510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K203741

B Applicant

Thermo Fisher Scientific

C Proprietary and Established Names

Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Cefiderocol in the dilution range of 0.03-64 µg/ml

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JWY, LRG, LTT	Class II	21 CFR 866.1640 - Antimicrobial Susceptibility Test Powder	MI - Microbiology

II Submission/Device Overview:

Purpose for Submission:
To update the breakpoints for Cefiderocol for members of the *Enterobacterales*
To modify the intended use to include the following additional indicated species: *Acinetobacter baumannii, Serratia marcescens*.

Measurand:

Cefiderocol in the dilution range of 0.03 – 64 µg/mL

Type of Test:

Automated quantitative or qualitative antimicrobial susceptibility test

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

III Intended Use/Indications for Use:

Intended Use(s):
See Indications for Use below.

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 Cefiderocol in the dilution range of 0.03-64 ug/mL for testing non-fastidious gram negative organisms on the Sensititre 18-24 hour MIC panel.

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

Escherichia coli
Enterobacter cloacae complex
Klebsiella pneumoniae
Proteus mirabilis
Pseudomonas aeruginosa
Acinetobacter baumannii
Serratia marcescens

Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

Limitations

Due to the occurrence of a very major error with Vizion read, isolates of A. baumannii that provide MICs of 1 µg/mL should be retested with an alternate method.

Studies of cefiderocol with Enterobacterales, Acinetobacter baumannii, and Pseudomonas aeruginosa were performed using the AIM autoinoculator inoculation method and ARIS/Autoreader/OptiRead and VIZION reading methods only. The use of alternative inoculation methods or alternative reading methods when testing cefiderocol have not been evaluated.

The ability of the Sensititre system to detect resistance to cefiderocol in the following species is unknown because resistant strains were not available at the time of comparative testing: P. mirabilis, S. marcescens and P. aeruginosa. Isolates yielding cefiderocol MIC results suggestive of a resistant interpretive category should be submitted to a reference laboratory for further testing.

Special Instrument Requirements:
Sensititre ARIS/Autoreader/OptiRead for automated read
Sensititre Vizion

IV Device/System Characteristics:

Device Description:

The Sensititre MIC and Breakpoint Susceptibility system is an *in vitro* diagnostic device for clinical susceptibility testing of non-fastidious gram negative isolates comprising of *Enterobacterales*, *Pseudomonas aeruginosa*, and other non-*Enterobacterales* and non-fastidious gram positive isolates comprising of *Staphylococcus* spp., *Enterococcus* spp., and Beta haemolytic *Streptococci* and not *S. pneumoniae*. The panels are multi-well microtiter plates dosed with dried stabilized antimicrobial agents at appropriate concentrations. It is a miniaturized version of the classic broth dilution method and can provide both qualitative and quantitative susceptibility results. A standardized organism suspension is prepared in cation-adjusted Mueller-Hinton broth with TES buffer; 100 µL of the organism suspension is inoculated into the antibiotic-containing well. After inoculation, plates are sealed with an adhesive seal, incubated at 34 to 36 °C for 20 to 24 hours and examined for bacterial growth. Results are read using the Vizion Reader or automatically on an ARIS/Autoreader/OptiRead using detection of fluorescence. The MIC result range for Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Cefiderocol is ≤0.03 to ≥64 µg/mL for all species.

Principle of Operation:

The Vizion allows the panel image to be displayed on a touch screen directly from a video camera and allows the user to visually determine MIC results. The Sensititre ARIS/Autoreader/OptiRead automated reading instruments utilize fluorescence technology which detects bacterial growth by monitoring the activity of specific surface enzymes produced by the test organisms. Growth is determined by generating a fluorescent product from a non-fluorescent (fluorogenic) substrate. The non-fluorescent substrate is prepared by conjugating a fluorescent compound to the specific enzyme substrates with a bond, which prevents fluorescence. The fluorophore is then said to be quenched. The plates are prepared with the substrate already added to the plate. Enzymatic action of the bacterial surface enzymes on the specific substrates cleave this bond releasing the fluorophore, which is now capable of fluorescence. The amount of fluorescence detected is directly related to the activity of the bacterial surface enzymes and therefore, to the bacterial growth. The substrate is included in the automated read inoculum broth.

