510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K260477

B Applicant

bioMérieux SA

C Proprietary and Established Names

ETEST Gepotidacin (GEP) (0.016-256 µg/mL)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JWY	Class II	21 CFR 866.1640 Antimicrobial susceptibility test powder.	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantial equivalence determination for the ETEST with gepotidacin at concentrations of 0.016-256 µg/mL for susceptibility testing of gram-positive and gram-negative organisms.

B Measurand:

Gepotidacin 0.016-256 µg/mL

C Type of Test:

Quantitative Antimicrobial Susceptibility Test growth-based detection

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

ETEST is a manual, quantitative technique for the determination of antimicrobial susceptibility of non-fastidious Gram-negative and Gram-positive aerobic bacteria and fastidious bacteria. 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 tested on agar media after overnight incubation.

Testing with ETEST Gepotidacin (GEP) (0.016-256 µg/mL) is indicated for Enterobacterales, *Staphylococcus saprophyticus*, *Enterococcus faecalis* and *Neisseria gonorrhoeae*, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC).

ETEST Gepotidacin (GEP) (0.016-256 µg/mL) demonstrated acceptable performance with the following microorganisms:

- *Escherichia coli*
- *Staphylococcus saprophyticus*
- *Enterococcus faecalis*
- *Neisseria gonorrhoeae*

C Special Conditions for Use Statement(s):

Rx – For prescription use only

Due to unacceptable categorical agreement (CA below 90%) and the occurrence of two (2) very major errors (2/11; 18.1%), *Klebsiella pneumoniae* should not be tested with the ETEST Geoptidacin (GEP) (0.016-256 µg/mL) and should be tested by an alternative method.

The ability of the ETEST Gepotidacin (GEP) (0.016-256 µg/mL) to detect resistance or non-susceptibilty with the following organisms is unknown because an insufficient number of resistant or non-susceptible isolates were encountered at the time of comparative testing: *Escherichia coli, Staphylococcus saprophyticus, Enterococcus faecalis*.

D Special Instrument Requirements:

Manual reading only.

IV Device/System Characteristics:

A Device Description:

ETEST is a thin, inert and non-porous plastic strip carrying the minimum inhibitory concentration (MIC) reading scale in µg/mL on one side and a predefined antibiotic gradient on the other side.

The ETEST gradient technology is based on a combination of the concepts of dilution and diffusion principles for susceptibility testing.

The ETEST is used to determine the antimicrobial susceptibility of bacteria. One side of the strip carries the MIC reading scale expressed in µg/mL. The other side of the strip contains a predefined continuous exponential gradient of antibiotic concentrations.

ETEST Gepotidacin contains a range of gepotidacin concentrations from 0.016 to 256 µg/mL.

B Principle of Operation:

When the ETEST strip is applied to an agar surface inoculated with bacteria, the preformed antibiotic gradient immediately transfers into the agar matrix, thereby forming a stable, continuous and exponential gradient of antibiotic concentrations directly underneath the strip. As bacteria growth becomes visible during incubation, a symmetrical inhibition ellipse centered along the strip appears. After incubation, the MIC value is read from the scale in terms of µg/mL at the point of complete inhibition of bacterial growth, i.e., where the pointed end of the ellipse intersects the strip. Since ETEST generates MIC values which may fall between two-fold dilutions for interpretation, the MIC value read must be recorded as the next highest two-fold dilution.

V Substantial Equivalence Information:

A Predicate Device Name(s):

ETEST Fosfomycin (FO) (0.032-512 µg/mL)

B Predicate 510(k) Number(s):

K210757

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device K260447	Predicate K210757
Device Trade Name	ETEST Gepotidacin (GEP) (0.016-256 µg/mL)	ETEST Fosfomycin (FO) (0.032-512 µg/mL)
General Device Characteristic Similarities		
Intended Use	ETEST is a manual, quantitative	Same

