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

A. 510(k) Number:

K183033

B. Purpose for Submission:

To obtain a substantial equivalence determination for the addition of Omadacycline at concentrations of 0.03 – 32 µg/mL to the Sensititre 18-24-hour MIC or Breakpoint Susceptibility System for testing gram negative or gram positive non-fastidious isolates

C. Measurand:

Omadacycline in the dilution range of 0.03 – 32 µg/mL.

D. Type of Test:

Quantitative Antimicrobial Susceptibility Test (AST), growth-based detection

E. Applicant:

ThermoFisher Scientific

F. Proprietary and Established Names:

Sensititre 18 – 24 hour MIC or Breakpoint Susceptibility System with Omadacycline in the dilution range of 0.03 – 32 µg/mL

G. Regulatory Information:

1. Regulation section:

   866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

   Class II

3. Product code:

   JWY – Manual Antimicrobial Susceptibility Test System

LRG – Instrument for Auto Reader and Instrumentation of Overnight Susceptibility Systems

LTT – Panels, Test, Susceptibility, Antimicrobial

4. Panel:

   83, Microbiology

H. Intended Use:

1. Intended use(s):

   The Sensititre MIC and Breakpoint Susceptibility system is an in vitro diagnostic product for clinical susceptibility testing of non-fastidious gram negative isolates comprising of *Enterobacteriaceae*, *Pseudomonas aeruginosa* and other non-*Enterobacteriaceae* and of non-fastidious gram positive isolates, comprising of *Staphylococcus* sp., *Enterococcus* sp., and Beta hemolytic Streptococci other than *S. pneumoniae*.

2. Indication(s) for use:

   The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System is an in vitro diagnostic product for clinical susceptibility testing of non-fastidious isolates.

   This 510(k) is for Omadacycline in the dilution range of 0.03 – 32 µg/mL for testing non-fastidious gram positive and gram negative organisms on the Sensititre 18-24 hour MIC panel.

   Omadacycline has been shown to be active both clinically and in vitro against the following organisms according to the FDA drug label:

   Gram negative bacteria
   Klebsiella pneumoniae
   Enterobacter cloacae

   Gram positive bacteria
   Enterococcus faecalis
   Staphylococcus lugdunensis
   Staphylococcus aureus

   Omadacycline has been shown to be active in vitro only against the non-fastidious bacteria listed below according to the FDA drug approved label:

   Gram negative bacteria
   Citrobacter koseri
   Citrobacter freundii

Klebsiella (Enterobacter) aerogenes
Escherichia coli
Klebsiella oxytoca

3. Special conditions for use statement(s):

For prescription use only

The following limitations are included in the labeling:

The testing of Omadacycline with Gram-negative and Gram-positive organisms was performed using the autoreader (OptiRead) and Vizion reading methods only. The use of an alternative reading method when testing Omadacycline has not been evaluated.

Studies of Omadacycline with gram negative and gram positive non-fastidious organsims were performed using the AIM autoinoculator. The use of an alternative inoculation system when testing meropenem/vaborbactam has not been evaluated.

The ability of the Sensititre system to detect resistance to Omadacycline in the following species is unknown because resistant strains were not available at the time of comparative testing: S. aureus (MRSA and MSSA), Enterococcus faecalis and S. lugdunensis. Isolates yielding omadacyline MIC results suggestive of a resistant interpretive category should be submitted to a reference laboratory for further testing.

Resistance mechanism characterization was not available for all organisms at the time of comparative testing, and therefore the performance of the Sensititre Omadacycline for non-fastidious gram-negative and gram-positive organisms is unknown for organisms harboring the following resistance mechanisms: tetB, tetK, tetL, tetM.

The safety and efficacy of Omadacycline in treating Acute Bacterial Skin and Skin Structure infections (ABSSSI) due to organisms other than K. pneumoniae and E. cloacae or Community Acquired Bacterial Pneumoniae (CABP) due to organisms other than K. pneumoniae may or may not have been established in adequate and well-controlled clinical trials. The clinical significance of susceptibility information in such instances is unknown.

The safety and efficacy of Omadacycline in treating Acute Bacterial Skin and Skin Structure infections (ABSSSI) due to organisms other than S. aureus (MRSA and MSSA, S. lugdunensis and E. faecalis or Community Acquired Bacterial Pneumoniae (CABP) due to organisms other than S. aureus (MSSA only) may or may not have been established in adequate and well-controlled clinical trials. The clinical significance of susceptibility information in such instances is unknown.

