510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K203336

B Applicant

Oxoid Limited (Part of Thermo Fisher Scientific)

C Proprietary and Established Names

Thermo Scientific Oxoid Omadacycline Disc (30µg) OMC30

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 Omadacycline Antimicrobial Susceptibility Test Disc.

B Measurand:

Omadacycline (30 µg) OMC30.

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:

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

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

For Acute Bacterial Skin and Skin Structure Infections (ABSSSI):

Enterobacter cloacae
Klebsiella pneumoniae
Staphylococcus aureus (including methicillin-resistant isolates)
Enterococcus faecalis
Streptococcus anginosus group (*Streptococcus anginosus* only)
Streptococcus pyogenes

For Community Acquired Bacterial Pneumonia (CABP):

Klebsiella pneumoniae
Staphylococcus aureus (including methicillin-susceptible isolates only)
Haemophilus species (Haemophilus influenzae, Haemophilus parainfluenzae)
Streptococcus pneumoniae

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Limitations:

- *The ability of the Thermo Scientific Oxoid Omadacycline Disc (30 µg) to detect resistance for Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in Staphylococcus aureus (including methicillin-resistant isolates), Enterococcus faecalis, Streptococcus pyogenes, Streptococcus anginosus group (S. anginosus only), and for Community Acquired Bacterial Pneumoniae (CABP), in Streptococcus pneumoniae is unknown because resistant strains were not avaible at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory for further testing.*

- *While the categorical agreement for Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) compared to FDA cleared disc device analysis was ≥ 90% for Staphylococcus aureus (MSSA and MRSA), Enterococcus faecalis, and Streptococcus pyogenes, categorical agreement for Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) compared to historical broth microdilution MIC values was below 90%, caused by the*

occurrence of false susceptible results and minor errors. If critical to patient care, testing should be performed using an alternate method, for the following antibiotic/organism combination(s) for ABSSSI: Omadacycline/S.aureus (MSSA and MRSA) which provides a zone of inhibition ≥ 19mm, Omadacycline/Enterococcus faecalis which provide a disc zone of inhibition of ≥ 17 mm , and for Omadacycline/Streptococcus pyogenes which provide a disc zone of inhibition ≥ 22 mm.

- *While the categorical agreement for Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) compared to FDA cleared disc device analysis was ≥ 90% for Haemophilus species, categorical agreement for Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) compared to historical Broth Microdilution MIC values was below 90%, caused by the occurrence of minor errors. If critical to patient care, results should be interpreted in conjunction with other clinical and laboratory information for the following antibiotic/organism combination(s) for CABP: Omadacycline/Haemophilus species which provide a zone of inhibition 17-19mm.*

- *Due to categorical agreement below 90% with the Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) when compared to both the FDA cleared comparator Disc and the historical Broth Microdilution MIC values cause by the occurrence of false susceptible results and minor errors, if critical to patient care, testing should be performed using an alternate method for the following antibiotic/organism combination(s) for CABP: Omadacycline/MSSA.*

D Special Instrument Requirements:

Not Applicable.

IV Device/System Characteristics:

A Device Description:

Thermo Scientific Omadacycline Disc (30µg) OMC30 comprise 6mm discs prepared by impregnating high quality absorbent paper with an accurately determined amount of Omadacycline. The Disc is clearly marked on both sides with the code OMC30. The code designates the agent (Omadacycline) and the drug content (30µg).

Thermo Scientific Oxoid discs are supplied in cartridges containing 50 discs 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 discs can be dispensed using a Thermo Scientific Oxoid Disc Dispenser.

B Principle of Operation:

A suitable therapeutic agent can be determined using filter paper discs 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 disc on the surface of the medium. The antibiotic within the disc diffuses into

the agar. After incubation, the zones of inhibition around the discs 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 Omadacycline 30µg (OMC30)

B Predicate 510(k) Number(s):

K183298

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device: K203336	Predicate: K183298
Device Trade Name	Thermo Scientific Oxoid Omadacycline Disc (30 µg) OMC30	HardyDisk AST Omadacycline 30µg (OMC30).
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	Omadacycline	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 M100-29th ed., *Performance Standards for Antimicrobial Susceptibility Testing*; Twenty-ninth Informational Supplement; 2019.

