510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K203700

B Applicant

Oxoid Limited (Part of Thermo Fisher Scientific)

C Proprietary and Established Names

Thermo Scientific Oxoid Cefiderocol Disc (30 µg) FDC30

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:

To obtain substantial equivalence determination for Cefiderocol Antimicrobial Test Disk

B Measurand:

Cefiderocol Disc (30 µg) FDC30

C Type of Test:

Antimicrobial Susceptibility Test Disc

Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

III Intended Use/Indications for Use:

A Intended Use(s):

See Indication for Use below.

B Indication(s) for Use:

Thermo Scientific Oxoid Antimicrobial Susceptibility Test (AST) Discs are used in the semi-quantitative agar diffusion test method for *in vitro* susceptibility testing.

Thermo Scientific Oxoid Cefiderocol Disc (30 µg) FDC30 can be used to determine susceptibility to Cefiderocol against the following bacteria for which Cefiderocol has been shown to be active both clinically and *in vitro*:

For Complicated Urinary Tract Infections (cUTI):
Gram-negative bacteria:
Enterobacter cloacae complex
Escherichia coli
Klebsiella pneumoniae
Proteus mirabilis
Pseudomonas aeruginosa

For Hospital Acquired Bacterial Pneumonia and Ventilator-associated bacterial pneumonia (HABPN VABP):

Gram-negative bacteria:
Escherichia coli
Klebsiella pneumoniae
Pseudomonas aeruginosa
Serratia marcescens

C Special Conditions for Use Statement(s):

- Rx - For Prescription Use Only

- Limitation:

  "*The ability of the Thermo Scientific Oxoid Cefiderocol disc to detect resistance in Enterobacterales group combined and P. aeruginosa 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 for further testing*".

- Footnotes:

  "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".

"Resistance mechanism characterization was not available at the time of comparative testing, and therefore the performance of the Thermo Scientific Oxoid Cefiderocol disc is unknown for Enterobacterales and P. aeruginosa with resistance mechanisms listed in the FDA drug label".

D Special Instrument Requirements:
Not applicable

IV Device/System Characteristics:

A Device Description:

Thermo Scientific Oxoid Cefiderocol Disc (30µg) FDC 30 comprise 6 mm disks prepared by impregnating high absorbent paper with accurately determined amounts of Cefiderocol. The disk is clearly marked on both sides with the code FDC30. The code designates the agent (Cefiderocol) and the drug content (30 µg).

Thermo Scientific Oxoid disks are supplied in cartridges containing 50 disks each; there are 5 cartridges per pack. Each cartridge is individually sealed together with a desiccant capsule in a foil covered see-through blister pack. Thermo Scientific Oxoid disks can be dispensed using a Thermo Scientific Oxoid Disk Dispenser.

B Principle of Operation:

A suitable therapeutic agent can be determined using filter paper disks impregnated with specified concentrations of antimicrobial agents placed on the surface of a suitable test medium. The test is performed by inoculating pure cultures of clinical isolates onto the test medium and placing the AST disk on the surface of the medium. 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 combinations being tested.

V Substantial Equivalence Information:

A Predicate Device Name(s):

HardyDisk AST Cefidericol 300µg (FDC30)

B Predicate 510(k) Number(s):

K193504

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device: K203700	Predicate: K193504
Device Trade Name	Thermo Scientific Oxoid Cefiderocol Disc (30 µg) FDC30	HardyDisk AST Cefiderocol 30 µg (FDA 30)
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Thermo Scientific Oxoid Antimicrobial Susceptibility Test Discs are used in the semi quantitative agar diffusion test method for in vitro susceptibility testing.	Same
Antimicrobial Agent	Cefiderocol	Same
Antimicrobial Agent Concentration	30 µg	Same
Interpretation	The user will interpret the zone diameter according to the established interpretive criteria for the drug	Same
Test Method	Semi quantitative agar diffusion test method using antimicrobial discs impregnated with an antimicrobial agent.	Same
Result Interpretation Method.	Measurement of zone size	Same
General Device Characteristic Differences		
Manufacturing Specifications	Oxoid's specifications	Hardy Diagnostics' specifications

VI Standards/Guidance Documents Referenced:

- CLSI M02-13th ed., "Performance Standards for Antimicrobial Disk Susceptibility Tests; Approved Standard"; January 2018
- CLSI M100-S29, Performance Standards for Antimicrobial Susceptibility Testing; Twenty-ninth Informational Supplement

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   Reproducibility was conducted at one external site using 15 organisms, tested in triplicate with two disk lots on three separate days using one lot of Mueller Hinton agar (MHA 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 lot x 3 days x 3 independent readers = 270 data point).