V Substantial Equivalence Information:

Predicate Device Name(s):

Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Cefiderocol in the dilution range of 0.03-64 µg/ml

Predicate 510(k) Number(s):

K193538

Comparison with Predicate(s):

Device & Predicate Device(s):	**Device K203741**	**Predicate K193538**
Device Trade Name	Sensititre 18-24 Hour Susceptibility System with Cefiderocol in the dilution range of 0.03-64 µg/mL	Same
General Device Characteristic Similarities		
Intended Use/Indications For Use	The Sensititre MIC or Breakpoint Susceptibility System is an in vitro diagnostic product for clinical susceptibility testing	Same
Technology	Broth microdilution (MIC) susceptibility test	Same
Specimen	Isolated colonies from pure culture	Same
Inoculation Method	Automated (AutoInoculator AIM) after preparation of a standard suspension	Same
Instrument	Automated on an ARIS/Autoreader/ OptiRead using fluorescence or on the Vizion by visual reading of growth.	Same
Incubation Temperature	34-36 °C	Same
Incubation Atmosphere	Ambient air	Same
Incubation Time, *Enterobacterales*	18-24 hours	Same
Reading Method	Detection of growth or detection of fluorescence	Same
Antimicrobial Agent	Cefiderocol 0.03 – 64 µg/mL	Same
P. aeruginosa Breakpoints	≤1, 2, ≥4	Same
General Device Characteristic Differences		
Indicated Species	*E. coli, E. cloacae, K. pneumoniae, P.*	*E. coli, E. cloacae, K. pneumoniae, P.*

	mirabilis, P. aeruginosa, Acinetobacter baumannii, Serratia marcescens	*mirabilis, P. aeruginosa*
Incubation Time, *A. baumannii*	20-24 hours	NA
Enterobacterales Breakpoints	≤4, 8, ≥16	≤2, 4, ≥8
A. baumannii Breakpoints	≤1, 2, ≥4	No breakpoints

VI Standards/Guidance Documents Referenced:

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

CLSI M07, Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, A10. 2015

M100, Performance Standards for Antimicrobial Susceptibility Testing, 29th ed. 2019

VII Performance Characteristics (if/when applicable):

Analytical Performance:

Precision/Reproducibility:

A reproducibility study of Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Cefiderocol was performed at three sites. A total of 11 isolates were evaluated including: *E. coli* (4 isolates), *K. pneumoniae* (3 isolates), *K. oxytoca* (1 isolate), *E. cloacae* (1 isolate), *A. baumannii* (1 isolate), *P. aeruginosa* (1 isolate). Each isolate was tested in triplicate over three days for a total of 297 data points. An additional reproducibility study was performed at a single site with 10 isolates including *E. coli* (3 isolates) *K. pneumoniae* (3 isolates) *E. cloacae* (2 isolates), *A. baumannii* (1 isolate) and *P. aeruginosa* (1 isolate) in triplicate with different operators for a total of 90 additional data points.

Plates were inoculated with the AutoInoculator/AIM after preparation of a standard suspension. All results were interpreted using Vizion and ARIS/Autoreader/OptiRead. The mode MIC was determined and the reproducibility was calculated based on the MIC values falling withing ± 1 doubling dilution of the mode MIC value.

There were 28 results that were considered "off-scale"; 27 of these results were from a single *E. coli* isolate for which all results (and therefore the mode MIC value) were off-scale. Best case reproducibility was greater than 95% for both read methods and was considered to be acceptable; worst case reproducibility was 88.3% and 87.8% for Vizion and Autoread, respectively but was

considered to be acceptable because the off-scale results were contributed by the single off-scale isolate.

Linearity:
Not Applicable

Analytical Specificity/Interference:
Not Applicable

Assay Reportable Range:
Not Applicable

Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):
Quality controls strains recommended by the CLSI were tested with cefiderocol at three sites and included *E. coli* ATCC 25922 and *P. aeruginosa* 27853. The QC strains were initially tested a minimum of 20 times per site and read using the Vizion and OptiRead (Table 1).