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 disc lots on three separate days using one lot of media (MHA, MHA + 5% SB, or HTM media). Each test was visually read by three independent readers with results blinded, resulting in 270 data points for evaluation (15 organisms x 2 disc lots x 1 media x 3 days x 3 independent readers = 270 data point). Colony counts was performed on all isolates.

The reproducibility study included the following species, indicated on the FDA-approved drug label: 1 isolate of *Staphylococcus lugdunensis*, 3 isolates of *Streptococcus pneumoniae*, 1 isolate of *Enterobacter cloacae* species complex, 1 isolate of *Streptococcus anginosus* group, 1 isolate of *Klebsiella pneumoniae*, 3 isolates of *Staphylococcus aureus*, 2 isolates of *Enterococcus faecalis* and 1 isolate of *Haemophilus influenzae, 1 Streptococcus pyogenes and 1 isolate of Enterobacter cloacae.*

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. Three isolates were >3mm above test mode with Thermo Scientific Oxoid Disc lot#1 and Disc lot#2. Results 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)	96.70% (87/90)	97.80% (88/90)	99% (89/90)	97.80% (264/270)

The reproducibility between disk lots and across readers 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, *Staphylococcus aureus* ATCC 25923, *Streptococcus pneumoniae* ATCC 49619, *Haemophilus influenzae* ATCC 49247 were tested a sufficient number of times (i.e., 20 replicates per lot per reader). One predicate disc lot and two Oxoid disc lots were used. Each test was visually read by three independent readers, resulting in 120 Oxoid disc data points and 60 predicate disc data points. The performance is shown in **Table 2** below.

Table 2: Quality Control Performance of Omadacycline (30µg)

	Zone Diameter in millimeter (mm)			
QC Organism	**Range**	**Comparator Disc (Predicate)[1]**	**Oxoid Lot A[2]**	**Oxoid Lot B[3]**
E. coli ATCC 25922 Expected Range: 22 – 28 mm	21			
	22		1	
	23	5	1	2
	24	32	22	20
	25	23	34	32
	26		2	6
	27			
	28			
	29			
	30			
Staphylococcus aureus ATCC 25923 Expected Range: 22 – 30	21			
	22	1	2	2
	23	3	2	3
	24	12	10	7
	25	20	16	18
	26	17	18	18
	27	6	8	7
	28	1	4	5
	29			
	30			

	Zone Diameter in millimeter (mm)			
QC Organism	**Range**	**Comparator Disc (Predicate)[1]**	**Oxoid Lot A[2]**	**Oxoid Lot B[3]**
Haemophilus influenzae ATCC 49247 Expected Range: 21-29 mm	21	1	1	1
	22	7	15	8
	23	38	25	26
	24	13	18	21
	25	1	1	4
	26			
	27			
	28			
	29			
	30			
Streptococcus pneumoniae ATCC 49619 Expected Range: 24 – 32	21			
	22			
	23			
	24			
	25	4	2	3
	26	8	7	9
	27	21	15	15
	28	18	26	25
	29	8	7	8
	30	1	3	
	31			
	32			

ATCC=American Type Culture Collection
[1]One comparator disk lot
[2]Two Oxoid disk lots were tested (lot A and lot B)
[3]Despite the lack of reliable disk diffusion breakpoints for S. pneumoniae with certain β-lactams, *S. pneumoniae* ATCC 49619 is the strain designated for QC of all disk diffusion tests with all *Streptococcus* spp.