4. Special instrument requirements:
   Sensititre AIM for device inoculation
   Sensititre VIZION or OptiRead for plate reading

I. Device Description:

Sensititre MIC Susceptibility MIC panels are multi-well microtiter plates, dosed with dried, stabilized antimicrobials. It is a miniaturized version of the classic broth dilution method and can provide both qualitative and quantitative susceptibility results. After inoculation, plates are sealed with an adhesive seal, incubated at 34 – 36 °C for 18 – 24 hours and examined for bacterial growth.

Antimicrobial susceptibility test results can be determined by reading growth using the digital device (VIZION) or automatically on an autoreader (OptiRead) using fluorescence.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Sensititre 18-24 hour Susceptibility System, Cefepime

2. Predicate 510(k) number(s):

   K962867

3. Comparison with predicate:

Table 1. Comparison with the Predicate Device

Similarities		
Item	**Device K183033 Sensititre 18-24 hour Susceptibility System Omadacycline**	**Predicate K962867 Sensititre 18-24 Hour Susceptibility System Cefepime**
Intended Use	The Sensititre MIC and Breakpoint Susceptibility system is an in vitro diagnostic product for clinical susceptibility testing of non-fastidious gram negative isolates, comprising of *Enterobacteriaceae, Pseudomonas aeruginosa*, and other non-*Enterobacteriaceae* and of non-fastidious gram positive isolates, comprising of *Staphylococcus* sp., *Enterococcus* sp., and Beta hemolytic *Streptococci* other than *S. pneumoniae*.	Same
Test Panel	96 well plate is dosed with selected antimicrobial agents and substrate for the fluorescent reads, then dried. The bacterial suspension in the appropriate broth is used to rehydrate the plate	Same
Test Organism	Non-fastidious gram-positive and gram-negative isolates	Same
Reading Methods	Results can be read using the following methods: 1) Automatically with the OptiRead (fluorescent substrate technology) 2) On the VIZION (digital viewing device)	Same

Differences		
Item	Device	Predicate
Antimicrobial Agent	Omadacycline	Cefepime
Incubation	18 hours, 35 ± 1° C	18-24 hours, 35 ± 1°C

K. Standard/Guidance Document Referenced (if applicable):

Guidance for Industry and FDA - Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems – August 28, 2009.

CLSI M100-S027: Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Seventh Informational Supplement

CLSI M7-A10: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard – Tenth Edition

L. Test Principle:

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System includes multi-well plastic microtiter plates that contain doubled dilution of antibacterial agents. Each plate includes antimicrobial agents at appropriate dilutions. Results can be read by the digital device, VIZION, or by use of an automated reader (OptiRead).

The VIZION allows the panel image to be displayed on a touch screen directly from a video camera and allows the user to manually determine MIC results. The Sensititre OptiRead utilizes fluorescence technology to read the microbroth dilution plates after 18 to 24 hours incubation. The technology involves the detection of bacterial growth by monitoring the activity of specific surface enzymes produced by the test organism. Growth is determined by generating a fluorescent product from a fluorogenic substrate. The substrate is prepared by conjugating a fluorescent compound to the specific enzyme substrates with a bond which prevents fluorescence. The enzymatic action of the bacterial surface enzymes on the substrate cleaves the bond releasing fluorescence. The amount of fluorescence detected is directly related to bacterial growth. The MIC is determined by observing the lowest dilution of antimicrobial agent that inhibits growth of the organism. The substrate can be added to the inoculum broth which is dispensed into the test plate at the same time as the test organism, or, the plates can be prepared with the substrate already added to each micro-well.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A reproducibility study was performed at four sites using a panel comprised of 12 strains of *Enterobacteriaceae:* (*K. pneumoniae* (four isolates), *E. cloacae* (one isolate), *E. coli* (five isolates) and *K. oxytoca* (two isolates). Thirteen gram positive isolates from indicated species were evaluated including *S. aureus* MSSA (five isolates) *S. aureus* MRSA (five isolates) and *E. faecalis* (three isolates). In addition, one non-indicated gram positive species was tested. All isolates were tested in triplicate over three days with each read method (i.e., VIZION and OptiRead). The Sensititre Aim inoculator was used for plate inoculation. The mode MIC value was determined and the reproducibility was calculated based on MIC values falling within ±1 dilution of the mode MIC value. Reproducibility was greater than 95% for both read methods with both gram-positive and gram-negative organisms and was considered to be acceptable.