The results demonstrate that the Sensititre 18-24 hour MIC or Breakpoint panel with Cefiderocol produced quality control results for *E. coli* ATCC 25922 in the recommended range >95% of the time (Table 1). Quality control results for *P. aeruginosa* ATCC 27853 were not in the recommended range 95% of the time using the reference method (57/62, 91.9% within range), VIZION (59/64, 92.2% within range) and OptiRead (55/62, 85.9% within range) methods during initial testing (Table 1). In order to address the lower performance for *P. aeruginosa* ATCC 27853 quality control, an additional quality control study was conducted which showed results within the expected range 100% of the time (Table 2). Quality control results are considered acceptable.

Table 1. QC Results for *E. coli* and *P. aeruginosa* with Cefiderocol with the Reference Method, Vizion and OptiRead

QC Organism	Cefiderocol Range (µg/mL)	Concentration (µg/mL)	Reference	Sensititre	
				Read method	
				VIZION	OptiRead
E. coli ATCC 25922[a]	0.06 -0.5 µg/mL	≤0.03	-	-	-
		0.06	-	1	1
		0.12	11	20	20
		0.25	50	41	40
		0.5	1	2	2
		1	0	0	1
P. aeruginosa ATCC 27853[b]	0.06 – 0.5 µg/mL	≤0.03	0	0	0
		0.06	0	0	0
		0.12	1	4	2
		0.25	22	30	27
		0.5	34	25	26
		1	5	5	9

[a] *E. coli* ATCC 25922 in-range QC results: Reference 100%, Vizion 100%, OptiRead 100%
[b] *P. aeruginosa* ATCC 27853 in-range QC results: Reference 57/62, 91.9%, Vizion 59/64, 92.2%, OptiRead 55/62, 85.9%

Table 2. Additional QC Results for *P. aeruginosa* with Cefiderocol and the Reference Method, Vizion and OptiRead

QC Organism	Cefiderocol Range (µg/mL)	Concentration (µg/mL)	Reference	Sensititre	
				Read method	
				VIZION	OptiRead
P. aeruginosa ATCC 27853[a]	0.06 – 0.5 µg/mL	≤0.03	0	0	0
		0.06	0	0	0
		0.12	0	2	1
		0.25	18	18	19
		0.5	2	0	0
		1	0	0	0

[a] *P. aeruginosa* ATCC 27853 in-range QC results: Reference 100%, Vizion 100%, OptiRead 100%

Inoculum Density: Inoculum density checks were performed a sufficient number of times; overall inoculum density results were acceptable.

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

Growth Failure: There were no growth failures in the Sensititre panels.

Detection Limit:
Not Applicable

Assay Cut-Off:
Not applicable

Comparison Studies:

Method Comparison with Predicate Device:

Testing of the Sensititre 18-24 hour MIC or Breakpoint panel with Cefiderocol was performed at two external sites and one internal site. Results were compared to results obtained with the CLSI broth microdilution reference panel. Sensititre panels were inoculated using AIM Autoinoculator and results were interpreted using both the Vizion and the ARIS/Autoreader/OptiRead. Reference panels were inoculated according to recommendations in the M07 CLSI document and results were interpreted manually using a mirrored reader. To address the inoculation and read methods for the Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Cefiderocol, the sponsor included the following limitation in the device labeling.

> *Studies of cefiderocol with Enterobacterales, Acinetobacter baumannii, and Pseudomonas aeruginosa were performed using the AIM autoinoculator inoculation method and ARIS/Autoreader/OptiRead and VIZION reading methods only. The use of alternative inoculation methods or alternative reading methods when testing cefiderocol have not been evaluated.*

The testing conditions for the reference method consisted of the following:

- **Media**: Testing of cefiderocol requires iron-depleted cation adjusted Mueller Hinton Broth (CAMHB). Chelation is used for iron depletion, which also removes other cations (i.e. calcium, magnesium and zinc). Following this process, cations are added back to concentrations of calcium 20-25 mg/L, magnesium 10-12.5 mg/L and zinc 0.5-1.0 mg/L.
- **Inoculum**: Inoculated per CLSI M07 guidelines
- **Incubation**: Reference panels were incubated at 35 ± 1° C in a non-CO_2 incubator for 18-24 hours; *Acinetobacter* spp. were incubated for 20-24 hours.