The Oxoid disk QC performance is > 95% 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 Omadacycline disc 30 µg (OMC 30) was compared with an FDA cleared disc of the same antimicrobial, mass/concentration, and content. The study was conducted at one external 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 disc of each test manufacturer (Oxoid and comparator FDA-cleared disc) utilizing Mueller-Hinton agar (MHA) [Fastidious isolates were tested on MHA+5% sheep blood for streptococci and on Haemophilus Test Medium (HTM) for *Haemophilus* spp], following the CLSI M02 13th edition method.

   Clinical:
   Clinical testing was performed at one U.S. site with both Thermo Scientific Oxoid Omadacycline Disc and the comparator FDA cleared disc using a total of 307 clinical isolates including: *K. pneumoniae* (25 isolates), *Enterobacter cloacae* (14 isolates), *Staphylococcus aureus* MRSA (25 isolates), *Enterococcus faecalis* (20 isolates), *Streptococcus pyogenes* (50 isolates), *Streptococcus anginosus* (26 isolates), *Staphylococcus aureus* MSSA (25 isolates), *Haemophilus influenzae* (37 isolates), *Haemophilus parainfluenzae* (37 isolates), *Streptococcus pneumoniae* (48 isolates).

   Challenge:
   Challenge testing was performed at one U.S site. A total of 91 challenge isolates were tested which included *K. pneumoniae* (10 isolates), *Enterobacter cloacae* (3 isolates), *Enterococcus faecalis* (8 isolates), *Streptococcus pyogenes* (10 isolates), *Staphylococcus aureus* MSSA (20), *Haemophilus influenzas* (19 isolates), *Streptococcus pneumoniae* (21 isolates).

   Performance results for the total of 398 clinical and challenge isolates are shown in **Table 3A** and **Table 3B** based on the breakpoint/disease indication (CABP or ABSSSI) for each organism or organism group, respectively.

Table 3A: Performance of Thermo Scientific Oxoid Omadacycline Disc vs. Comparator FDA Cleared Disc with ABSSSI Breakpoints

`	Total	CA#	%CA	#S	#I	#R	MIN	MAJ	VJM
Enterobacterales[1] [Breakpoints (S, I, R in mm): ≥18, 16-17, ≤15]									
Clinical	39	35	89.7	24	5	10	4	0	0
Challenge	13	12	92.3	6	5	2	1	0	0
Combined	52	47	**90.4**	30	10	12	5	0	0
***Staphylococcus aureus* (including MRSA isolates) [Breakpoints (S, I, R in mm): ≥21, 19-20, ≤18]**									
Clinical	50	48	96	47	3	0	2	0	0
Challenge	20	19	95	18	1	1	1	0	0
Combined	70	67	**95.7**	65	4	1	3	0	0
***Enterococcus faecalis* [Breakpoints (S, I, R in mm): ≥18, 16-17, ≤15]**									
Clinical	20	19	95	18	2	0	1	0	0

`	Total	CA#	%CA	#S	#I	#R	MIN	MAJ	VJM
Challenge	8	8	100	8	0	0	0	0	0
Combined	28	27	**96.4**	26	2	0	1	0	0
Streptococcus anginosus **[Breakpoints (S, I, R in mm): ≥ 24, 18-23, ≤17]**									
Clinical	26	26	100.0	26	0	0	0	0	0
Challenge									
Combined	26	26	**100.0**	26	0	0	0	0	0
Streptococcus pyogenes **[Breakpoints (S, I, R in mm): ≥19, 16-18, ≤15]**									
Clinical	50	50	100.0	50	0	0	0	0	0
Challenge	10	10	100.0	10	0	0	0	0	0
Combined	60	60	**100.0**	60	0	0	0	0	0

[1]*K. pneumoniae* and *E. cloacae* only.

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 disc result interpretation agrees exactly with the comparator result interpretation.

For Acute Bacterial Skin and Skin Structure Infections (ABSSSI):

- The performance of the Thermo Scientific Oxoid Omadacycline disc as compared to the FDA cleared comparator disc for Enterobacterales (*Klebsiella pneumoniae* and *Enterobacter cloacae* only) (**Table 3A**) is acceptable with 90.4% CA. There were five minor errors and no major or very major discrepancies.