Device & Predicate Device(s):	Device K260447	Predicate K210757
	technique for the determination of antimicrobial susceptibility of non-fastidious Gram-negative and Gram-positive aerobic bacteria and fastidious bacteria. 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 tested on agar media after overnight incubation.	
Test Methodology	Quantitative antimicrobial susceptibility test to determine the *in vitro* susceptibility of microorganisms	Same
Test Design	Predefined exponential gradient of the dried and stabilized antibiotic covers a continuous range of two-fold dilutions of the conventional MIC method	Same
Inoculum	Isolated colonies from culture in a suspension equivalent to 0.5 McFarland. Inoculum is applied to agar with swab manually or with rotation plate for even distribution of inoculum.	Same
Inoculation Method	Manual	Same
Read Method	Manual; the point where the edge of the ellipse intersects the test strip.	Same
Results	MIC (µg/mL)	Same
General Device Characteristic Differences		
Antimicrobial Agents	Gepotidacin	Fosfomycin
Drug Concentration Range	0.016-256 µg/mL	0.032-512 µg/mL
Tested Species	*Escherichia coli*, *Staphylococcus saprophyticus*, *Enterococcus faecalis* and *Neisseria gonorrhoeae*	*Escherichia coli, Enterococcus faecalis*

Predetermined Change Control Plan (PCCP):

To support the implementation of changes to FDA-recognized susceptibility test interpretive criteria (i.e., breakpoints), this submission included a predetermined change control plan (PCCP) with a breakpoint change protocol that was reviewed and accepted by FDA in submission K250274 cleared on April 30, 2025.This protocol addresses future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm). The protocol outlined the specific procedures and acceptance criteria that bioMérieux intends to use to evaluate the ETEST Gepotidacin (GEP) (0.016-256 µg/mL) when revised breakpoints for the indicated drug are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, bioMérieux will update the ETEST Gepotidacin (GEP) (0.016-256 µg/mL) label to include (1) the new breakpoints, (2) an updated performance section after re-evaluation of data in this premarket notification with the new breakpoints, and (3) any new limitations as determined by their evaluation.

VI Standards/Guidance Documents Referenced:

- FDA Class II Special Controls Guidance Document: Antimicrobial Susceptibility (AST) Systems; Guidance for Industry and FDA (Issued August 28, 2009).
- CLSI M07 12th Edition - Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically.
- CLSI M100 35th Edition - Performance Standards for Antimicrobial Susceptibility Testing.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Reproducibility testing was conducted at three sites using 26 on-scale isolates (10 *E. coli*, 2 *K. pneumoniae*, 2 *E. faecalis*, 2 *S. saprophyticus*, and 10 *N. gonorrhoeae*). Each isolate was tested in triplicate over three days for a total of at least 270 data points. The mode MIC value was determined for each isolate, and the reproducibility was calculated based on the number of MIC values that fell within ±1 doubling dilution of the mode. The testing resulted in overall reproducibility of 100% for both the best and worst cases. The results were acceptable.

2. Linearity:

   N/A

3. Analytical Specificity/Interference:

   N/A

4. Detection Limit and Assay Reportable Range:

N/A

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Inoculum Density Check:
The inoculum was prepared to achieve turbidity equivalent to a 0.5 McFarland standard. Colony counts were performed periodically at each site for all QC replicates, from at least one replicate of each reproducibility isolate on each of the three days of testing, and from a minimum of 10% of the contemporary clinical isolates tested. The inoculum densities were acceptable.

Purity Check:
Verification of isolate purity was conducted on all clinical, challenge, QC and reproducibility organism suspensions for each ETEST and from each growth control well of the broth microdilution reference panel. All organism suspensions for both the broth microdilution reference panels and ETEST were pure.

Growth or Device Failure:
No device failures occurred in the ETEST Gepotidacin (GEP) (0.016-256 µg/mL) clinical trial.

Quality Control Testing:
The CLSI-recommended quality control (QC) strains *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, *Staphylococcus aureus* ATCC 29213 and *Neisseria gonorrhoeae* ATCC 49226 were tested at a minimum of 20 times per site. The QC strains were tested using both ETEST and broth microdilution (BMD) reference methods. The results are summarized in **Table 1**.

