



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

**I Background Information:**

**A 510(k) Number**

K251337

**B Applicant**

Thermo Fisher Scientific (Oxoid Ltd.)

**C Proprietary and Established Names**

Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10

**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:**

In this Traditional 510(k) submission, Oxoid Limited (part of Thermo Fisher Scientific) seeks the following:

1. To obtain a substantial equivalence determination for gepotidacin antimicrobial susceptibility test disk.
2. To 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 Disks

## III Intended Use/Indications for Use:

### A Intended Use(s):

See Indications for Use below.

### B Indication(s) for Use:

Thermo Scientific Oxoid Antimicrobial Susceptibility Test Disks are used in the semi-quantitative agar diffusion test method for *in vitro* susceptibility testing. Used in a diagnostic workflow to aid clinicians in determining potential treatment options for patients suspected of having a microbial infection, these discs are intended to determine susceptibility against microorganisms for which specific drugs have been shown to be active both clinically and *in vitro*.

The Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 is intended to determine susceptibility of Enterobacterales, *Staphylococcus saprophyticus*, and *Enterococcus faecalis* to gepotidacin, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC). The Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 demonstrated acceptable performance to determine susceptibility to gepotidacin against the following microorganisms:

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*

### C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Due to categorical agreement below 90% with the Thermo Scientific Oxoid Gepotidacin (10 µg) GEP 10 when compared to the Broth Microdilution MIC values caused by the occurrence of minor and very major errors, if critical to patient care, testing should be performed using an alternate method for the following antibiotic/organism combination: Gepotidacin/*Klebsiella pneumoniae*

The current absence of resistant *Staphylococcus saprophyticus* and *Enterococcus faecalis* isolates precludes defining any results other than “Susceptible”. For these species, isolates yielding results other than “Susceptible” should be submitted to a reference laboratory for further testing.

The ability of the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 to detect resistance with the following combination(s) is unknown because an insufficient number of resistant strains

were encountered at the time of comparative testing: Gepotidacin 10 µg and Enterobacterales group. If such a strain is encountered, it should be submitted to a reference laboratory for further testing.

**D Special Instrument Requirements:**

Not applicable.

**IV Device/System Characteristics:**

**A Device Description:**

Thermo Scientific Oxoid Gepotidacin Disc (10 µg) which is designated with the code GEP10 is a high quality 6mm diameter white filter paper disk that is impregnated with 10 µg gepotidacin. The disks are clearly marked on both sides with GEP10, designating the agent and the drug content. The disks are supplied in plastic cartridges containing 50 disks each. Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 is intended to be used for *in vitro* agar diffusion susceptibility testing.

**B Principle of Operation:**

A suitable therapeutic agent for *in vitro* use can be determined using filter paper disks impregnated with specified concentrations of antimicrobial agents placed on the surface of a suitable test medium. Pure cultures of clinical isolates are inoculated onto the test medium, and the AST disk placed on the surface. The antibiotic within the disk diffuses into the agar. After incubation, the zones of inhibition around the disks are measured and compared against recognized zone diameter ranges for the specific antimicrobial agent/organism combination under test.

**V Substantial Equivalence Information:**

**A Predicate Device Name(s):**

Thermo Scientific Oxoid Sulbactam/Durlobactam Disc (10/10 µg) SUD20

**B Predicate 510(k) Number(s):**

K232276

**C Comparison with Predicate(s):**

Device & Predicate Device(s):	Device: <u>K251337</u>	Predicate: <u>K232276</u>
Device Trade Name	Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10	Thermo Scientific Oxoid Sulbactam/Durlobactam Disc (10/10 µg) SUD20
General Device Characteristic Similarities		

Device & Predicate Device(s):	Device: <u>K251337</u>	Predicate: <u>K232276</u>
Intended Use	Antimicrobial Susceptibility Test Discs used in the semi-quantitative agar diffusion test method for <i>in vitro</i> susceptibility testing.	Same
Test Method	Antimicrobial susceptibility testing using paper disks impregnated with an antimicrobial agent.	Same
Methodology	Disk diffusion susceptibility test protocol requires the user to determine categorical interpretations (S/I/R) using the measured zone diameters.	Same
Inoculum	Prepared from pure isolated colonies to match the turbidity equivalent of a 0.5 McFarland.	Same
Inoculation Method	Dip a sterile swab into the prepared inoculums and streak an appropriate agar plate's surface three times. Add the disks impregnated with the antimicrobial agent to the surface of the plate. The temperature, atmospheric conditions, and duration of incubation are dependent on the organism tested.	Same
Reading Method	The user will interpret the zone diameters according to established interpretive criteria for the drug.	Same
<b>General Device Characteristic Differences</b>		
Antimicrobial Agent	Gepotidacin	Sulbactam/Durlobactam
Concentration	10 µg	10/10 µg

#### **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 K231806 cleared on March 22, 2024. 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 Thermo Fisher Scientific (Oxoid Ltd.) intends to use to evaluate the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 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, Thermo Fisher Scientific (Oxoid Ltd.) will update the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 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:

- CLSI M02-14th ed. *Performance Standards for Antimicrobial Disk Susceptibility Tests* (March 2024).
- CLSI M100-35th ed. *Performance Standards for Antimicrobial Susceptibility Testing* (January 2025).

