510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K261853

B Applicant

Liofilchem, Inc.

C Proprietary and Established Names

Gepotidacin GEP 10 µg

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JTN	Class II	21 CFR 866.1620 - Antimicrobial Susceptibility Test Disc	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

1. Obtain a substantial equivalence determination for Gepotidacin GEP 10 µg for susceptibility testing of Enterobacterales, *Enterococcus faecalis*, and *Staphylococcus saprophyticus*
2. Establish a Pre-Determined Change Control Plan (PCCP) to address future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage

B Measurand:

Gepotidacin 10 µg

C Type of Test:

Antimicrobial Susceptibility Test Disc

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

Gepotidacin GEP 10 µg is an *in vitro* semi-quantitative method for antimicrobial susceptibility of clinical isolates tested on agar media using overnight incubation.

The Gepotidacin GEP 10 µg is intended to determine susceptibility of Enterobacterales, *Enterococcus faecalis*, and *Staphylococcus saprophyticus* to gepotidacin, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC). Gepotidacin at a concentration of 10 µg should be interpreted at 16-18 hours of incubation.

The Gepotidacin GEP 10 µg demonstrated acceptable performance with the following organisms*:*

Enterobacterales (*Citrobacter freundii, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Morganella morganii, Proteus mirabilis, Providencia rettgeri*)

Enterococcus faecalis

Staphylococcus saprophyticus

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

The ability of the Antibiotic Disc to detect resistance or non-susceptibility to antimicrobials as shown below is unknown because resistant strains were not available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory.

Gepotidacin: Enterococcus faecalis, Staphylococcus saprophyticus

D Special Instrument Requirements:

Not applicable

IV Device/System Characteristics:

A Device Description:

Gepotidacin GEP 10 µg is made of special high-quality paper impregnated with a predefined concentration. The disks are clearly marked on both sides with “GEP 10,” designating the agent and the drug content. The disks are supplied in plastic cartridges containing 50 disks each. Gepotidacin GEP 10 µg is intended to be used for *in vitro* agar diffusion susceptibility testing.

B Principle of Operation:

Liofilchem Antibiotic Discs are applied to the surface of a culture medium inoculated with a pure colony suspension of the microorganisms under examination. The simultaneous growth of the bacteria and diffusion of the antimicrobials compounds forms a zone of inhibition of growth. After incubation, the plates are examined, the zone diameter around each disk are examined and compared with the standard inhibition zone diameter. The microorganisms are defined as being susceptible, intermediate or resistant to the tested antimicrobial agents.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10

B Predicate 510(k) Number(s):

K251337

C Comparison with Predicate(s):

Device & Predicate Device(s):	**Device: K261853**	**Predicate: K251337**
Device Trade Name	Gepotidacin GEP 10 µg	Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10
General Device Characteristic Similarities		
Intended Use	Semi-quantitative susceptibility to antimicrobial agents against Enterobacterales, *Enterococcus faecalis*, and *Staphylococcus saprophyticus*	Same
Test Method	Antimicrobial susceptibility testing using paper disks impregnated with an antimicrobial agent	Same
Plate Media	Mueller Hinton Agar	Same
Disc Material	High quality paper impregnated with a predefined concentration of antimicrobial agent	Same
Inoculation	Isolated colonies from a culture in a suspension equivalent to 0.5 McFarland. Inoculum is applied to agar with swab manually or with rotation plate	Same
Reading Method	Measurement of inhibition zone diameter in mm	Same

Device & Predicate Device(s):	Device: K261853	Predicate: K251337
Result Interpretation	Categorical interpretation (S/I/R) as determined by the measured zone diameters according to established interpretive criteria for the drug	Same
Incubation	35°C ± 2°C for 16-18 hours	Same
Antimicrobial Agent	Gepotidacin	Same
General Device Characteristic Differences		
Test Organisms	Enterobacterales (*Citrobacter freundii, Enterobacter cloacae* complex, *Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Morganella morganii, Proteus mirabilis, Providencia rettgeri*) *Enterococcus faecalis* *Staphylococcus saprophyticus*	Enterobacterales (*Citrobacter freundii* complex*, Citrobacter koseri, Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Morganella morganii, Proteus mirabilis*, and *Providencia rettgeri*) *Staphylococcus saprophyticus* *Enterococcus faecalis*