Table 1. Quality Control Test Results for ETEST Gepotidacin (GEP)

QC Organism	Expected Range (µg/mL)	Concentration (µg/mL)	Reference BMD (All sites)	ETEST (All sites)
Escherichia coli ATCC 25922	1-4	<1		
		1	57	25
		2	25	61
		4	1	0
		>4		
Enterococcus faecalis ATCC 29212	1-4	<1		
		1	28	11
		2	43	73
		4	10	0
		>4		
Staphylococcus aureus ATCC 29213	0.125-1	<0.125		
		0.125	0	14
		0.25	55	67
		0.50	25	4

QC Organism	Expected Range (µg/mL)	Concentration (µg/mL)	Reference BMD (All sites)	ETEST (All sites)
		1	2	0
		>1		
Neisseria gonorrhoeae ATCC 49226	0.25-1	<0.25		
		0.25	21	47
		0.50	64	47
		1	0	0
		>1		

The Quality Control results were within the recommended range 100% of the time, which is acceptable.

6. Assay Cut-Off:

N/A

B Comparison Studies:

1. Method Comparison with Predicate Device:

Results obtained with ETEST Gepotidacin (GEP) (0.016-256 µg/mL) were compared to results obtained with the CLSI broth microdilution (BMD) reference panel for Enterobacterales, *S. saprophyticus*, and *E. faecalis*. ETEST results were compared to results obtained with the CLSI agar dilution reference method for *N. gonorrhoeae*. The BMD reference panel and the agar dilution reference plates were prepared and interpreted according to recommendations outlined in the CLSI M07 *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically* 12th ed. At the end of incubation, the MIC value obtained from the ETEST (determined based on where the complete inhibition of growth intersects the strip) was compared to MIC results obtained with the reference methods. Testing was performed following the ETEST instructions for use.

The testing conditions for ETEST with Enterobacterales*, S. saprophyticus*, and *E. faecalis* consisted of the following:

- Inoculum: Direct colony suspension to achieve a suspension equivalent to a 0.5 McFarland standard suspension in 0.85% NaCl
- Medium: Mueller Hinton agar
- Incubation: 35±2ºC for 16-20 hours in aerobic conditions

The testing conditions for ETEST with *N. gonorrhoeae* consisted of the following:

- Inoculum: Direct colony suspension to achieve a suspension equivalent to a 0.5 McFarland standard suspension in Mueller Hinton Broth
- Medium: GC chocolate agar with defined supplements
- Incubation: 35±2ºC for 20-24 hours in 5% CO_2 conditions

Clinical testing was performed at three external sites (two US sites and one OUS site) and one internal site. A total of 903 isolates (763 clinical isolates and 140 challenge isolates) were

tested (including 383 *Escherichia coli,* 110 *Staphylococcus saprophyticus*, 110 *Enterococcus faecalis*, and 300 *Neisseria gonorrhoeae*). The clinical testing included 24.1% contemporary (218/903; isolated no longer than 6 months prior to testing) and 60.4% stock (545/903; no time limit on time from isolation prior to testing) clinical isolates. A total of 140 challenge isolates were also evaluated at one internal site using ETEST Gepotidacin (GEP) and the reference methods.

The performance of 903 clinical and challenge isolates is summarized in **Table 2.**

Table 2. Performance of ETEST Gepotidacin (GEP)*

	Tot*	No. EA	EA %	Eval Tot	No. Eval EA	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
Enterobacterales (*E. coli*) [Breakpoints (µg/mL): ≤ 16 (S), 32 (I), ≥64 (R)]													
Clinical	307	295	96.1	307	295	96.1	306	99.6	0	303	1	0	0
Challenge	76	75	98.7	76	75	98.7	76	100	0	76	0	0	0
Combined	383	370	96.6	383	370	96.6	382	99.7	0	379	1	0	0
***Staphylococcus saprophyticus* [Breakpoints (µg/mL): ≤ 0.25 (S)]**													
Clinical	104	103	99.0	104	103	99.0	104	100	0	104	0	0	0
Challenge	6	6	100	6	6	100	6	100	0	6	0	0	0
Combined	110	109	99.1	110	109	99.1	110	100	0	110	0	0	0
***Enterococcus faecalis* [Breakpoints (µg/mL): ≤ 4 (S)]**													
Clinical	104	102	98.1	104	102	98.1	104	100	0	104	0	0	0
Challenge	6	6	100	6	6	100	6	100	0	6	0	0	0
Combined	110	108	98.2	110	108	98.2	110	100	0	110	0	0	0
***Neisseria gonorrhoeae* [Breakpoints (µg/mL): ≤ 1 (S), 2 (I), ≥4 (R)]**													
Clinical	248	238	96.0	248	238	96.0	247	99.6	1	244	1	0	0
Challenge	52	50	96.2	52	50	96.5	51	98.1	6	44	1	0	0
Combined	300	288	96.0	300	288	96	298	99.3	7	288	2	0	0

* Testing with the optional ETEST tools was not evaluated during the ETEST Gepotidacin clinical studies.