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

#### 1. Precision/Reproducibility:

Reproducibility was conducted at one internal site using 15 organisms, tested in triplicate with two disk lots on three separate days using one lot of media (Mueller Hinton Agar media). Each test was visually read by three independent readers with results blinded, resulting in 270 data points for evaluation (15 organisms x 2 disk lots x 1 media x 3 days x 3 independent readers = 270 data points). Colony counts were performed on all isolates.

The reproducibility study included Enterobacterales, *Staphylococcus saprophyticus*, and *Enterococcus faecalis* consisting of the following species: three (3) isolates each of *E. coli*, *K. pneumoniae*, and *E. faecalis*; two (2) isolates each of *C. freundii*, *P. mirabilis*, and *S. saprophyticus*.

Reproducibility was calculated as the percent of results which were within  $\pm 3$  mm difference in zone diameter comparing each test result with the modal zone diameter value. The reproducibility across disk lots is  $>95\%$  and meets the acceptance criteria. Results are shown in **Table 1** below.

**Table 1: Reproducibility Summary**

Between Disk Lots			Across Readers <sup>1</sup>			
Lot A	Lot B	All Lots	Reader#1	Reader#2	Reader#3	All Readers
97.0% (131/135)	97.0% (131/135)	97.0% (262/270)	97.8% (88/90)	95.6% (86/90)	97.8% (88/90)	97.0% (262/270)

<sup>1</sup>Two disk lots were read by each reader.

2. Linearity:

Not applicable.

3. Analytical Specificity/Interference:

Not applicable.

4. Assay Reportable Range:

Not applicable.

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

**Quality Control (QC) Testing:**

The CLSI quality control (QC) isolates, *Escherichia coli* ATCC 25922 and *Staphylococcus aureus* ATCC 25923 were tested. Two Oxoid disk lots were used and at least 20 replicates per lot per reader were tested. Each test was visually read by at least three independent readers, resulting in 274 Oxoid disk data points. The Oxoid disk QC performance for disk diffusion method was acceptable at > 95%. The performance is shown in **Table 2** below.

**Table 2: Quality Control Performance of Gepotidacin (10 µg)**

QC Organism	Zone Diameter in millimeter (mm)		
	Range	Oxoid Lot A <sup>1</sup>	Oxoid Lot B <sup>1</sup>
<i>E. coli</i> ATCC 25922  Expected Range: 18-26 mm	17		
	18		
	19		
	20		1
	21	3	1
	22	2	1
	23	15	22
	24	21	17
	25	21	20
	26	7	7
	27		
<i>S. aureus</i> ATCC 25923  Expected Range: 23-29 mm	22		
	23	1	1
	24	3	2
	25	11	9
	26	20	28
	27	13	8
	28	13	13
	29	7	7
	30		

ATCC=American Type Culture Collection

<sup>1</sup>Two Oxoid disk lots were tested (lot A and lot B)

Broth micro dilution (BMD) for QC isolates was performed as per CLSI M07 on every day of the clinical study to provide assurance of the data obtained from the reference method. The QC performance for the reference BMD method was acceptable at > 95%. The performance is shown in **Table 3** below.

**Table 3: Quality Control Performance of Gepotidacin by BMD Method**

QC Organism	MIC (µg/mL)	Results
<i>E. coli</i> ATCC 25922 Expected MIC Range: 1-4 µg/mL	0.5	
	1	16
	2	3
	4	
	8	
<i>S. aureus</i> ATCC 29213 Expected MIC Range: 0.12-1 µg/mL	0.06	
	0.12	2
	0.25	10
	0.5	3
	1	1
	2	
<i>E. faecalis</i> ATCC 29212 Expected MIC Range: 1-4 µg/mL	0.5	
	1	
	2	16
	4	1
	8	

ATCC=American Type Culture Collection

#### **Inoculum Density Check:**

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

#### **Stability:**

A real-time stability study was conducted 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 within the expected range which is acceptable. Stability and storage information is provided in the package insert.

#### 6. Detection Limit:

Not applicable.