- The performance of the Thermo Scientific Oxoid Omadacycline disc as compared to the FDA cleared comparator disc for *Staphylococcus aureus* (including methicillin-resistant isolates) (**Table 3A**) is acceptable with 95.7% CA. There were three minor errors and no major or very major discrepancies.

- The performance of the Thermo Scientific Oxoid Omadacycline disc as compared to the FDA cleared comparator disc for *E. faecalis, Streptococcus anginosus* and *Streptococcus pyogenes* (**Table 3A**) is acceptable with 100% CA respectively. There were no minor, major, or very major discrepancies.

Table 3B: Performance of Oxoid Disc vs. Comparator Disc with CABP Breakpoints

	Total	CA#	%CA	#S	#I	#R	MIN	MAJ	VJM
***Klebsiella pneumoniae* [Breakpoints (S, I, R in mm): ≥18, 16-17, ≤15]**									
Clinical	25	23	92	13	4	8	2	0	0
Challenge	10	9	90	5	4	1	1	0	0
Combined	35	32	91.4	18	8	9	3	0	0
***Staphylococcus aureus* (MSSA isolates only) [Breakpoints (S, I, R in mm): ≥ 23, 21-22, ≤20]**									
Clinical	25	21	84	19	4	2	4	0	0
Challenge	20	19	95	16	2	2	1	0	0
Combined	45	40	88.9	35	6	4	5	0	0
***Haemophilus species*[1] [Breakpoints (S, I, R in mm): ≥ 20, 17-19, ≤16]**									
Clinical	74	71	95.95	58	14	2	4	0	0
Challenge	19	16	84.21	10	6	3	3	0	0
Combined	93	87	93.5	68	20	5	7	0	0
***Streptococcus pneumoniae* [Breakpoints (S, I, R in mm): ≥25, 23-24, ≤22]**									
Clinical	48	46	95.83	44	4	0	2	0	0
Challenge	21	21	100	20	1	0	0	0	0
Combined	69	67	97.1	64	5	0	2	0	0

[1]*Haemophilus* species includes *H. influenzae* and *H. parainfluenzae*

For Community Acquired Bacterial Pneumonia (CABP):

- The performance of the Thermo Scientific Oxoid Omadacycline disc as compared to the FDA cleared comparator disc (for *Klebsiella pneumoniae* only) performance is acceptable with 91.4% CA (**Table 3B**). There were three minor errors and no major or very major discrepancies.

- The performance of the Thermo Scientific Oxoid Omadacycline disc as compared to the FDA cleared comparator disc for *Staphylococcus aureus* (MSSA isolates only) has a low CA of 88.9% due to five minor errors (**Table 3B**). There were no major or very major discrepancies. Refer to limitation below under secondary analysis.

- The performance of the Thermo Scientific Oxoid Omadacycline disc as compared to the FDA cleared comparator disc for *Haemophilus species* is acceptable with 93.5% CA (**Table 3B**). There were seven minor errors and no major or very major discrepancies.

- The performance of the Thermo Scientific Oxoid Omadacycline disc as compared to the FDA cleared comparator disc for *Streptococcus pneumoniae* performance is acceptable with 97.1% CA (**Table 3B**). There were two minor errors 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".

Resistance Isolates:

A total of 398 clinical and challenge isolates were tested. However, no resistant isolates were available for testing for some organisms. 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 Omadacycline Disc (30 µg) to detect resistance for Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in Staphylococcus aureus (including methicillin-resistant isolates), Enterococcus faecalis, Streptococcus pyogenes, Streptococcus anginosus group (S. anginosus only), and for Community Acquired Bacterial Pneumoniae (CABP), in Streptococcus pneumoniae 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 Omadacycline has been shown to be active were not tested. This was addressed in the device labeling by adding the following footnote:

"*The performance of the Thermo Scientific Oxoid Omadacycline (30 µg) disc was not evaluated with challenge isolates harboring resistance mechanisms listed in the FDA drug label*".