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) that was reviewed and accepted by FDA. This PCCP addresses future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage (FDA-Recognized Antimicrobial Susceptibility Test Interpretive Criteria). The PCCP outlined the specific procedures and acceptance criteria that Liofilchem, Inc. intends to use to evaluate the Gepotidacin GEP 10 µg when revised breakpoints for gepotidacin are published on the FDA STIC webpage. The PCCP included with the submission indicated that if specific criteria are met, Liofilchem, Inc. will update the Gepotidacin GEP 10 µg device label to include the new breakpoints.

VI Standards/Guidance Documents Referenced:

- CLSI M100-Ed35. *Performance Standards for Antimicrobial Susceptibility Testing* (January 2025).
- CLSI M02-14th ed. *Performance Standards for Antimicrobial Disk Susceptibility Tests* (March 2024).
- CLSI M07-Ed12. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically* (March 2024).

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Reproducibility testing of the Gepotidacin GEP 10 µg was performed using a panel of gram-positive and gram-negative isolates from species indicated for testing with the device (3 *Enterococcus faecalis*, 2 *Staphylococcus saprophyticus*, 2 *Enterobacter cloacae*, 2 *Escherichia coli*, 2 *Klebsiella pneumoniae,* 2 *Morganella morganii,* 1 *Citrobacter freundii,* 1 *Proteus mirabilis*). Testing was performed at one internal site using 15 organisms, including 10 gram-negative organisms and 5 gram-positive organisms. Each isolate was tested using two disc lots and one media lot (Mueller Hinton agar media) on three separate days. Each test was visually read by three independent readers with results blinded, resulting in 270 data points for evaluation (15 isolates x 3 independent readers x 3 days x 2 disc lots x 1 media lot x 1 site = 270 data points).

   Reproducibility was calculated as the percentage of results which were within ±3 mm difference in zone diameter comparing test results with the modal zone diameter value. The reproducibility performance between disc lots and across readers was 100% and is acceptable. Results are shown in **Table 1**.

Table 1. Reproducibility for Gepotidacin GEP 10 µg

Between Disc Lots			Across Readers			
Lot #1	**Lot #2**	**All Lots**	**Reader #1**	**Reader #2**	**Reader #3**	**All Readers**
135/135 (100%)	135/135 (100%)	270/270 (100%)	90/90 (100%)	90/90 (100%)	90/90 (100%)	270/270 (100%)

2. Linearity:

   Not applicable.

3. Analytical Specificity/Interference:

   Not applicable.

4. Detection Limit and Assay Reportable Range:

   Not applicable.

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

   Quality Control (QC) Testing:
   The CLSI-recommended quality control (QC) strains *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923 were tested by disk diffusion using two Gepotidacin GEP 10 µg lots and at least 20 replicates per lot per reader. Each test was visually read by three independent readers. Results were compared to broth microdilution reference method. The QC performance of Gepotidacin GEP 10 µg was acceptable at > 95%. The performance is shown in **Table 2.**

Table 2. Quality Control Performance of Gepotidacin GEP 10 µg

QC Organism	Expected Range	Zone Diameter in millimeter (mm)		
		Range	Lot #1	Lot #2
Escherichia coli ATCC 25922	18-26 mm	17		
		18		
		19	-	-
		20	-	-
		21	-	-
		22	3	3
		23	19	23
		24	38	34
		25	-	-
		26	-	-
		27	-	-
Staphylococcus aureus ATCC 25923	23-29 mm	22	-	-
		23	-	-
		24	-	-
		25	-	-
		26	16	19
		27	32	20
		28	12	11
		29	-	-
		30	-	-

The CLSI-recommended quality control (QC) strains *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, and *Staphylococcus aureus* ATCC 29213 were tested by broth microdilution (BMD) as per CLSI M07 each day of the clinical study to provide assurance of the data quality obtained by the reference method. The QC performance for the BMD reference method was acceptable at ≥95%. The performance is shown in **Table 3** below.