b. Linearity/assay reportable range:

Not applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Quality control strains recommended by the CLSI were tested with Omadacycline at four sites. The QC organisms tested were *E. coli* ATCC 25922, *S. aureus* ATCC 29213 and *E. faecalis* ATCC 29212. The QC strains were tested a minimum of 20 times per site and read using the VIZION and OptiRead. The results demonstrate that the Sensititre 18-24 hour MIC or Breakpoint panel with Omadacycline produced quality control results in the recommended range >95% of the time (Table 2).

Table 2. Quality Control Results for Sensititre 18 – 24 hour MIC or Breakpoint Susceptibility System with Omadacycline with the VIZION and OptiRead Methods.

QC Organism	Omadacycline Range (µg/mL)	Concentration (µg/mL)	Reference	Sensititre	
				Read method	
				VIZION	OptiRead
E. coli ATCC 25922	0.25 - 2	0.12	0	0	0
		0.25	26	4	1
		0.5	53	75	76
		1	1	1	3
		2	0	0	0
		4	0	0	0
S. aureus ATCC 29213	0.12 -1	0.06	0	0	0
		0.12	4	3	3
		0.25	71	58	71
		0.5	3	20	7
		1	0	0	0
		2	0	0	0
E. faecalis ATCC 29212	0.06 – 0.5	0.03	0	0	0
		0.06	12	0	3
		0.12	52	41	71
		0.25	14	39	7
		0.5	0	1	0
		1	0	0	0

Inoculum Density. Inoculum density checks were performed a sufficient number of times; all organism suspensions were in the acceptable range.

Purity checks. Purity checks were performed on all isolates following plate inoculation. Only results from pure cultures were evaluated.

Growth Failure: All gram-negative and gram-positive isolates tested showed growth in the Sensititre panels.

d. Detection limit:

Not applicable

e. Analytical specificity:

Not applicable

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Results obtained with Sensititre 18 – 24 hour MIC or Breakpoint Susceptibility System with Omadacycline were compared to results obtained with the CLSI broth microdilution reference panel. Drug dilutions were prepared using fresh Mueller Hinton broth as indicated in CLSI M100, 28th ed. Clinical testing was performed at four sites, three of which were in the U.S. A total of 365 clinical *Enterobacteriaceae* isolates were tested comprised of the following species: *K. pneumoniae* (96 isolates), *E. cloacae* (41 isolates), *E. coli* (108 isolates), *Citrobacter* spp. (57 isolates), *K. aerogenes* (20 isolates), and *K oxytoca* (43 isolates). A total of 390 gram positive clinical isolates were tested comprised of the following species: *S. aureus* (MSSA, 201 isolates, MRSA 199 isolates), *S. lugdunensis* (20 isolates), and *E. faecalis* (60 isolates). All of the clinical isolates tested were fresh isolates. During the course of the clinical trial, all Sensititre dried MIC panels were inoculated using the Sensititre Autoinoculator (AIM) and the same panel was read on both the VIZION (manual read) and the OptiRead in a blinded manner. The sponsor added the following limitations to the device labeling to reflect these inoculation and read methods:

> *Studies of Omadacyline with gram positive and gram negative organisms were performed using the AIM autoinoculator. The use of an alternative inoculation system when testing Omadacycline has not been evaluated.*
>
> *The testing of Omadacycline with Gram-negative and Gram-positive organisms was performed using the autoreader (OptiRead) and VIZION reading methods only. The use of an alternative reading method when testing Omadacycline has not been evaluated.*

A total of 194 challenge isolates were tested at a single site. Species tested included *K. pneumoniae* (28 isolates), *E. cloacae* (11 isolates), *E. coli* (16 isolates), *Citrobacter* spp. (8 isolates), *K. aerogenes* (7 isolates), *K. oxytoca* (5 isolates), *S. aureus* (MSSA, 50 isolates, MRSA 50 isolates), *S. lugdunensis* (14 isolates), and *E. faecalis* (5 isolates).