Secondary Analysis:

A secondary analysis of the results obtained with the 392 clinical and challenge isolates was also performed. The analysis was conducted to assess the qualitative categorical agreement (CA) of the Oxoid Omadacycline disc diffusion results compared to the reference broth microdilution (BMD) results (based on historical data from BMD testing performed at the initial recovery of isolates during the drug clinical trial).

Analysis of the Oxoid disc when tested against the MIC value for each isolate showed a high number of categorical errors. It was determined that isolates showing very high major errors (VMJ) and minor errors should be retested as it was hypothesized that the MIC for these historical isolates was likely to have changed since they were first tested.

An additional study was performed which consisted of triplicate testing of the BMD method in addition of a control set representing ~25% of isolates with concordant results (percentage calculated based on the total number of concordant results). The categorical interpretations of

the disc diffusion value and mode MIC values were used to determine the categorical agreement.

The results of the Oxoid Omadacycline Disc versus MICs including retests of isolates showing very major and minor discrepancies are summarized below based on the breakpoint/disease indication (CABP or ABSSSI) for each organism or organism group.

For Acute Bacterial Skin and Skin Structure Infections (ABSSSI):

- The analysis of the Oxoid disc data when compared to the reference BMD method for Enterobacterales (*Klebsiella pneumoniae* and *Enterobacter cloacae* only) is acceptable with 92.3% CA. There were no major errors. There were three minor and one very major discrepancies (1/12 = 8.3%). This VMJ error rate was considered acceptable as this was due to single *Enterobacter cloacae* isolate and the %CA met the FDA acceptance criteria of >90%.

- The analysis of the Oxoid disc data when compared to the reference BMD method for *Streptococcus anginosus* is acceptable with 100% CA. There were no minor, major, or very major discrepancies.

- The analysis of the Oxoid disc data when compared to the reference BMD method for *Staphylococcus aureus* (MSSA and MRSA) had a low CA of 82.9% due to the high number of minor errors (9) and three very major errors (3/5 60%). There were no major errors. Refer to limitation below.

- The analysis of the Oxoid disc data when compared to the reference BMD method for *E. faecalis* had a low CA of 75% due to six minor and one very major discrepancies (1/2 50%). There were no major errors. Refer to limitation below.

- The analysis of the Oxoid disc data when compared to the reference BMD method for *Streptococcus pyogenes* had a low CA of 88.3% due to six minor and one very major discrepancies (1/1 100%). There were no major errors. Refer to limitation below.

  To address the low CA due to categorical errors (i.e., minor errors, very major errors) obtained with *Staphylococcus aureus* (MSSA and MRSA), *Enterococcus faecalis* and *Streptococcus pyogenes*, the following limitation was added to the device labeling:

  > *"While the categorical agreement for Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) compared to FDA cleared disc device analysis was ≥ 90% for Staphylococcus aureus (MSSA and MRSA), Enterococcus faecalis, and Streptococcus pyogenes, categorical agreement for Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) compared to historical broth microdilution MIC values was below 90%, caused by the occurrence of false susceptible results and minor errors. If critical to patient care, testing should be performed using an alternate method, for the following antibiotic/organism combination(s) for ABSSSI: Omadacycline/S.aureus (MSSA and MRSA) which provides a zone of inhibition ≥ 19mm, Omadacycline/Enterococcus faecalis which*

provide a disc zone of inhibition of ≥ 17 mm, and for Omadacycline/Streptococcus pyogenes which provide a disc zone of inhibition ≥ 22 mm".

For Community Acquired Bacterial Pneumonia (CABP):

- The analysis of the Oxoid disc data when compared to the reference BMD method for *Klebsiella pneumoniae* is acceptable with 91.43% CA. There were three minor errors and no major or very major discrepancies.

