510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K250789

B Applicant

Thermo Fisher Scientific (Oxoid Ltd.)

C Proprietary and Established Names

Thermo Scientific Oxoid Aztreonam/Avibactam Disc (30/20 µg) AZA50

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 Scientific) seeks the following:

1. Obtain a substantial equivalence determination for aztreonam/avibactam antimicrobial susceptibility test disk.
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:

Aztreonam/Avibactam 30/20 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 Discs 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 Aztreonam/Avibactam Disc (30/20 µg) AZA50 is intended to determine susceptibility of Enterobacterales to Aztreonam/Avibactam, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC). The Thermo Scientific Oxoid Aztreonam/Avibactam Disc (30/20 µg) AZA50 demonstrated acceptable performance to determine susceptibility to Aztreonam/Avibactam against the following microorganisms:

Enterobacterales (*Citrobacter freundii* complex*, Escherichia coli, Enterobacter cloacae* complex*, Klebsiella pneumoniae, Klebsiella oxytoca, Serratia marcescens,* and *Proteus mirabilis*)

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

Thermo Scientific Oxoid Aztreonam/Avibactam Disc (30/20 µg) which is designated with the code AZA50 is a high quality 6mm diameter white filter paper disk that is impregnated with 30/20 µg aztreonam/avibactam. The disks are clearly marked on both sides with AZA50, designating the agent and the drug content. The disks are supplied in plastic cartridges containing 50 disks each. Thermo Scientific Oxoid Aztreonam/Avibactam Disc (30/20 µg) AZA50 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: K250789	Predicate: K232276
Device Trade Name	Thermo Scientific Oxoid Aztreonam/Avibactam Disc (30/20 µg) AZA50	Thermo Scientific Oxoid Sulbactam/Durlobactam Disc (10/10 µg) SUD20
General Device Characteristic Similarities		
Intended Use	Antimicrobial Susceptibility Test Discs used in the semi quantitative agar diffusion test method for *in vitro* 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
Inoculum 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	Same

Device & Predicate Device(s):	Device: K250789	Predicate: K232276
	antimicrobial agent to the surface of the plate. The temperature, atmospheric conditions and duration of incubation are dependent on the organism tested.	
Reading Method	The user will interpret the zone diameters according to established interpretive criteria for the drug.	Same
General Device Characteristic Differences		
Antimicrobial Agent	Aztreonam/Avibactam	Sulbactam/Durlobactam
Concentration	30/20 µg	10/10 µg

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 lot x 3 days x 3 independent readers = 270 data points). Colony counts were performed on all isolates.

The reproducibility study included Enterobacterales consisting of the following species: three isolates each of *E. cloacae, E. coli, and K. pneumoniae*; two isolates each of *C. freundii* and *K. oxytoca;* and one isolate each of *P. mirabilis* and *S. marcescens.*

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

Table 1: Reproducibility Summary

Between Disk Lots			Across Readers[1]			
Lot A	**Lot B**	**All Lots**	**Reader#1**	**Reader#2**	**Reader#3**	**All Readers**
98.5% (133/135)	100.0% (135/135)	99.3% (268/270)	98.9% (89/90)	98.9% (89/90)	100.0% (90/90)	99.3% (268/270)

[1]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-recommended quality control (QC) isolate *Klebsiella pneumoniae* ATCC 700603 and CLSI QC isolates *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC 35218, and *Pseudomonas aeruginosa* ATCC 27853 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 280 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 Aztreonam/Avibactam Disk (30/20 µg)

	Zone Diameter in millimeter (mm)		
QC Organism	**Range**	**Oxoid Lot A[1]**	**Oxoid Lot B[1]**
E. coli ATCC 25922 Expected Range: 32–38 mm	31		
	32		
	33	5	6
	34	20	18
	35	21	22
	36	16	13
	37	6	9
	38	2	2
	39		
E. coli ATCC 35218 Expected Range: 31–38 mm	30		
	31		1
	32	2	3
	33	3	6
	34	22	18
	35	27	23
	36	14	15
	37	1	3
	38	1	1
	39		
	23		

	Zone Diameter in millimeter (mm)		
QC Organism	**Range**	**Oxoid Lot A[1]**	**Oxoid Lot B[1]**
P. aeruginosa ATCC 27853 Expected Range: 24–30 mm	24	1	1
	25	15	26
	26	31	24
	27	11	10
	28	9	6
	29	3	3
	30		
	31		
K. pneumoniae ATCC 700603 Expected Range: 26–32 mm	25		
	26		
	27	4	6
	28	26	23
	29	22	20
	30	12	12
	31	5	8
	32	1	1
	33		

