510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K252014

B Applicant

Thermo Fisher Scientific

C Proprietary and Established Names

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Amikacin in the dilution range of 0.25-256 µg/mL

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

To obtain substantial equivalence determination for The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Amikacin in the dilution range of 0.25-256 µg/mL with updated FDA-recognized breakpoints for *Acinetobacter* spp., Enterobacterales, and *Pseudomonas aeruginosa* and modified dilution range from that cleared in K860753.

B Measurand:

Amikacin in the dilution range of 0.25 to 256 µg/mL

C Type of Test:

Quantitative antimicrobial susceptibility test (AST) growth-based detection

III Intended Use/Indications for Use:

A 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 *Acinetobacter* species, Enterobacterales, *Pseudomonas aeruginosa*, and other non-Enterobacterales and of non-fastidious Gram positive isolates, comprising of *Staphylococcus* spp., *Enterococcus* spp., and beta-haemolytic Streptococci other than *S. pneumoniae*.

B 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 amikacin in the dilution range of 0.25-256 µg/mL for testing non-fastidious gram-negative isolates on The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System. Testing is indicated for *Acinetobacter* spp., Enterobacterales, and *Pseudomonas aeruginosa*, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC) webpage.

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Amikacin in the dilution range of 0.25-256 µg/mL demonstrated acceptable performance with the following organisms:

Acinetobacter spp. (*Acinetobacter baumannii*)

Enterobacterales (*Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex, *Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Serratia marcescens*)

Pseudomonas aeruginosa

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

The following limitation was applied to amikacin testing in the appropriate section of the device labeling that references other drugs:

> *Studies of the following drugs were performed with the AIM Autoinoculator and read using the ARIS HiQ/OptiRead and Vizion. The use of an alternative inoculation system or alternative read methods has not been evaluated.*

Due to the insufficient number of resistant of *C. freundii*, *C. koseri*, *E. cloacae* complex, *E. coli*, *K. aerogenes*, *K. oxytoca*, *M. morganii*, *P. vulgaris*, and *S. marcescens* isolates evaluated, the following limitation was applied to amikacin testing in the appropriate section of the device labeling that references other drugs:

The ability of the Sensititre system to detect resistance or non-susceptibility to antimicrobics as shown below is unknown because an insufficient number of resistant or non-susceptible strains were available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory.

D Special Instrument Requirements:

Sensititre AIM for device inoculation
Sensititire Vizion digital viewing device
Sensititre ARIS HiQ/OptiRead automated plate reader

IV Device/System Characteristics:

A Device Description:

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility Plate System is an antimicrobial susceptibility test. Each plate is dosed with dried, stabilized antimicrobial agents at appropriate dilutions. It is a micro-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.

B Principle of Operation:

The Sensititre 18-24 hour MIC Susceptibility plates are multi-well plastic microtiter plates that contain doubled dilutions of antibacterial agents. Each plate includes antimicrobial agents at appropriate dilutions. Results can be read using the digital viewing device (Vizion) or by use of an automated plate reader (ARIS HiQ/OptiRead).

The Sensititre Vizion digital viewing device 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 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 non-fluorescent 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 bound non-fluorescent substrate cleaves the bond releasing fluorescence. The amount of fluorescence detected is directly related to the activity of bacterial growth. The MIC is determined by observing the lowest dilution of antimicrobial agent that inhibits growth of the organism. The non-fluorescent (fluorogenic) 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.

Sensititre 18-24 hour MIC plates can either be read automatically on an ARIS HiQ/OptiRead using fluorescence or by visual reading of growth on the Vizion digital viewing device.

V Substantial Equivalence Information:

A Predicate Device Name(s):
The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Lefamulin in the dilution range of 0.008-16 µg/mL

B Predicate 510(k) Number(s):
K192729

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device K252014	Predicate K192729
Device Trade Name	The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Amikacin in the dilution range of 0.25-256 µg/mL	The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Lefamulin in the dilution range of 0.008-16 µg/mL
General Device Characteristic Similarities		
Intended Use	The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of non-fastidious bacterial isolates.	Same
Test panel	Each 96 well plate is precision 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
Incubation	18-24 hours	Same
Read Method	Results can be read using fluorescence with the ARIS HiQ/OptiRead or by visual reading of growth with the Vizion.	Same
General Device Characteristic Differences		
Antibiotic and Dilution Range	Amikacin 0.25-256 µg/mL	Lefamulin 0.008-16 µg/mL
Test Organisms	*Acinetobacter* spp. (*Acinetobacter baumannii*) Enterobacterales (*Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex,	*Staphylococcus aureus* (methicillin-susceptible isolates)

	Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae, Morganella morganii, Proteus mirabilis, Proteus vulgaris, Providencia rettgeri, Providencia stuartii, Serratia marcescens) *Pseudomonas aeruginosa*	

VI Standards/Guidance Documents Referenced:

CLSI M07, "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard - Eleventh Edition", (January 2018)

CLSI M100, "Performance Standards for Antimicrobial Susceptibility Testing; 34th Edition", (March 2024)

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

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

   A reproducibility study of The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Amikacin was performed at three sites using a panel of twenty-five (25) gram-negative isolates from species indicated for use with the device (six *Escherichia coli*, five *Klebsiella pneumoniae*, four *Pseudomonas aeruginosa*, three *Serratia marcescens*, two *Enterobacter cloacae*, two *Acinetobacter baumannii*, one *Citrobacter koseri*, one *Proteus mirabilis,* and one *Providencia stuartii*). All isolates were tested in triplicate over three days for a total of 252 data points with each read method (i.e., automatically with the ARIS HiQ/OptiRead and visually with the Vizion). The Sensititre AIM Autoinoculator was used for Sensititre plate inoculation. The mode MIC value was determined, and the reproducibility was calculated based on MIC values falling within ±1 doubling dilution of the mode MIC value. The reproducibility studies for both the ARIS HiQ/OptiRead and Vizion read methods demonstrated acceptable performance of ≥95%.