EA – Essential Agreement
CA – Category Agreement
S – Susceptible
R - Resistant
Eval – Evaluable MICs
min – Minor Errors
maj – Major Errors
vmj – Very Major Errors

Essential agreement (EA) occurs when the MIC result of the reference method and that of the ETEST Gepotidacin (GEP) are within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on scale for both the reference method and the ETEST Gepotidacin (GEP) or those in which an off-scale result is at least two doubling dilutions from the on-scale result. Category agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the ETEST Gepotidacin (GEP).

Enterobacterales

ETEST Gepotidacin (GEP) (0.016-256 µg/mL) performance for 383 *Escherichia coli* isolates (clinical and challenge) was acceptable with an EA of 96.6% and CA of 99.7%. There was one (1) minor error and no major or very major errors.

An insufficient number of resistant *Escherichia coli* isolates were available for evaluation. The sponsor included the following limitation in the device labeling:

> *The ability of the ETEST Gepotidacin (GEP) (0.016-256 µg/mL) to detect resistance or non-susceptibility with the following organisms is unknown because an insufficient number of resistant or non-susceptible strains were encountered at the time of comparative testing: Escherichia coli*

During the clinical study, 115 *Klebsiella pneumoniae* isolates (clinical and challenge) were tested with ETEST Gepotidacin (GEP) (0.016-256 µg/mL). The EA was 90.4% and the CA was 80.9%. There were 21 minor, no major, and two (2/11=18.1%) very major errors, which is not acceptable. Reporting limitations were not appropriate to mitigate the unacceptable very major error rate. The sponsor removed this organism from the Indications for Use, and the following limitation is included in the device labeling to address testing of this species:

> *Due to an unacceptable categorical agreement (CA below 90%) and the occurrence of two very major errors (2/11;18.1%), Klebsiella pneumoniae should not be tested with the ETEST Gepotidacin (GEP) (0.016-256 µg/mL) and should be tested by an alternative method*.

Staphylococcus saprophyticus

ETEST Gepotidacin (GEP) (0.016-256 µg/mL) performance for 110 *Staphylococcus saprophyticus* isolates (clinical and challenge) is acceptable with an EA of 99.1% and CA of 100%. There were no potential minor, potential major, or potential very major errors. Errors are considered potential since no interpretive category other than "susceptible only" is defined for *S. saprophyticus* with gepotidacin.

An insufficient number of non-susceptible *Staphylococcus saprophyticus* isolates were available for evaluation. The sponsor included the following limitation in the device labeling:

> *The ability of the ETEST Gepotidacin (GEP) (0.016-256 µg/mL) to detect resistance or non-susceptibility with the following organisms is unknown because an insufficient number of resistant or non-susceptible strains were encountered at the time of comparative testing: Staphylococcus saprophyticus.*

Enterococcus faecalis

ETEST Gepotidacin (GEP) (0.016-256 µg/mL) performance for 110 *Enterococcus faecalis* isolates (clinical and challenge) is acceptable with an EA of 98.2% and CA of 100%. There were no potential minor, potential major, or potential very major errors. Errors are considered potential since no interpretive category other than "susceptible only" is defined for *E. faecalis* with gepotidacin.

An insufficient number of non-susceptible *Enterococcus faecalis* isolates were available for evaluation. The sponsor included the following limitation in the device labeling:

The ability of the ETEST Gepotidacin (GEP) (0.016-256 µg/mL) to detect resistance or non-susceptibility with the following organisms is unknown because an insufficient number of resistant or non-susceptible strains were encountered at the time of comparative testing: Enterococcus faecalis.

Neisseria gonorrhoeae

ETEST Gepotidacin (GEP) (0.016-256 µg/mL) performance for 300 *Neisseria gonorrhoeae* isolates (clinical and challenge) is acceptable with an EA of 96.0% and CA of 99.3%. There were two (2) minor, no major, or very major errors.