ATCC=American Type Culture Collection
[1]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 clinical study to provide assurance of the data quality 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 Aztreonam/Avibactam by BMD Method

QC Organism	MIC (µg/mL)	Results
E. coli ATCC 25922 Expected MIC Range: 0.03/4-0.12/4 µg/mL	0.016/4	
	0.03/4	
	0.06/4	13
	0.12/4	1
	0.25/4	
E. coli ATCC 35218 Expected MIC Range: 0.016/4-0.06/4 µg/mL	0.008/4	
	0.016/4	5
	0.03/4	7
	0.06/4	2
	0.12/4	
P. aeruginosa ATCC 27853 Expected MIC Range: 2/4-8/4 µg/mL	1/4	
	2/4	
	4/4	11
	8/4	3
	16/4	
K. pneumoniae ATCC 700603 Expected MIC Range: 0.06/4-0.5/4 µg/mL	0.03/4	
	0.06/4	
	0.12/4	11

QC Organism	MIC (µg/mL)	Results
	0.25/4	3
	0.5/4	
	1/4	

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. The real time stability test is on-going.

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 Aztreonam/Avibactam Disc (30/20 µg) AZA50 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 two internal testing sites. 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 310 Enterobacterales clinical isolates [*C. freundii* (30 isolates), *E. cloacae* (51 isolates), *E. coli* (70 isolates), *K. oxytoca* (48 isolates), *K. pneumoniae* (60 isolates), *P. mirabilis* (31 isolates), and *S. marcescens* (20 isolates)].

   Challenge:
   Challenge testing was performed at one U.S site and one OUS site using a total of 75 Enterobacterales challenge isolates [*C. freundii* (11 isolates), *E. cloacae* (13 isolates), *E. coli* (13 isolates), *K. oxytoca* (11 isolates), *K. pneumoniae* (12 isolates), *P. mirabilis* (5 isolates), and *S. marcescens* (10 isolates)].

   Performance results for the total 385 clinical and challenge isolates are shown in **Table 4**.

Table 4: Performance of Thermo Scientific Oxoid Aztreonam/Avibactam Disk vs. Reference BMD Based on Categorical Result Interpretation

	Total	CA#	%CA	#S	#I	#R	MIN	MAJ	VJM
Enterobacterales [Disk Breakpoints (mm): ≥21 (S), 18-20 (I), ≤17 (R)]									
Clinical	310	308	99.4%	308	1	1	2	0	0
Challenge	75	74	98.7%	73	2	0	1	0	0
Combined	385	382	99.2%	381	3	1	3	0	0

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

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 Aztreonam/Avibactam Disc (30/20 µg) AZA50 disk as compared to the MIC for Enterobacterales (**Table 4**) is acceptable with 99.2% CA. There were three minor errors and no major or very major discrepancies.

Testing/Reporting Non-Indicated Species:
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".*

Resistance Isolates:
A total of 385 clinical and challenge isolates were tested when the Thermo Scientific Oxoid Aztreonam/Avibactam Disc (30/20 µg) AZA50 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 Aztreonam/Avibactam Disc (30/20 µg) AZA50 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: Aztreonam/Avibactam (30/20 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 Aztreonam/Avibactam Disc (30/20 µg) AZA50. The following mechanisms were evaluated: aac(3), aac(6'), AcrF, ACT, ANT, APH(3'), APH(6), ARR, cAmpC, cat, CMY, CRE, CTX, dfrA, DHA, EmrD, ere(A), erm(B), IMP, KdeA, KPC, mcr, mph(A), NDM, OmpK36m OqxA, OXA, qacEdelta1, QepA4, QnrS1, rmtF1, SHV, SME, sul1, sul2, TEM, tet(B), and VIM alleles.

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 aztreonam/avibactam are listed in **Table 5**.

Table 5. FDA Identified Interpretive Criteria for Aztreonam/Avibactam

	Minimum Inhibitory Concentration (µg/mL)[a]			Zone Diameter (mm)[a]		
Organism	**S**	**I**	**R**	**S**	**I**	**R**
Enterobacterales	≤ 4/4	8/4	≥ 16/4	≥ 21	18-20	≤ 17

[a] 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.

To support the implementation of changes to FDA-recognized susceptibility test interpretive criteria (i.e., breakpoints), this submission included a breakpoint change protocol that was reviewed and accepted by FDA. 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 Scientific Oxoid intends to use to evaluate the Thermo Scientific Oxoid Aztreonam/Avibactam Disc (30/20 µg) AZA50 when revised breakpoints for aztreonam/avibactam are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, Thermo Scientific Oxoid will update the Thermo Scientific Oxoid Aztreonam/Avibactam Disc (30/20 µg) AZA50 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.