510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K260696

B Applicant

Liofilchem s.r.l.

C Proprietary and Established Names

MTS Gepotidacin 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 Liofilchem MIC Test Strip (MTS) Gepotidacin at concentrations of 0.016 to 256 µg/mL for susceptibility testing of Enterobacterales, *Enterococcus faecalis*, and *Staphylococcus saprophyticus*.

B Measurand:

Gepotidacin in the dilution range of 0.016 to 256 µg/mL

C Type of Test:

Quantitative antimicrobial susceptibility test (AST) growth-based detection

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The MTS (MIC Test Strip) Gepotidacin 0.016-256 µg/mL is a quantitative method intended for *in vitro* determination of antimicrobial susceptibility of bacteria. MTS consists of specialized paper impregnated with a predefined concentration gradient of an antimicrobial agent, which is used to determine the minimum inhibitory concentration (MIC) in µg/mL of antimicrobial agents against bacteria as tested on agar media using overnight incubation and manual reading procedures. MTS Gepotidacin at concentrations of 0.016-256 µg/mL should be interpreted at 16-20 hours of incubation.

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

The MTS Gepotidacin 0.016-256 µg/mL has demonstrated acceptable performance with the following organisms:

Enterobacterales (*Citrobacter freundii* complex*, Escherichia coli,* and *Klebsiella pneumoniae*)

Enterococcus faecalis

Staphylococcus saprophyticus

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

The ability of the MTS Gepotidacin to detect the following resistant or nonsusceptible isolates is unknown because an insufficient number of resistant or nonsuceptible isolates were available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory.

Gepotidacin: E. coli, C. freundii complex, E. faecalis

D Special Instrument Requirements:

N/A – Manual reading only

IV Device/System Characteristics:

A Device Description:

MTS Gepotidacin 0.016-256 µg/mL is made of special high-quality paper impregnated with a predefined concentration gradient of gepotidacin across 15 two-fold dilutions like those used by conventional MIC methods. One side of the strip is labeled with the gepotidacin code (GEP) and

the MIC reading scale in µg/mL. MIC values are determined by identifying the drug concentration at which growth of the ellipse ends. The MIC Test Strip (MTS) is single use only.

B Principle of Operation:

MTS are made of specialized high-quality paper impregnated with a predefined concentration gradient of antibiotic, across 15 two-fold dilutions like those of a conventional MIC method. When the MTS is applied onto an inoculated agar surface, the preformed exponential gradient of antimicrobial agent diffuses into the agar. After 16-20 hours incubation, a symmetrical inhibition ellipse centered along the strip is formed. The MIC is read manually directly from the scale in terms of µg/mL at the point where the edge of the inhibition ellipse intersects the strip MTS.

Growth along the entire gradient (i.e., no inhibition ellipse) indicates that the MIC value is greater than or equal to (≥) the highest value on the scale. An inhibition ellipse that intersects below the lower end of the scale is read as less than (<) the lowest value. An MIC of 0.125 µg/mL is considered to be the same as 0.12 µg/mL for reporting purposes. An MTS MIC value which falls between standard two-fold dilutions must be rounded up to the next standard upper two-fold value before categorization.

V Substantial Equivalence Information:

A Predicate Device Name(s):

Liofilchem MIC Test Strip (MTS)-Vancomycin 0.016 -256 µg/mL

B Predicate 510(k) Number(s):

K153687

C Comparison with Predicate(s):

Device & Predicate Device(s):	**Device: K260696**	**Predicate: K153687**
Device Trade Name	MTS Gepotidacin 0.016-256 µg/mL	Liofilchem MIC Test Strip (MTS)-Vancomycin 0.016-256 µg/mL
General Device Characteristic Similarities		
Plate Media	Mueller Hinton Agar	Same
MTS Strip Material	High quality paper impregnated with a predefined concentration of gradient antimicrobial agent	Same
Inoculation	Isolated colonies from culture in a suspension equivalent to 0.5 McFarland. Inoculum is applied to agar with swab manually	Same

Device & Predicate Device(s):	Device: K260696	Predicate: K153687
Reading	Manual; Interpret the MIC as 100% inhibition	Same
Result	MIC in µg/mL	Same
General Device Characteristic Differences		
Intended Use	Quantitative susceptibility to antimicrobial agents against specified gram-negative and gram-positive organisms	Quantitative susceptibility to antimicrobial agents against specified gram-positive organisms
Antimicrobial Agent	Gepotidacin (GEP)	Vancomycin (VA)
Incubation	35°C ± 2°C for 16-20 hours	35°C ± 2°C for 24 hours

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 K252114 cleared on October 2, 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 Liofilchem intends to use to evaluate the MTS Gepotidacin 0.016-256 µg/mL when revised breakpoints for gepotidacin are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, Liofilchem will update the MTS Gepotidacin 0.016-256 µg/mL device 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:

- Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA (August 2009).
- CLSI M07-Ed12. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically (March 2024).
- CLSI M100-Ed35. Performance Standards for Antimicrobial Susceptibility Testing (January 2025).