#### 7. Assay Cut-Off:

Not applicable.

### **B Comparison Studies:**

#### 1. Method Comparison with Predicate Device:

The qualitative Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 disk diffusion results were compared to the qualitative categorical interpretation (S/I/R) based on the minimum inhibitory concentration (MIC) values obtained from reference broth microdilution (BMD) to assess the categorical agreement (CA) and error rates. The study was conducted at

one internal testing site. Seven independent operators participated in reading of test results to mimic multiple testing sites. Testing was performed utilizing Mueller-Hinton agar (MHA) per CLSI M02 guidelines. The reference BMD method was performed per CLSI M07 guidelines.

#### Clinical:

Clinical testing was performed using a total of 375 Enterobacterales clinical isolates [*C. koseri* (10 isolates), *C. freundii* (25 isolates), *E. cloacae* (10 isolates), *E. coli* (100 isolates), *K. aerogenes* (10 isolates), *K. oxytoca* (10 isolates), *K. pneumoniae* (159 isolates), *M. morganii* (10 isolates), *P. mirabilis* (31 isolates), and *P. rettgeri* (10 isolates)], 24 *Staphylococcus saprophyticus* clinical isolates, and 33 *Enterococcus faecalis* clinical isolates.

#### Challenge:

Challenge testing was performed using a total of 171 Enterobacterales challenge isolates [*C. koseri* (10 isolates), *C. freundii* (10 isolates), *E. cloacae* (10 isolates), *E. coli* (15 isolates), *K. aerogenes* (10 isolates), *K. oxytoca* (10 isolates), *K. pneumoniae* (72 isolates), *M. morganii* (10 isolates), *P. mirabilis* (14 isolates), and *P. rettgeri* (10 isolates)], one (1) *Staphylococcus saprophyticus* challenge isolates, and 16 *Enterococcus faecalis* challenge isolates.

Performance results for the 546 clinical and challenge Enterobacterales isolates, 25 clinical and challenge *S. saprophyticus* isolates, and 49 clinical and challenge *E. faecalis* isolates are shown in **Table 4**.

**Table 4: Performance of Thermo Scientific Oxoid Gepotidacin Disk vs. Reference BMD Based on Categorical Result Interpretation (All isolates)**

	Total	CA#	%CA	#S	#I	#R	MIN	MAJ	VMJ
<b>Enterobacterales</b>									
<b>[Disk Breakpoints (mm): ≥12 (S), 8-11 (I), ≤7 (R)]</b>									
Clinical	375	351	93.6%	343	20	12	23	0	1
Challenge	171	152	88.9%	119	23	29	17	1	1
Combined	546	503	92.1%	462	43	41	40	1	2
	Total	CA#	%CA	#S	#NS		MIN	MAJ	VMJ
<b><i>Staphylococcus saprophyticus</i></b>									
<b>[Disk Breakpoints (mm): ≥23 (S)]</b>									
Clinical	24	24	100.0%	24	0		0	0	0
Challenge	1	1	100.0%	1	0		0	0	0
Combined	25	25	100.0%	25	0		0	0	0
	Total	CA#	%CA	#S	#NS		MIN	MAJ	VMJ
<b><i>Enterococcus faecalis</i></b>									
<b>[Disk Breakpoints (mm): ≥14 (S)]</b>									
Clinical	33	33	100.0%	33	0		0	0	0
Challenge	16	16	100.0%	16	0		0	0	0
Combined	49	49	100.0%	49	0		0	0	0

**CA** – Category Agreement

**S** – Susceptible isolates

**MAJ** – major errors

**VMJ** – very major errors

**MIN** – minor errors

**NS** – Non-susceptible isolates

**I** – Intermediate isolates

**R** – Resistant isolates

Category Agreement (CA) is when the Thermo Scientific Oxoid disk result interpretation agrees exactly with the MIC result interpretation.



The performance of the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 disk as compared to the MIC for *Staphylococcus saprophyticus* (Table 4) is acceptable with 100.0% CA.

The performance of the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 disk as compared to the MIC for *Enterococcus faecalis* (Table 4) is acceptable with 100.0% CA.

The performance of the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 disk as compared to the MIC for all Enterobacterales isolates (Table 4) is acceptable with 92.1% CA. There were 40 minor errors, one major error (1/462; 0.2%), and two very major errors (2/9; 22.2%).