Table 3. Broth Microdilution Quality Control Summary for Gepotidacin

QC Organism	Expected Range (µg/mL)	Concentration (µg/mL)	Reference Results
Escherichia coli ATCC 25922	1-4 µg/mL	0.5	-
		1	105
		2	15
		4	-
		8	-
Enterococcus faecalis ATCC 29212	1-4 µg/mL	0.5	-
		1	11
		2	106
		4	3
		8	-
	0.12-1 µg/mL	0.06	-
		0.12	4
		0.25	76

QC Organism	Expected Range (µg/mL)	Concentration (µg/mL)	Reference Results
Staphylococcus aureus ATCC 29213		0.5	36
		1	4
		2	

Inoculum Density Check:
Colony counts were conducted for all QC and reproducibility isolates, as well as 10% of clinical isolates. All counts were within the expected range.

Stability:
A real-time stability study was performed with the device stored in the storage conditions recommended in the package insert. Three lots of disks were tested throughout the 36-month claimed shelf life, and microbiological and chemical performance results were acceptable. Stability and storage information is provided in the package insert.

6. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

The qualitative Gepotidacin GEP 10 µg results were compared to the qualitative categorical interpretation (S/I/R) based on the minimum inhibitory concentration (MIC) values obtained from the broth microdilution (BMD) reference method to assess the categorical agreement (CA) and error rates. The study was conducted at one internal testing site. Three independent operators participated in reading test results with isolates evenly distributed to mimic multiple testing sites. Testing was performed utilizing Mueller Hinton agar media. The BMD reference method was performed per CLSI M07 guidelines.

Isolated colonies from an overnight agar plate were suspended in saline to achieve a 0.5 McFarland standard turbidity (approximately 10^8 CFU/mL). Testing conditions consisted of incubation of the inoculated Mueller Hinton agar plate in an inverted position at 35°C ±2°C for 16-18 hours. At the end of the appropriate incubation, the Gepotidacin GEP 10 µg categorical interpretations as determined by zone edges at the point of complete inhibition (inhibition zone) were compared to categorical interpretations as determined by MIC results obtained with the CLSI broth microdilution reference method.

Clinical:
Clinical testing was performed using a total of 386 clinical isolates including 267 Enterobacterales (19 *Citrobacter freundii*, 16 *Enterobacter cloacae* complex, 94 *Escherichia coli,* 16 *Klebsiella aerogenes*, 4 *Klebsiella oxytoca*, 60 *Klebsiella pneumoniae,* 16

Morganella morganii, 33 *Proteus mirabilis*, and 9 *Providencia rettgeri*), 55 *Enterococcus faecalis*, and 64 *Staphylococcus saprophyticus.* The clinical testing included 116 (30.1%) contemporary isolates (isolated no longer than 6 months prior to testing) and 270 (69.9%) stock isolates (isolated more than 6 months prior to testing).

Challenge:
Challenge testing was performed at one site using a total of 82 challenge isolates including 75 Enterobacterales (1 *Citrobacter freundii*, 9 *Enterobacter cloacae* complex, 11 *Escherichia coli,* 1 *Klebsiella aerogenes*, 1 *Klebsiella oxytoca*, 43 *Klebsiella pneumoniae,* 1 *Morganella morganii*, and 8 *Proteus mirabilis*), 3 *Enterococcus faecalis*, and 4 *Staphylococcus saprophyticus.*

Performance results for the total 468 clinical and challenge isolates are shown in **Table 4.**

Table 4. Performance of Gepotidacin GEP 10 µg with Clinical and Challenge Isolates