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Reproducibility testing of the MTS Gepotidacin was performed using a panel of 18 gram-positive and gram-negative isolates from species indicated for use with the device (5 *Enterococcus faecalis*, 5 *Staphylococcus saprophyticus*, 4 *Escherichia coli*, 3 *Klebsiella*

pneumoniae, and 1 *Citrobacter freundii*). Testing was performed in triplicate at three sites on three separate days for a total of 483 data points (18 isolates x 3 replicates x 3 days of testing = 162 data points/site). Results were used to determine site to site and overall reproducibility.

The mode MIC value was determined, and the reproducibility was calculated based on the number of MIC values that fell within ±1 doubling dilution of the mode MIC value. All MIC results were on scale. The overall reproducibility results for MTS Gepotidacin were 99.4%, which is acceptable.

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):

   Inoculum Density Check:
   The inoculum is prepared from an overnight agar plate into saline to achieve turbidity equivalent to a 0.5 McFarland standard. The inoculum is applied to agar with a sterile swab manually. Colony counts are performed periodically at each site for all QC replicates.

   Inoculum density checks were performed, and the colony counts obtained for each QC strain were within the recommended range of approximately 1 x 10^8 CFU/mL. Colony counts are also determined from one replicate of each reproducibility isolate on each of the three days of testing and from a minimum of 10% of the clinical strains tested and showed similar ranges.

   Purity Checks:
   Purity checks are performed on all isolates following MTS inoculation. All isolates were determined to be pure in both the broth microdilution reference panels and the MTS agar plates.

   Growth Rate:
   All clinical and challenge isolates grew in both the reference broth microdilution panels and the MTS agar plates.

   Quality Control:
   The CLSI-recommended quality control (QC) strains *Escherichia coli* ATCC 25922, *Enterococcus faecalis* ATCC 29212, and *Staphylococcus aureus* 29213 were tested at three sites for a minimum of 20 times at each site by both the MTS and the reference method. The results demonstrate that MTS Gepotidacin can produce quality control results in the recommended range ≥95% of the time which is acceptable (**Table 1**).

Table 1. QC Results for Gepotidacin with CLSI-Recommended QC Strains

QC Organism	Expected Range (µg/mL)	Concentration (µg/mL)	Reference BMD (All sites)	MTS (All sites)
Escherichia coli ATCC 25922	1-4 µg/mL	0.5	-	-
		1	317	64
		2	69	354
		4	3	10
		8	-	-
Enterococcus faecalis ATCC 29212	1-4 µg/mL	0.5	-	-
		1	28	4
		2	69	88
		4	2	1
		8	-	-
		16	1	-
Staphylococcus aureus ATCC 29213	0.12-1 µg/mL	0.06	-	-
		0.12	8	26
		0.25	352	306
		0.5	27	71
		1	3	-
		2	-	1

6. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Results obtained with MTS Gepotidacin 0.016-256 µg/mL were compared to results obtained from frozen reference MIC panels. Reference MIC panels are prepared, tested, and interpreted as outlined in the CLSI M07 *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically* 12th ed.

   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 16-20 hours. At the end of the appropriate incubation, the MIC value where the edge of the inhibition ellipse intersects the strip was compared to MIC results obtained with the CLSI reference broth microdilution method.

   Clinical:
   Clinical testing with MTS Gepotidacin was performed at four external U.S. sites, and the reference method was performed at three of the four sites. A total of 13,205 clinical isolates were evaluated including: 12,383 Enterobacterales (44 *C. freundii* complex, 8,661 *E. coli*, 3,608 *K. pneumoniae*), 71 *E. faecalis*, and 821 *S. saprophyticus* isolates. The clinical testing

included 5,821 (44.1%) contemporary isolates (isolated no longer than 6 months prior to testing) and 7,384 (55.9%) stock isolates (isolated over 6 months prior to testing).

Challenge:
Challenge testing was performed at one external U.S. site. A total of 205 clinical isolates were evaluated including: 122 Enterobacterales (7 *C. freundii* complex, 95 *E. coli*, 20 *K. pneumoniae*), 35 *E. faecalis*, and 50 *S. saprophyticus* isolates.

Results of MTS Gepotidacin testing with clinical and challenge isolates are shown in **Table 2**.