When evaluating results by individual species, *Klebsiella pneumoniae* had a CA <90% due to the occurrence of minor and very major errors which is unacceptable. To address the minor and very major errors, the following limitation was included in the device labeling:

*Due to categorical agreement below 90% with the Thermo Scientific Oxoid Gepotidacin (10 µg) GEP 10 when compared to the Broth Microdilution MIC values caused by the occurrence of minor and very major errors, if critical to patient care, testing should be performed using an alternate method for the following antibiotic/organism combination: Gepotidacin/Klebsiella pneumoniae.*

In alignment with the above mitigation, performance was also evaluated with *Klebsiella pneumoniae* isolates (159 clinical and 72 challenge) excluded from the clinical study. Performance results for the remaining total 315 clinical and challenge isolates is shown in Table 5.

**Table 5: Performance of Thermo Scientific Oxoid Gepotidacin Disk vs. Reference BMD Based on Categorical Result Interpretation (excluding *K. pneumoniae*)**

	Total	CA#	%CA	#S	#I	#R	MIN	MAJ	VMJ
Enterobacterales									
[Disk Breakpoints (mm): ≥12 (S), 8-11 (I), ≤7 (R)]									
Clinical	216	211	97.7%	212	3	1	5	0	0
Challenge	99	96	97.0%	96	1	2	2	0	1
Combined	315	307	97.5%	308	4	3	7	0	1

CA – Category Agreement  
S – Susceptible isolates  
MAJ – major errors  
VMJ – very major errors

MIN – minor errors  
NS – Non-susceptible isolates  
I – Intermediate isolates  
R – Resistant isolates

The performance of the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 disk as compared to the MIC for Enterobacterales excluding *Klebsiella pneumoniae* (Table 5) is acceptable with 97.5% CA. There were seven minor errors and one very major (VMJ) error (1/3; 33.3%).

When evaluating results by individual species, the one VMJ error was observed for *Enterobacter cloacae*, resulting in a VMJ rate of 50.0% (1/2). Due to the limited number of

resistant isolates tested with this species, the error was considered random. This is addressed with the following footnote to the Performance Characteristics table in the device labeling:

*One very major error (VMJ) was observed with gepotidacin when testing Enterobacter cloacae that resulted in an unacceptable VMJ rate (50.0%, 1/2). This was considered random due to the limited number of resistant Enterobacter cloacae isolates tested.*

#### **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 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”.*

#### **Non-susceptible Isolates Tested:**

Due to the lack of an interpretive category other than susceptible for gepotidacin with *Staphylococcus saprophyticus* and *Enterococcus faecalis*, the following limitation was included in the device labeling:

*The current absence of resistant Staphylococcus saprophyticus and Enterococcus faecalis isolates precludes defining any results other than “Susceptible”. For these species, isolates yielding results other than “Susceptible” should be submitted to a reference laboratory for further testing.*

#### **Resistance Isolates:**

A total of 315 clinical and challenge isolates were tested when the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 was compared to the interpretive category based on MIC values for Enterobacterales. However, an insufficient number of resistant isolates were available for testing. To address the lack of resistant strains encountered during the clinical evaluation, the following limitation was added in the device labeling:

*The ability of the Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10 to detect resistance with the following combination(s) is unknown because an insufficient number of resistant strains were encountered at the time of comparative testing: Gepotidacin 10 µg and Enterobacterales group. If such a strain is encountered, it should be submitted to a reference laboratory for further testing.*

**Resistance Mechanisms in Challenge Isolates:**

Challenge isolates of Enterobacterales harboring various molecular mechanisms of resistance were evaluated with Thermo Scientific Oxoid Gepotidacin Disc (10 µg) GEP10. The following mechanisms were evaluated: AmpC, CMY alleles, CRE-, dfrA1, ESBL, IMP, KPC alleles, MAL-1, NDM alleles, OmpK36, OXA-48, OXY-2-7, SHV-5, and TEM-1.

**2. Matrix Comparison:**

Not applicable.

**C Clinical Studies:****1. Clinical Sensitivity:**

Not applicable.

**2. Clinical Specificity:**

Not applicable.

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

Not applicable.

**D Clinical Cut-Off:**

Not applicable.

**E Expected Values/Reference Range:**

The FDA recognized susceptibility interpretive criteria for gepotidacin are listed in **Table 6**.

**Table 6. FDA Identified Interpretive Criteria for Gepotidacin**

Organism	Minimum Inhibitory Concentration (µg/mL) <sup>a</sup>			Zone Diameter (mm) <sup>a</sup>		
	S	I	R	S	I	R
Enterobacterales	≤ 16	32	≥ 64	≥ 12	8-11	≤ 7
<i>Staphylococcus saprophyticus</i>	≤ 0.25	-	-	≥ 23	-	-
<i>Enterococcus faecalis</i>	≤ 4	-	-	≥ 14	-	-

<sup>a</sup> [FDA STIC Webpage](#)

**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.