	Tot	CA #	% CA	# S	# I	# R or NS	min	maj	vmj
Enterobacterales [Breakpoints (mm): ≥12 (S), 8-11 (I), ≤7 (R)]									
Clinical	267	257	96.3	227	18	22	10	0	0
Challenge	75	71	94.7	51	20	4	4	0	0
Total	342	328	95.9	278	38	26	14	0	0
***Enterococcus faecalis* [Breakpoints (mm): ≥14 (S)]**									
Clinical	55	55	100	55	n/a	0	n/a	0	0
Challenge	3	3	100	3	n/a	0	n/a	0	0
Total	58	58	100	58	n/a	0	n/a	0	0
***Staphylococcus saprophyticus* [Breakpoints (mm): ≥23 (S)]**									
Clinical	64	64	100	64	n/a	0	n/a	0	0
Challenge	4	4	100	4	n/a	0	n/a	0	0
Total	68	68	100	68	n/a	0	n/a	0	0

CA – Category Agreement
S – Susceptible Isolates
I – Intermediate Isolates
R – Resistant Isolates
NS – Nonsusceptible Isolates
min – Minor Errors
maj – Major Errors
vmj – Very Major Errors

Category agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of Gepotidacin GEP 10 µg.

The overall performance of Gepotidacin GEP 10 µg as compared to the broth microdilution reference method results for Enterobacterales is acceptable with 95.9% CA. There were fourteen (14) minor errors, no major errors, and no very major errors.

The overall performance of the Gepotidacin GEP 10 µg as compared to the broth microdilution reference method results for *Enterococcus faecalis* is acceptable with 100.0% CA.

The overall performance of the Gepotidacin GEP 10 µg as compared to the broth microdilution reference method results for *Staphylococcus saprophyticus* is acceptable with 100.0% CA.

Resistant Isolates:
Due to the insufficient number of nonsusceptible *E. faecalis* and *S. saprophyticus* evaluated during the Gepotidacin GEP 10 µg clinical study, the following limitation is included in the device labeling:

The ability of the Antibiotic Disc to detect resistance or non-susceptibility to antimicrobials as shown below is unknown because resistant strains were not available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory.
Gepotidacin: Enterococcus faecalis, Staphylococcus saprophyticus

Resistance Mechanisms in Challenge Isolates
Challenge isolates of Enterobacterales, *Enterococcus faecalis*, and *Staphylococcus saprophyticus* harboring various molecular mechanisms of resistance were evaluated with Gepotidacin GEP 10 µg. The following mechanisms were evaluated: colistin resistance, vancomycin resistance, AmpC, CMY-4, CTX-M-2, CTX-M-15, DHA-1, ESBL, IMP-1, IMP-4, KPC, KPC-2, KPC-3, KPC-6, MBL, NDM, NDM-1, NDM-5, NDM-6, NDM-7, NCM-A, OXA-2, OXA-9, OXA-10, OXA-30, OXA-48, OXA-181, OXA-232, SHV, SHV-1, SHV-11, SHV-12, SHV-26, SHV-28, SHV-83, SHV-OSBL, TEM, TEM-1, and VIM-1.

Testing/Reporting MICs for Species Not Listed in the Indications for Use
For this review, the interpretive 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 included in the Warnings and Precautions section of the device 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 labeling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.

2. Matrix Comparison:

Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

Not applicable.

2. Clinical Specificity:

Not applicable.

3. Clinical Cut-Off:

Not applicable.

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

Not applicable.

D Expected Values/Reference Range:

Table 5. FDA-Recognized Interpretive Criteria for Gepotidacin

Organism	Minimum Inhibitory Concentration (µg/mL)[a]			Disk Diffusion (Zone diameters in mm)[a]		
	S	I	R	S	I	R
Enterobacterales	≤16	32	≥64	≥12	8-11	≤7
Enterococcus faecalis	≤4	-	-	≥14	-	-
Staphylococcus saprophyticus	≤0.25	-	-	≥23	-	-

[a]According to FDA STIC Webpage, 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.