For the *Enterobacteriaceae,* results were evaluated for essential agreement (EA) and category agreement (CA). For CA evaluation, the same breakpoints for both Community Acquired Bacterial Pneumonia (CABP) and Acute Bacterial Skin and Skin Structure Infections (ABSSSI) (≤4, 8, ≥16) were used as noted on the FDA-Recognized Susceptibility Test Interpretive Criteria Website (STIC) (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm575163.htm). The results from clinical and challenge testing determined with the

VIZION demonstrated a combined EA of 100% and CA of 96.6%. A total of 438 isolates were determined to have evaluable results; the EA of evaluable results was 100% (Table 3). Clinical and challenge isolate results for the *Enterobacteriaceae* determined with OptiRead demonstrated a combined EA of 99.8% and CA of 96.6%. A total of 438 isolates were determined to have evaluable results; the EA of evaluable results was 99.8% (Table 5).

For *S. aureus* (MSSA) results were evaluated for essential agreement (EA) and category agreement (CA). For CA evaluation, the STIC-recognized breakpoints for CABP, the combined MIC results from clinical and challenge testing determined with the VIZION demonstrated EA of 100% and CA 90.4%; EA of evaluable results was 100% (Table 4). For MIC results determined with OptiRead, the combined results from clinical and challenge testing demonstrated an EA of 99.2% and CA of 100%; EA of evaluable results was 99.2% (Table 6).

For *S. aureus* (MSSA and MRSA) evaluated using the STIC-recognized breakpoints for ABSSSI, combined MIC results of clinical and challenge testing read using VIZION demonstrated an EA of 99.4% and CA of 97.8%; EA of evaluable results was 99.4% (Table 4). Using OptiRead, results demonstrated an EA of 98.4% and CA of 98.8%; EA of evaluable result was 98.4% (Table 6).

MIC results for isolates of *S. lugdunensis* were evaluated using STIC-recognized breakpoints for ABSSSI only and showed 100% EA and CA for results read on both VIZION and OptiRead (Tables 4 and 6).

MIC results for isolates of *E. faecalis* were evaluated using STIC-recognized breakpoints for ABSSSI only. Results obtained using VIZION demonstrated an EA of 93.8% and CA of 92.3%; EA of evaluable was 97.7% (Table 4). For results obtained using OptiRead, EA was 95.9% and CA was 93.8%; EA of evaluable was 100% (Table 6).

For all gram-positive organisms, an insufficient number of resistant strains were encountered during the clinical evaluation. The sponsor included the following limitation in the device labeling:

> *The ability of the Sensititre system to detect resistance to Omadacycline in the following species is unknown because resistant strains were not available at the time of comparative testing: S. aureus (MRSA and MSSA), Enterococcus faecalis and S. lugdunensis. Isolates yielding omadacyline MIC results suggestive of a resistant interpretive category should be submitted to a reference laboratory for further testing.*

Table 3. Performance of Gram Negative Clinical and Challenge Isolates, ABSSSI and CABP Breakpoints, Read Using VIZION

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Enterobacteriaceae* ABSSSI and CABP breakpoints (≤4, 8, ≥16) [a]**													
Clinical	365	365	100.0	363	363	100.0	353	96.7	18	333	12	0	0
Challenge	75	75	100.0	75	75	100.0	72	96.0	8	54	3	0	0
Total	440	440	100.0	438	438	100.0	425	96.6	26	387	15	0	0

[a] Includes *K. pneumoniae, E. cloacae, E. coli, Citrobacter* spp., *K. aerogenes* and *K. oxytoca*

EA – Essential Agreement (+/- 1 dilution)
CA – Category Agreement
EVAL – Evaluable isolates
R – Resistant isolates

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 Sensititre panel 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 the Sensititre panel. Category agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the Sensititre panel.

Table 4. Performance of Gram Positive Clinical and Challenge Isolates, CABP and ABSSSI Breakpoints, Read Using VIZION