MIC Trending Analysis

Using the combined clinical and challenge data, an analysis of trending was conducted for all indicated species. Results are analyzed to determine if species-related trends were observed (**Table 3**). This trending calculation considers MIC values that are determined to be one or more doubling dilutions lower or higher compared to the reference method irrespective of whether the device MIC values are on-scale or not. Results that are not clearly at least one dilution lower, at least one dilution higher or in exact agreement with the CLSI reference method are not considered in the trending analysis.

Species for which the difference between the percentage of isolates with higher vs. lower readings was ≥ 30% and for which the confidence interval was determined to be statistically significant were considered to show evidence of trending. Trending that provides higher or lower MIC values compared to the reference is addressed in labeling.

Table 3. Trending Observed with ETEST Gepotidacin (GEP)

Organism Name	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No.	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)*	Trending Noted
Escherichia coli	383	94 (24.5%)	237	52 (13.6%)	-11% (-16%, -5%)	No
Staphylococcus saprophyticus	110	37 (33.7%)	68	5 (4.6%)	-29% (-39%, -19%)	No
Enterococcus faecalis	110	30 (27.3%)	69	11 (10%)	-17% (-27%, -7%)	No
Neisseria gonorrhoeae	300	108 (36%)	150	42 (14%)	-22% (-29%, -15%)	No

Analysis of trending indicated that MIC values tended to be in exact agreement with the reference MIC values. No trending was noted.

Testing/Reporting MICs For Species Not Listed in Indications for Use

For this review, the interpretative criteria are applied to the organisms/organism groups according to the FDA STIC website. As required under 511A(2)(2)(B) of the Federal Food, Drug and Cosmetic Act, the following statement is added in the precautions section of labeling to address testing and reporting of species not listed in the device Indications for Use:

Per the FDA-Recognized Susceptibility Test Interpretive Criteria website, the safety and efficacy of antimicrobial drugs for which antimicrobial susceptibility is tested by this AST device, may or may not have been established in adequate and well-controlled clinical trials for treating clinical infections due to microorganisms outside of those found in the indications and usage in the drug label. The clinical significance of susceptibility information in those instances is unknown. The approved labelling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.

Inoculator and ETEST Strip Applicator Options
Culture media plates for ETEST can be inoculated and streaked by swabs manually or with the RETRO C80 inoculator. ETEST strips can be applied onto inoculated media using forceps, the NEMA C88 vacuum pen or the automatic Applicator SIMPLEX C76.

The ETEST studies for gepotidacin used manual inoculation with swabs and applied ETEST strips with forceps at all test sites. The following statement is included as a footnote to the performance table in the device labeling:

Testing with the optional ETEST tools was not evaluated during the ETEST Gepotidacin clinical studies.

Resistant Isolates
A total of seven (7) Neisseria *gonorrhoeae* resistant isolates (one clinical and six challenge) were available in the ETEST Gepotidacin performance evaluation studies.

Resistance Mechanism Characterization
Challenge isolates of *Escherichia coli*, *Enterococcus faecalis*, and *Neisseria gonorrhoeae* harboring various mechanisms of resistance were evaluated with ETEST Gepotidacin (GEP) (0.016-256 µg/mL). The following antimicrobial resistance mechanisms were evaluated: penicillinase, ciprofloxacin resistance, acquired carbapenemases (i.e., KPC, NDM, OXA-, and OXA-48), reduced permeability, high-level Amp-C β-lactamase, ESBL, and vancomycin resistance enterococci (VanA and VanB).

2. Matrix Comparison:

   N/A

C Clinical Studies:

1. Clinical Sensitivity:

   N/A

2. Clinical Specificity:

   N/A

3. Clinical Cut-Off

   N/A

4. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

N/A

D Expected Values/Reference Range:

The FDA recognized susceptibility interpretive criteria for gepotidacin are listed in **Table 4**.

Table 4. FDA Recognized Interpretive Criteria for Gepotidacin

	Minimum Inhibitory Concentration (µg/mL)[a]		
Organisms	**S**	**I**	**R**
Enterobacterales	≤16	32	≥64
Staphylococcus saprophyticus	≤0.25	-	-
Enterococcus faecalis	≤4	-	-
Neisseria gonorrhoeae	≤1	2	≥4

[a]According to the FDA STIC Webpage https://www.fda.gov/drugs/development-resources/fda-recognized-antimicrobial-susceptibility-test-interpretive-criteria

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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