Table 2. Performance of MTS Gepotidacin with Clinical and Challenge Isolates

	Tot	EA No.	EA %	Eval Tot	Eval EA No.	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
Enterobacterales [≤16 (S), 32 (I), ≥64 (R)]													
Clinical	12313	12014	97.6	12306	12007	97.6	12138	98.6	61	12065	174	0	1
Challenge	122	122	100	113	113	100	107	87.7	15	97	15	0	0
Total	12435	12136	97.6	12419	12120	97.6	12245	98.5	76	12162	189	0	1
***E. faecalis* [≤4 (S)]**													
Clinical	71	70	98.6	70	69	98.6	71	100	2	69	0	0	0
Challenge	35	35	100	35	35	100	35	100	0	35	0	0	0
Total	106	105	99.1	105	104	99.1	106	100	2	104	0	0	0
***S. saprophyticus* [≤0.25 (S)]**													
Clinical	821	806	98.2	821	806	98.2	819	99.8	4	817	0	0	2
Challenge	50	50	100	50	50	100	50	100	2	48	0	0	0
Total	871	856	98.3	871	856	98.3	869	99.8	6	865	0	0	2

EA – Essential Agreement
CA – Category Agreement
R – Resistant
S – Susceptible
Eval – Evaluable MIC Results
min – Minor Discrepancies
maj – Major Discrepancies
vmj – Very Major Discrepancies

Essential agreement (EA) occurs when the result of the reference method and that of the MTS Gepotidacin 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 MTS Gepotidacin 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 MTS Gepotidacin.

Enterobacterales

For Enterobacterales, the combined clinical and challenge results (12,435 isolates) were acceptable with an EA of 97.6% and CA of 98.5%. There were 189 minor errors, no major errors, and one very major error (1/76 = 1.3%). Performance is acceptable.

Enterococcus faecalis

For *E. faecalis*, the combined clinical and challenge results (106 isolates) were acceptable with an EA of 99.1% and CA of 100%. There were no 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. Performance is acceptable.

Staphylococcus saprophyticus

For *S. saprophyticus*, the combined clinical and challenge results (871 isolates) were acceptable with an EA of 98.3% and CA of 99.8%. There were no potential major errors and two potential very major errors (2/6 = 33.3%). Errors are considered potential since no interpretive category other than "susceptible only" is defined for *S. saprophyticus* with gepotidacin. Due to the lack of an intermediate interpretive criteria, further analysis of the errors is performed, and adjustments are made by considering the MIC values where the errors occurred. Both potential very major errors had an MIC value that was in essential agreement with the reference MIC value; therefore, the adjusted potential very major error rate is 0%, and performance is acceptable.

MIC Trending Analysis

A trending analysis was conducted using the combined data (clinical and challenge) obtained for Enterobacterales, *Enterococcus faecalis,* and *Staphylococcus saprophyticus.* This trending calculation takes into account MIC values that are determined to be one or more doubling dilutions lower or higher than 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 MIC 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.

Evaluation of results for species within Enterobacterales, *E. faecalis*, and *S. saprophyticus* with MTS Gepotidacin are summarized in **Table 3**.

Table 3. Trending Analysis for MTS Gepotidacin

Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (95% CI)	Trending Noted
C. freundii complex	51	13, (25.5)	31	7, (13.7)	-12% (-27% to 4%)	No
E. coli	8577	636, (7.3)	3893	4226, (48.3)	41%, (40% to 42%)	Yes, high
E. faecalis	105	5, (4.8)	83	17, (16.2)	11%, (3% to 20%)	No
K. pneumoniae	3620	871, (24.1)	2090	659, (18.2)	-6%, (-8% to -4%)	No
S. saprophyticus	871	114, (13.1)	423	334, (38.4)	25%, (21% to 29%)	No

A trend toward higher MIC readings was observed for *E. coli* with MTS Gepotidacin compared to the CLSI broth microdilution reference method. To address the MIC trending, the following footnote to the performance table was included in the device labeling:

MTS Gepotidacin MIC values tended to be in exact agreement or at least one doubling dilution higher when testing E. coli

Resistant Isolates
Due to the insufficient number of resistant or nonsusceptible *C. freundii* complex, *E. coli*, and *E. faecalis* evaluated during the MTS Gepotidacin clinical study, the following limitation is included in the device labeling:

The ability of the MTS Gepotidacin to detect the following resistant or nonsusceptible isolates is unknown because an insufficient number of resistant or nonsusceptible isolates were available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory:

Gepotidacin: E. coli, C. freundii complex, E. faecalis

Resistance Mechanisms in Challenge Isolates
Challenge isolates of Enterobacterales, *Enterococcus faecalis*, and *Staphylococcus saprophyticus* harboring various molecular mechanisms of resistance were evaluated with MTS Gepotidacin 0.016- 256 µg/mL. The following mechanisms were evaluated: ampicillin resistance, oxacillin resistance, vancomycin resistance, CMY-2, CMY-6, CMY-42, CTX-M-9, CTX-M-15, ESBL, KPC, KPC-2, KPC-3, mcr-1, NDM, NDM-1, OXA-1, OXA-30, OXA-48, SHV-1, SHV-12, SHV-31, TEM-1, TEM-16, TEM-164S, and VEB-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 4. FDA-recognized Interpretive Criteria for Gepotidacin

Organisms	Minimum Inhibitory Concentration (µg/mL)[a]		
	Susceptible	Intermediate	Resistant
Enterobacterales	≤16	32	≥64
Enterococcus faecalis	≤4	-	-
Staphylococcus saprophyticus	≤0.25	-	-

[a]According to 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.