The testing conditions for the Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Cefiderocol consisted of the following:

- **Media**: The medium in the dried Sensititre panels was prepared using an alternative preparation method to produce a final composition that was in accordance with CLSI recommendations.
- **Inoculum**: A standardized suspension (0.5McFarland) suspension was prepared from a fresh primary agar plate in sterile water. Ten µL of the standardized suspension was transferred to 11 mL of cation adjusted Mueller Hinton broth with TES buffer. Fifty µL of the broth suspension was inoculated into the panel wells using the AutoInoculator/AIM.
- **Incubation**: As above for the reference method.

A total of 283 clinical isolates belonging to the *Enterobacterales* were evaluated including: *E. coli* (90 isolates), *E. cloacae* complex (74 isolates), *K. pneumoniae* (89 isolates), *P. mirabilis* (15 isolates), and *S. marcescens* (15 isolates). In addition 45 clinical isolates of *Acinetobacter baumannii* and 60 clinical isolates of *P. aeruginosa* were evaluated. Challenge testing included testing of 87 isolates of *Enterobacterales* including *E. coli* (29 isolates); *E. cloacae* (16 isolates), *K. pneumoniae* (27) isolates, *P. mirabilis* (10 isolates), and *S. marcescens* (5 isolates). In addition 10 challenge isolates of *A. baumannii* and 21 challenge isolates of *P. aeruginosa* were evaluated.

For *Enterobacterales* read using Vizion, the combined clinical and challenge results were acceptable at 93.8% and 95.1% for EA and CA, respectively, with no major or very major errors. EA and CA were also acceptable for *P. aeruginosa* read using Vizion at 97.5% and 95.1% for EA and CA, respectively with no major or very major errors. For Vizion with *A. baumannii*, the EA was acceptable at 98.2%; however the CA was low at 81.8% with nine of ten errors being minor errors (7.7%). A single very major error was observed with *A. baumannii* and Vizion (Table 3). To address the very major error the following limitation was added to the device labeling:

> *Due to the occurrence of a very major error with Vizion read, isolates of A. baumannii that provide MICs of 1 µg/mL should be retested with an alternate method.*

To address the potential for minor errors with Vizion read with *A. baumannii* the following footnote was added to the performance table:

> *Category errors when testing A. baumannii with Vizion were mostly due to minor errors (Vizion 9/55, 16.4%). One of 14 resistant A. baumannii isolate gave a very major error.*

For *Enterobacterales* read using ARIS/Autoreader/OptiRead, the combined clinical and challenge results were acceptable at 93.0% and 95.1%, for EA and CA, respectively, with no major or very major errors. EA and CA were also acceptable for *P. aeruginosa* read on ARIS/Autoreader/OptiRead at 97.5% and 92.6% for EA and CA, respectively with no major or very major errors. For ARIS/Autoreader/OptiRead with *A. baumannii,* the EA was acceptable at 94.5%; however the CA was low at 81.8% with all errors being minor errors (Table 4).

To address the potential for minor errors with ARIS/Autoreader/OptiRead with *A. baumannii* the following footnote was added to the performance table:

> *Category errors when testing A. baumannii with Vizion were mostly due to minor errors (ARIS/Autoreader/OptiRead 10/55, 18.2%).*

Table 3. Cefiderocol Results for *Enterobacterales*, *A. baumannii* and *P. aeruginosa* with Vizion