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Staphylococcus aureus* (MSSA) - CABP breakpoints (≤0.25, 0.5, ≥1)**													
Clinical	201	201	100.0	200	200	100.0	178	88.6	1	191	23	0	0
Challenge	50	50	100.0	50	50	100.0	49	98.0	0	50	0	0	0
Total	251	251	100.0	250	250	100.0	227	90.4	1	241	23	0	0
***Staphylococcus aureus* (MSSA) - ABSSSI breakpoints (≤0.5, 1, ≥2)**													
Clinical	201	201	100.0	200	200	100.0	200	99.5	0	200	1	0	0
Challenge	50	50	100.0	50	50	100.0	50	100.0	0	50	0	0	0
Total	251	251	100.0	250	250	100.0	250	99.6	0	250	1	0	0
***Staphylococcus aureus* (MRSA) - ABSSSI breakpoints (≤0.5, 1, ≥2)**													
Clinical	199	197	99.0	199	197	99.0	192	96.6	2	184	7	0	0
Challenge	50	49	98.0	50	49	98.0	47	94.0	0	48	3	0	0
Total	249	246	98.8	249	246	98.8	239	96.0	2	232	10	0	0
***Staphylococcus aureus* (MSSA and MRSA) - ABSSSI breakpoints (≤0.5, 1, ≥2)**													
Clinical	400	398	99.5	399	397	99.5	392	98.0	2	384	8	0	0
Challenge	100	99	99.0	100	99	99.0	97	97.0	0	98	3	0	0
Total	500	497	99.4	499	496	99.4	489	97.8	2	482	11	0	0
***Staphylococcus lugdunensis* ABSSSI breakpoints – (≤0.12, 0.25, ≥0.5)**													
Clinical	20	20	100.0	20	20	100.0	20	100.0	0	20	0	0	0
Challenge	14	14	100.0	14	14	100.0	14	100.0	3	11	0	0	0
Total	34	34	100.0	34	34	100.0	34	100.0	3	31	0	0	0
***Enterococcus faecalis* - ABSSSI breakpoints (≤0.25, 0.5, ≥1)**													
Clinical	60	56	93.3	55	53	96.4	55	91.7	1	58	5	0	0
Challenge	5	5	100.0	5	5	100.0	5	100.0	1	4	0	0	0

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
Total	65	61	93.8	60	58	96.7	60	92.3	2	62	5	0	0

Table 5. Performance of Gram Negative Clinical and Challenge Isolates, Read Using OptiRead

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Enterobacteriaceae* ABSSSI and CABP breakpoints (≤4, 8, ≥16)**													
Clinical	365	364	99.7	364	363	99.7	348	95.3	18	333	16	1	0
Challenge	75	75	100.0	75	75	100.0	67	89.3	8	54	8	0	0
Total	440	439	99.8	439	438	99.8	415	94.3	26	387	24	1	0

Table 6. Performance of Gram Positive Clinical and Challenge Isolates, CABP and ABSSSI Breakpoints, Read Using OptiRead

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Staphylococcus aureus* (MSSA) - CABP breakpoints (≤0.25, 0.5, ≥1)**													
Clinical	201	199	99.0%	200	198	99.0%	187	93.0%	1	191	14	0	0
Challenge	50	50	100.0%	50	50	100.0%	50	100.0%	0	50	0	0	0
Total	251	249	99.2%	250	248	99.2%	237	94.4%	1	241	14	0	0
***S. aureus* (MSSA) - ABSSSI breakpoints (≤0.5, 1 ≥2)**													
Clinical	201	199	99.0	200	198	99.0	201	100.0	0	200	0	0	0
Challenge	50	50	100.0	50	50	100.0	50	100.0	0	50	0	0	0
Total	251	249	99.2	250	248	99.2	251	100.0	0	250	0	0	0
***S. aureus* (MRSA) - ABSSSI breakpoints (≤0.5, 1 ≥2)**													
Clinical	199	195	98.0	199	195	98.0	195	98.0	2	184	4	0	0
Challenge	50	48	96.0	50	48	96.0	48	96.0	0	48	2	0	0
Total	249	243	97.6	249	243	97.6	243	97.6	2	232	6	0	0
***S. aureus* (MSSA and MRSA) - ABSSSI breakpoints (≤0.5, 1 ≥2)**													
Clinical	400	394	98.5	399	393	98.5	396	99.0	2	384	4	0	0
Challenge	100	98	98.0	100	98	98.0	98	98.0	0	98	2	0	0
Total	500	492	98.4	499	491	98.4	494	98.8	2	482	6	0	0
***S. lugdunensis* - ABSSSI breakpoints (≤0.12, 0.25, ≥0.5)**													
Clinical	20	20	100.0	20	20	100.0	20	100.0	0	20	0	0	0
Challenge	14	14	100.0	14	14	100.0	14	100.0	3	11	0	0	0
Total	34	34	100.0	34	34	100.0	34	100.0.	3	31	0	0	0
***E. faecalis* - ABSSSI breakpoints (≤0.25, 0.5, ≥1)**													
Clinical	60	58	96.7	55	55	100.0	56	93.3	1	58	4	0	0
Challenge	5	5	100.0	5	5	100.0	5	100.0	1	4	0	0	0
Total	65	63	96.9	60	60	100.0	61	93.8	2	62	4	0	0