   The reproducibility study included 11 Enterobacterales (5 *Enterobacter cloacae*, 6 *Klebsiella pneumoniae*) and 4 *Pseudomonas aeruginosa isolates.*

   Reproducibility was calculated as the percent of results which were within ±3 mm difference in zone diameter comparing test results with the modal zone diameter value. Summary results between disk lots and across readers are shown in **Table 1** below.

Table 1: Reproducibility Summary

Between Disk Lots			Across Readers			
Lot #1	**Lot #2**	**All Lots**	**Reader 1**	**Reader #2**	**Reader #3**	**All Readers**
97.8% (132/135)	97.8% (132/135)	97.8% (264/270)	98.9% (89/90)	98.9% (89/90)	98.9% (89/90)	98.9% (267/270)

   The reproducibility between disk lots and across reader is >95% and meets the acceptance criteria.

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-recommended quality control (QC) isolates, *Escherichia coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were tested a sufficient number of times (i.e., 20 replicates per lot per reader). One predicate disk lot and two Oxoid disk lots were used. Each test was visually read by three independent readers, resulting in 128 Oxoid disk data points (64 data points per lot) and 64 predicate disk data points. The performance is shown in **Table 2**.

Table 2: Quality Control Performance

	Zone Diameter in millimeter (mm)			
QC Organism	**Range**	**Comparator Disc[1]**	**Oxoid Lot A[2]**	**Oxoid Lot B[2]**
E. coli ATCC 25922 Expected Range: 25-31mm	21			
	22			
	23			
	24			
	25	5	5	5
	26	14	9	12
	27	17	14	13
	28	14	15	16
	29	9	12	9
	30	5	7	8
	31		2	1
P. aeruginosa ATCC 27853 Expected Range: 22 – 31	21			
	22			
	23	6	3	6
	24	15	10	10
	25	15	16	15
	26	16	16	10
	27	11	11	15
	28	1	8	8
	29			
	30			
	31			

ATCC=American Type Culture Collection
[1]One comparator disk lot.
[2]Two Oxoid disk lots were tested (Lot A and Lot B).

The Oxoid disk QC performance is > 95% (100%, 64/64 within the expected range for each disk lot) and is acceptable.

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.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:

   Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

The Oxoid disk Cefiderocol disc 30 µg (FDC30) was compared with an FDA cleared disc (predicate) of the same antimicrobial, mass/concentration, and content. The study was conducted at one testing site. Three independent operators participated in reading of test results with isolates evenly distributed to mimic testing at multiple sites. Testing was performed with one lot of disk of each test manufacturer (Oxoid and comparator FDA-cleared disk) utilizing Mueller Hinton agar (MHA media) following the CLSI M02-A13 method.

Clinical:
Clinical testing was performed at one U.S. site with both Thermo Scientific Cefiderocol and the Hardydisk using a total of 323 clinical isolates including 224 *Enterobacterales* (30 isolates of *Enterobacter cloacae* complex, 93 isolates of *E. coli*, 81 isolates of *K. pneumoniae*, 10 isolates of *P. mirabilis*, 10 isolates of *Serratia marcescens*) and 99 clinical isolates of *P. aeruginosa* .

Challenge:
Challenge testing was performed at one internal site. A total of 75 challenge isolates were tested which included 49 isolates of *Enterobacterales* (14 isolates of Enterobacter cloacae complex, 7 isolates of E. coli, 28 isolates of K. pneumoniae) and 26 isolates of ***P. aeruginosa.***

Results for the total 398 clinical and challenge isolates with representative species from each organism group are shown in **Table 3**.

Table 3: Overall Performance of the TF Oxoid Cefiderocol Disc vs. HardyDisk.