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Enterobacterales* (≤4, 8, ≥16 µg/mL)**													
Clinical	283	267	94.3	210	194	92.4	277	97.9	3	276	6	0	0
Challenge	87	80	92.0	74	67	90.5	75	86.2	11	62	12	0	0
Total	370	347	93.8	284	261	91.9	352	95.1	14	338	18	0	0
***Acinetobacter baumannii* (≤1, 2, ≥4 µg/mL)**													
Clinical	45	44	97.8	42	41	97.6	35	77.8	10	29	9	0	1
Challenge	10	10	100.0	9	9	100.0	10	100.0	3	6	0	0	0
Total	55	54	98.2	51	50	98.0	45	81.8	13	35	9	0	1
***Pseudomonas aeruginosa* (≤1, 2, ≥4 µg/mL)**													
Clinical	60	58	96.7	58	56	96.6	59	98.3	0	58	1	0	0
Challenge	21	21	100.0	21	21	100.0	18	85.7	0	20	3	0	0
Total	81	79	97.5	79	77	97.5	77	95.1	0	78	4	0	0

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. Cefiderocol Results for *Enterobacterales*, *A. baumannii* and *P. aeruginosa* with ARIS/Autoreader/OptiRead.

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Enterobacterales* (≤4, 8, ≥16 µg/mL)**													
Clinical	283	264	93.3	208	189	90.9	278	98.2	3	276	5	0	0
Challenge	87	80	92.0	74	67	90.5	74	85.1	11	62	13	0	0
Total	370	344	93.0	282	256	90.8	352	95.1	14	338	18	0	0
***Acinetobacter baumannii* (≤1, 2, ≥4 µg/mL)**													
Clinical	45	42	93.3	43	40	93.0	35	77.8	10	29	10	0	0
Challenge	10	10	100.0	9	9	100.0	10	100.0	4	6	0	0	0
Total	55	52	94.5	52	49	94.2	45	81.8	14	35	10	0	0
***Pseudomonas aeruginosa* (≤1, 2, ≥4 µg/mL)**													
Clinical	60	58	96.7	59	57	96.6	58	96.7	0	58	2	0	0
Challenge	21	21	100.0	21	21	100.0	17	81.0	0	20	4	0	0
Total	81	79	97.5	80	78	97.5	75	92.6	0	78	6	0	0

Resistant Strains
For *P. mirabilis, S. marcescens* and *P. aeruginosa*, no resistant isolates were available for evaluation during clinical or challenge testing. The sponsor included the following limitation in the device labeling:

> *The ability of the Sensititre system to detect resistance to cefiderocol in the following species is unknown because resistant strains were not available at the time of comparative testing: P. mirabilis, S. marcescens and P. aeruginosa. Isolates yielding cefiderocol MIC results suggestive of a resistant interpretive category should be submitted to a reference laboratory for further testing.*

MIC Trending

A trending analysis was conducted using the combined data (clinical and challenge) obtained for both Vizion and ARIS/Autoreader/OptiRead 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 than the reference method irrespective of whether the device MIC values are on-scale or not. Results that are not clearly at least one dilution lower, at least one dilution higher or in exact agreement with the CLSI reference method are not considered in the trending analysis.

Organism groups for which the difference between the percentage of isolates with higher vs. lower readings was > 30% and for which the confidence interval was determined to be statistically significant were considered to show evidence of trending. Trending that showed higher or lower MIC values compared to the reference is addressed in the labeling.

Evaluation of results for ARIS/Autoreader/OptiRead showed low trending for *E. coli* and the *E. cloacae* complex and high trending for *P. aeruginosa* and *A. baumannii*. Evaluation of results for Vizion read showed low trending for *E. coli* and high trending for *S. marcescens* and *A. baumannii*. Results for *P. mirabilis* showed low trending for both read methods but results were not statistically significant. (Table 5)

To address trending, the sponsor included the following footnotes to the performance table:

> For ARIS/Autoreader/OptiRead:
> *Cefiderocol MIC values tended to be in exact agreement or at least one dilution higher when testing P. aeruginosa and A. baumannii with ARIS/Autoreader/OptiRead compared to the CLSI reference broth microdilution method. MIC values tended to be in exact agreement or one dilution lower when testing E. coli, and E. cloacae complex.*
>
> For Vizion:
> *Cefiderocol MIC values tended to be in exact agreement or at least one dilution higher when testing S. marcescens and A. baumannii with Vizion compared to the CLSI reference broth microdilution method. MIC values tended to be in exact agreement or at least one dilution lower when testing E. coli.*