To address the testing of non-indicated species the following footnotes were included in the device labeling:

> *The safety and efficacy of Omadacycline in treating Acute Bacterial Skin and Skin Structure infections (ABSSSI) due to organisms other than K. pneumoniae and E. cloacae or Community Acquired Bacterial Pneumoniae (CABP) due to organisms other than K. pneumoniae may or may not have been established in adequate and well-controlled clinical trials. The clinical significance of susceptibility information in such instances is unknown.*
>
> *The safety and efficacy of Omadacycline in treating Acute Bacterial Skin and Skin Structure infections (ABSSSI) due to organisms other than S. aureus (MRSA and MSSA, S. lugdunensis and E. faecalis or Community Acquired Bacterial Pneumoniae (CABP) due to organisms other than S. aureus (MSSA only) may or may not have been established in adequate and well-controlled clinical trials. The clinical significance of susceptibility information in such instances is unknown.*

Resistance Mechanisms

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

> *Resistance mechanism characterization was not available for all organisms at the time of comparative testing, and therefore the performance of the Sensititre Omadacycline for non-fastidious gram-negative and gram-positive organisms is unknown for organisms harboring the following resistance mechanisms: tetB, tetK, tetL, tetM.*

MIC Trending

An analysis of trending was conducted using the combined clinical and challenge data for each organism group. This trending calculation takes into account MIC values that are determined to be one or more doubling dilutions lower or higher compared to the reference method irrespective of whether the device MIC values are on-scale or not. Trending results are shown in Table 7 for *Enterobacteriaceae* and for gram positive organisms in Table 8. Results for *Enterobacteriaceae* were also stratified by species to determine if particular trends were observed. The acceptable percent difference between higher and lower dilution readings is <30%.

Gram-negative

Table 7. Trending in *Enterobacteriaceae*, Clinical and Challenge Isolates

Read Method	Organism	Total evaluable for trending	≥ 1 dilution lower No. (%)	Exact No (%)	≥ 1 dilution higher No (%)
VIZION	*K. pneumoniae*[a]	122	11(9.0)	77 (63.1)	34 (27.9)
	E. cloacae[b]	52	3 (5.8)	41 (78.9)	8 (15.4)
	K. oxytoca[c]	48	2 (4.2)	39 (81.3)	7 (14.6)
	K. aerogenes[d]	27	2 (7.4)	22 (81.5)	3 (11.1)
	Citrobacter spp.[e]	65	2 (3.1)	34 (52.3)	29 (44.6)
	E. coli[f]	124	14 (11.3)	73 (58.9)	37 (29.8)
	All *Enterobacteriaceae*[g]	438	34 (7.8)	286 (65.3)	118 (26.9)
OptiRead	*K. pneumoniae*[h]	123	17 (13.8)	71 (57.7)	35 (28.5)
	E. cloacae[i]	52	5 (9.6)	40 (76.9)	7 (13.5)
	K. oxytoca[j]	48	5 (10.4)	35 (72.9)	8 (16.7)
	K. aerogenes[k]	27	3 (11.1)	22 (81.5)	2 (7.4)
	Citrobacter spp.[l]	65	6 (9.2)	29 (44.6)	30 (46.2)
	E. coli[m]	124	23 (18.6)	71 (57.3)	30 (24.2)
	All *Enterobacteriaceae*[n]	439	59 (13.4)	268 (61.1)	112 (25.5)