	Total	CA#	CA%	S (#)	I (#)	R (#)	Vmj	Maj	Min
Enterobacterales Combined									
Clinical	224	223	99.55	222	2	0	0	0	1
Challenge	49	49	100	48	1	0	0	0	0
Combined	273	272	**99.6**	270	3	0	0	0	1
P. aeruginosa									
Clinical	99	93	93.94	93	6	0	0	0	6
Challenge	26	26	100	23	3	0	0	0	0
Combined	125	119	**95.2**	116	9	0	0	0	6

CA – Category Agreement
S – Susceptible isolates
R – Resistant isolates
MIN – minor errors
MAJ – major errors
VMJ – very major errors

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

The overall performance of The Oxoid Cefiderocol disc as compared to the predicate disc for *Enterobacterales* group (Table 3) is acceptable with 99.6% CA. There were one minor discrepancy and no major or very major discrepancies.

The overall performance of The Oxoid Cefiderocol disc as compared to the predicate disc for *P. aeruginosa* (Table 3) is acceptable with 95.2% CA. There were six minor discrepancies and no major or very major discrepancies.

As required under 511A(b)(2)(C)(ii)(I) of the Federal Food, Drug and Cosmetic Act, the following statement is included as a footnote to the performance table in the device labeling to address testing of non-indicated species:

> *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.*

Number of Resistant Isolates Tested:

A total of 398 organisms combined challenge and clinical (273 for *Enterobacteriaceae* and 125 for *P. aeruginosa*) were tested. However, no resistant isolates were available for testing. To address the lack of resistant strains encountered during the clinical evaluation, the sponsor added the following limitation in the device labeling:

"The ability of the Thermo Scientific Oxoid Cefiderocol disc to detect resistance in Enterobacterales group combined and P. aeruginosa 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 for further testing".

Resistance Mechanisms in Challenge Isolates:

Challenge isolates harboring the resistance mechanisms against which Cefiderocol has been shown to be active were not tested. The sponsor added the following footnote to the device labeling:

"Resistance mechanism characterization was not available at the time of comparative testing, and therefore the performance of the Thermo Scientific Oxoid Cefiderocol disc is unknown for Enterobacterales and P. aeruginosa with resistance mechanisms listed in the FDA drug label".

Secondary Analysis:

A secondary analysis of the total 398 combined clinical and challenge isolates was also performed (273 *Enterobacterales* and 125 *P. aeruginosa*). The analysis was conducted to compare qualitative categorical agreement of the Oxoid disc and the predicate disk with the reference MIC values (based on historical data from testing performed at the initial recovery of isolates during the drug clinical trials). Because of the similarities between the Oxoid disk and the comparator disk with respect to content, drug concentration and test methods, a

similar analysis was also conducted with the comparator FDA-cleared disk diffusion results compared to the MIC values obtained by reference method.

Analysis of the Oxoid disk data for the *Enterobacterales* isolates showed an overall 98.9% CA, which is acceptable. There were three minor errors and no major or very major discrepancies observed with the Thermo Scientific Oxoid disc when compared to the MIC interpretive criteria.

Analysis of the Oxoid disk data for *P. aeruginosa* isolates showed an overall 97.6% CA, which is acceptable. There were three minor errors and no major or very major discrepancies observed with the Thermo Scientific Oxoid disc when compared to the MIC interpretive criteria.

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-identified interpretive criteria for Cefiderocol are listed in **Table 4**.

Table 4: FDA- Identified Interpretative Criteria Cefiderocol[1]

Pathogen	Disk Diffusion (mm)			Minimum Inhibitory Concentrations (mcg/mL)		
	S	I	R	S	I	R
Enterobacteriaceae[2,3]	≥16	9-15	≤8	≤4	8	≥ 16
P. aeruginosa	≥22	13-21	≤12	≤1	2	≥ 4

S = Susceptible; I = Intermediate; R = Resistant

[1] According to FDA STIC Website.

[2] Clinical efficacy was shown for *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Enterobacter cloacae* complex in patients with complicated urinary tract infections (cUTI).
[3] Clinical efficacy was shown for *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae* complex, and *Serratia marcescens* in patients with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP).

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.