Table 5. Trending Observed for *Enterobacterales*, *A. baumannii* and *P. aeruginosa* with Vizion and ARIS/Autoreader/OptiRead

Read Method	Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
Vizion	*E. coli*	93	47 (50.5)	28 (30.1)	18 (19.4)	-31.2 (-43.2 to -17.6)	Yes Low
	E. cloacae complex	87	35 (40.2)	33 (37.9)	19 (21.8)	-18.4 (-31.2 to -4.6)	No
	K. pneumoniae	98	35 (35.7)	39 (39.8)	24 (24.5)	-11.2 (-23.6 to 1.6)	No
	P. mirabilis	10	5 (50.0)	3 (30.0)	2 (20.0)	-30.0 (-60.0 to 10.7)	Yes Low*
	S. marcescens	20	3 (15.0)	8 (40.0)	9 (45.0)	30.0 (1.5 to 53.0)	Yes High
	A. baumannii	52	7 (13.5)	20 (38.5)	25 (48.1)	34.6 (17.1 to 49.5)	Yes High
	P. aeruginosa	80	12 (15.0)	39 (48.8)	29 (36.3)	21.3 (7.8 to 33.8)	No
Autoread	*E. coli*	92	51 (55.4)	26 (28.3)	15 (16.3)	-39.1 (-50.7 to -25.6)	Yes Low
	E. cloacae complex	86	40 (46.5)	32 (37.2)	14 (16.3)	-30.2 (-42.5 to -16.5)	Yes Low
	K. pneumoniae	96	45 (46.9)	30 (31.3)	21 (21.9)	-25.0 (-37.2 to -11.6)	No
	P. mirabilis	10	5 (50.0)	3 (30.0)	2 (20.0)	-30.0 (-60.0 to 10.7)	Yes Low*
	S. marcescens	20	4 (20.0)	7 (35.0)	9 (45.0)	25.0 (-3.9 to 49.0)	No
	A. baumannii	53	5 (9.4)	29 (37.7)	28 (52.8)	43.4 (26.4 to 57.3)	Yes High
	P. aeruginosa	81	9 (11.1)	37 (45.7)	35 (43.2)	32.1 (18.7 to 44.1)	Yes High

* Not statistically significant

Resistance Mechanisms Tested
Isolates with the following resistance mechanisms were included in the reproducibility study:

TEM-1, TEM-4, TEM-10, TEM-12, SHV-1, SHV-2, SHV-11, SHV-12, SHV-83, 164S TEM, CTX-M-1, CTX-M-9, CTX-M-15, NDM, KPC-3, OMPC, OMPK-36

Testing/Reporting MIC for Non-indicated Species:
For this review, the interpretative 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 added to the Precautions section of the device labeling:

> *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 labelling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.*

Matrix Comparison:
Not applicable

Clinical Studies:

Clinical Sensitivity:
Not applicable

Clinical Specificity:
Not applicable

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

Clinical Cut-Off:
Not applicable

Expected Values/Reference Range:

Table 6. FDA-Identified Interpretive Criteria for Cefiderocol

Organism	Interpretive Criteria for Cefiderocol (µg/mL)		
	Susceptible	Intermediate	Resistant
Enterobacterales	≤4	8	≥16
P. aeruginosa	≤1	2	≥4
Acinetobacter baumannii complex	≤1	2	≥4

[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 the breakpoint change protocol that was reviewed and accepted by FDA during review of K193538. 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 ThermoFisher intends to use to evaluate the Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Cefiderocol in the dilution range of 0.03 – 64 µg/mL when revised breakpoints for cefiderocol are published on the FDA STIC webpage. The breakpoint change protocol included

with the submission indicated that if specific criteria are met, ThermoFisher will update the cefiderocol 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.