- The analysis of the Oxoid disc data when compared to the reference BMD method for *Streptococcus pneumoniae* is acceptable with 97.10% CA. There were two minor errors and no major or very major discrepancies.

- The analysis of the Oxoid disc data when compared to the reference BMD method for *Staphylococcus aureus* (methicillin-susceptible isolates only) had a low CA of 84.4% due to six minor and one very major error. There were no major errors. The following limitation was added to the device labeling:

  "Due to categorical agreement below 90% with the Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) when compared to both the FDA cleared comparator Disc and the historical Broth Microdilution MIC values cause by the occurrence of false susceptible results and minor errors, if critical to patient care, testing should be performed using an alternate method for the following antibiotic/organism combination(s) for CABP: Omadacycline/MSSA".

- The analysis of the Oxoid disc data when compared to the reference BMD method for *Haemophilus* spp had a low CA of 80.6% mainly due to 18 minor errors. There were no major or very major discrepancies. The following limitation was added to the device labeling:

  "While the categorical agreement for Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) compared to FDA cleared disc device analysis was ≥ 90% for Haemophilus species, categorical agreement for Thermo Scientific Oxoid Omadacycline Disc 30 µg (OMC 30) compared to historical Broth Microdilution MIC values was below 90%, caused by the occurrence of minor errors. If critical to patient care, results should be interpreted in conjunction with other clinical and laboratory information for the following antibiotic/organism combination(s) for CABP: Omadacycline/Haemophilus species which provide a zone of inhibition 17-19mm".

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 Omadacycline are listed in **Table 4A and 4B** below.

Table 4A: FDA Identified Interpretive Criteria for Omadacycline[1] for ABSSSI

Pathogen	Disk Diffusion (mm)			Minimum Inhibitory Concentrations (mcg/mL)		
	S	I	R	S	I	R
Enterobacteriaceae[2,3]	≥18	16-17	≤15	≤4	8	≥ 16
Staphylococcus aureus (including MRSA isolates)	≥21	19-20	≤18	≤ 0.5	1.0	≥ 2.0
Staphylococcus lugdunensis	≥29	26-28	≤25	≤ 0.12	0.25	≥0.5
Enterococcus faecalis	≥18	16-17	≤15	≤ 0.25	0.5	≥ 1.0
Streptococcus anginosus group[4]	≥24	18-23	≤17	≤ 0.12	0.25	≥ 0.5
Streptococcus pyogenes	≥19	16-18	≤15	≤ 0.12	0.25	≥ 0.

S = Susceptible; I = Intermediate; R = Resistant

[1] According to FDA STIC Website.
[2] *Klebsiella pneumoniae* and *Enterobacter cloacae* only
[3] Omadacycline is not active in vitro against *Morganella* spp., *Proteus* spp., and *Providencia* spp.
[4] *Streptococcus anginosus* group includes *S. anginosus*, *S. intermedius*, and *S. constellatus* but only *S. anginosus* is included in the intended use.

Table 4B: FDA Recognized Interpretive Criteria for Omadacycline[1] for CABP

Pathogen	Disk Diffusion (mm)			Minimum Inhibitory Concentrations (mcg/mL)		
	S	I	R	S	I	R
Enterobacteriaceae[2,3]	≥18	16-17	≤15	≤4	8	≥ 16
Staphylococcus aureus (MSSA isolates only)	≥23	21-22	≤20	≤ 0.25	0.5	≥ 1.0
Haemophilus species[4]	≥20	17-19	≤16	≤2	4	≥ 8
Streptococcus pneumoniae	≥25	23-24	≤22	≤0.12	0.25	≥ 0.5

S = Susceptible; I = Intermediate; R = Resistant

[1] According to FDA STIC Website.
[2] Omadacycline is not active in vitro against *Morganella* spp., *Proteus* spp., and *Providencia* spp.
[3] *Klebsiella pneumoniae* only
[4] *Haemophilus* species includes *H. influenzae* and *H. parainfluenzae*.

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.