[a] Difference between the higher and lower dilutions for *K. pneumoniae* is:18.9%
[b] Difference between the higher and lower dilutions for *E. cloacae* is: 9.6%
[c] Difference between the higher and lower dilutions for *K. oxytoca* is: 10.4%
[d] Difference between the higher and lower dilutions for *K. aerogenes* is: 3.7%
[e] Difference between the higher and lower dilutions for *Citrobacter* spp. is 41.5%
[f] Difference between the higher and lower dilutions for *E. coli* is 18.6%
[g] Difference between the higher and lower dilutions for *Enterobacteriaceae* (Manual Read) is 19.2%
[h] Difference between the higher and lower dilutions for *K. pneumoniae* is: 14.6%
[i] Difference between the higher and lower dilutions for *E. cloacae* is:3.9%
[j] Difference between the higher and lower dilutions for *K oxytoca* is 6.2%
[k] Difference between the higher and lower dilutions for *K. aerogenes* is -3.7%
[l] Difference between the higher and lower dilutions for *Citrobacter* spp. is 36.9%
[m] Difference between the higher and lower dilutions for *E. coli* is 5.7%
[n] Difference between the higher and lower dilutions for *Enterobacteriaceae* (Auto Read) is 12.1%

Gram-positive

Table 8. Trending in *Staphylococcus* spp. and *E. faecalis*

Read Method	Organism	Total evaluable for trending	≥ 1 dilution lower No. (%)	Exact No (%)	≥ 1 dilution higher No (%)
Vizion	*S. aureus* (MSSA)[a]	250	18 (7.2)	132 (52.8)	100 (40.0)
	S. aureus (MRSA)[b]	249	12 (4.8)	142 (57.0)	95 (38.2)
	S. aureus[c]	499	30 (6.0)	274 (54.9)	195 (39.1)
	S. lugdunensis[d]	34	2 (5.9)	24 (70.6)	8 (23.5)
	E. faecalis[e]	60	0	33 (55.0)	27 (45.0)
OptiRead	*S. aureus* (MSSA)[f]	250	34 (13.6)	138 (55.2)	78 (31.2)
	S. aureus (MRSA)[g]	249	24 (9.6)	137 (55.0)	88 (35.3)
	S. aureus[h]	499	58 (11.6)	275 (55.1)	166 (33.3)
	S. lugdunensis[i]	34	16 (47.1)	17 (50.0)	1 (2.9)
	E. faecalis[j]	60	8 (13.3)	36 (60.0)	16 (26.7)

[a] Difference between the higher and lower dilutions for *S. aureus* (MSSA) is: 32.8%
[b] Difference between the higher and lower dilutions for *S. aureus* (MRSA) is: 33.3%
[c] Difference between the higher and lower dilutions for *S. aureus* (MSSA and MRSA) is: 33.1%
[d] Difference between the higher and lower dilutions for *S. lugdunensis* is: 17.7%
[e] Difference between the higher and lower dilutions for *E. faecalis* is: 45.0%
[f] Difference between the higher and lower dilutions for *S. aureus* (MSSA) is: 17.6%
[g] Difference between the higher and lower dilutions for *S. aureus* (MRSA) is: 25.7%
[h] Difference between the higher and lower dilutions for *S. aureus* (MSSA and MRSA) is: 22.6%
[i] Difference between the higher and lower dilutions for *S. lugdunensis* is: -44.1%
[j] Difference between the higher and lower dilutions for *E. faecalis* is: 13.3%

A trend toward higher MIC readings was observed for *Citrobacter spp* with both Vizion and OptiRead. A trend toward higher MIC readings was observed for *S. aureus* (MRSA and MSSA and *E. faecalis* with Vizion; a trend toward lower MIC readings was observed for *S. lugdunensis* with OptiRead. The sponsor included the following footnotes to the performance table to address the trending observed for Omadacycline.

Omadacycline MIC values tended to be in exact agreement or at least one dilution higher when testing Citrobacter spp. with OptiRead compared to the CLSI reference broth microdilution. MIC values tended to be in exact agreement or one dilution lower when testing S. lugdunensis.

Omadacycline MIC values tended to be in exact agreement or at least one dilution higher when testing Citrobacter spp., S. aureus (MRSA and MSSA) and E. faecalis with Vizion compared to the CLSI reference broth microdilution.

b. Matrix comparison:

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

Table 9. Interpretive Criteria for Omadacycline

Organism	Infection Type	FDA Interpretive Criteria for Omadacycline MIC (µg/mL)		
		S	I	R
Enterobacteriaceae[a]	CABP and ABSSSI	≤4	8	≥18
S. aureus (MSSA only)	CABP	≤0.25	0.5	≥1
S. aureus (MSSA and MRSA)	ABSSSI	≤0.5	1	≥2
S. lugdunensis	ABSSSI	≤0.12	0.25	≥0.5
E. faecalis	ABSSSI	≤0.25	0.5	≥1

N. Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.