demonstrated that the device system could produce QC results in the recommended range.

Quality Control results demonstrated the ability of the device to produce acceptable results >95% of the time.

Quality Control Table for Gram Negative Isolates

ORGANISM	Conc ug/mL	Reference	Etest®
<i>E. coli</i> ATCC 25922 Expected Range : 0.015 – 0.064 µg/mL	0.016	47	35
	0.032	23	35
<i>P. aeruginosa</i> ATCC 27853 Expected Range : 0.12 – 0.5 µg/mL	0.125	25	27
	0.25	45	43
	0.5	1	1

Quality Control Table for Anaerobes

ORGANISM	Conc ug/mL	Reference	Etest®
<i>B. fragilis</i> ATCC 25285 Expected Range: 0.12 – 0.5 µg/mL	0.125	52	61
	0.25	13	4
<i>B. thetaoitaomicron</i> ATCC 29741 Expected Range: 0.125 – 1 µg/mL	0.125	6	21
	0.25	39	38
	0.5	20	6

A 0.5 McFarland is used to determine the correct inoculum. Colony counts for the clinical/stock isolates were performed periodically at each site to demonstrate that the inoculum procedure results were in the expected CFU/mL range. All colony count inoculum check means results were within the acceptable ranges.

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:*

CLSI recommended broth microdilution and agar dilution media were utilized as the reference methods, and were used to compare with the Etest® results.

Clinical testing was performed at three sites. The testing included fresh/stock, clinical aerobic Gram negative isolates; and fresh/stock clinical isolates of *Bacteroides* species. Approximately 60% of the Clinical strains were fresh isolates. The Challenge isolates selected for testing each organism group was appropriate for this antibiotic. Challenge testing was performed at one site. Low numbers from each organism group were tested, although the

overall numbers were sufficient. The performance of the study is demonstrated below.

Summary Table

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#NS
<i>A. baumannii</i>	189	189	100	133	133	100	133	131	98.5	104
<i>P. aeruginosa</i>	171	169	98.8	123	121	98.4	123	119	96.7	80
<i>Enterobacteriaceae</i>	358	357	99.7	354	353	99.7	354	353	99.7	19
<i>Bacteroides spp.</i>	266	266	100	258	258	100	258	256	99.2	21

EA - Essential Agreement

NS – Not Susceptible

CA - Category Agreement

EA is when there is agreement between the reference method and the Etest® panel within plus or minus one serial two-fold dilution of antibiotic. Category agreement (CA) is when the Etest® panel result interpretation agrees exactly with the reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the Etest® and the reference and have on-scale EA.

The no growth rate is <10% for all organisms tested.

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:

<i>Enterobacteriaceae</i>	≤0.5
<i>P. aeruginosa</i>	≤2
<i>Acinetobacter baumannii</i>	≤1
<i>Anaerobes</i>	≤1

* **Limitation statement:** The current absence of resistant isolates precludes defining any category other than “Susceptible”. Isolates yielding MIC results suggestive of “Nonsusceptible” category should be subjected to additional testing.

However, in the *in vitro* diagnostic studies, 104/189 *Acinetobacter baumannii* isolates, and 80/171 *P. aeruginosa* isolates were identified as Nonsusceptible (NS).

N. Proposed Labeling:

The expected value range, interpretive criteria and QC are included in the package insert. The labeling is sufficient and satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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