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):

The CLSI-recommended quality control (QC) strains *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 were tested at three sites. The QC strains were tested a minimum of 20 times per site and read automatically with the ARIS HiQ/OptiRead and visually with the Vizion. The QC strains were also tested with the reference method. The results demonstrate that The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Amikacin produced quality control results within the recommended range >95% of the time (**Table 1**).

Table 1. Quality Control Results for *E. coli* and *P. aeruginosa* with Amikacin with the Reference Method, ARIS HiQ/OptiRead, and Vizion

QC Organism	Expected Range (µg/mL)	Concentration (µg/mL)	Reference	ARIS HiQ/ OptiRead	Vizion
Escherichia coli ATCC 25922	0.5-4 µg/mL	≤0.25	-	-	-
		0.5	-	-	-
		1	6	11	6
		2	66	94	95
		4	12	9	13
		≥8	-	-	-
Pseudomonas aeruginosa ATCC 27853	1-4 µg/mL	≤0.5	-	-	-
		1	4	11	1
		2	75	103	108
		4	5	-	5
		≥8	-	-	-

Inoculum Density: Inoculum density checks were performed for all QC, reproducibility, challenge, and clinical isolates tested. Only results from cultures with appropriate inoculum densities were reported.

Purity Checks: Purity checks were performed for all QC, reproducibility, challenge, and clinical isolates tested. Only results from pure cultures were reported.

Growth Failure: There were no growth failures.

ARIS HiQ/OptiRead Invalid (No fluorescence): There were no invalids for *Acinetobacter* spp., Enterobacterales, or *P. aeruginosa* that did not produce adequate fluorescence by the ARIS HiQ/OptiRead.

6. Detection Limit:

Not applicable.

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Testing of The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Amikacin was performed at three external sites. Results were compared to those obtained with the CLSI broth microdilution reference method. Sensititre panels were inoculated using only the AIM Autoinoculator and results were read automatically by the ARIS HiQ/OptiRead and visually by the Vizion. Reference panels were inoculated according to recommendations in the M07 CLSI document and results were read manually using a mirrored reader.

No inoculation system other than the AIM Autoinoculator and no read methods other than ARIS HiQ/OptiRead and Vizion was used in the comparative study. To address the inoculation method and read method limitation, the following limitation was applied to amikacin testing in the appropriate section of the device labeling that references other drugs:

> *Studies of the following drugs were performed with the AIM Autoinoculator and read using the ARIS HiQ/OptiRead and Vizion. The use of an alternative inoculation system or alternative read methods has not been evaluated.*

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

- Media: per CLSI M07 guidelines for *Acinetobacter* spp., Enterobacterales and *Pseudomonas aeruginosa*
- Inoculum: Inoculated per CLSI M07 guidelines
- Incubation: 34-36°C in a non-CO_2 incubator for 20-24 hours (*Acinetobacter* spp.) or 16-20 hours (Enterobacterales and *Pseudomonas aeruginosa*)

Inoculation and incubation procedure for *Acinetobacter* spp., Enterobacterales (excluding *Proteus* spp., *Providencia* spp., and *Morganella* spp.) and *Pseudomonas aeruginosa*

- Media: cation-adjusted Mueller Hinton broth with TES buffer (CAMHBT)
- Inoculum: A suspension approximating a 0.5 McFarland standard was prepared in 5 mL sterile water. Ten (10) µL of the standardized suspension was transferred to 11 mL of CAMHBT. Susceptibility plates were inoculated with 50 µL of the final organism suspension using the Sensititre AIM Autoinoculator.
- Incubation: 34-36°C in a non-CO_2 incubator for 18-24 hours (20-24 hours for *Acinetobacter* spp.)

Inoculation and incubation procedure for *Proteus* spp., *Providencia* spp., and *Morganella* spp.

- Media: cation-adjusted Mueller Hinton broth with TES buffer (CAMHBT)
- Inoculum: A suspension approximating a 0.5 McFarland standard was prepared in 5 mL sterile water. One (1.0) µL of the standardized suspension was transferred to 11 mL of

CAMHBT. Susceptibility plates were inoculated with 50 µL of the final organism suspension using the Sensititre AIM Autoinoculator.

- Incubation: 34-36°C in a non-CO_2 incubator for 18-24 hours

ARIS HiQ/OptiRead:

A total of 686 gram-negative clinical isolates comprised of *A. baumannii* (60 isolates), Enterobacterales (30 *C. freundii*, 45 *C. koseri*, 60 *E. cloacae* complex, 75 *E. coli*, 60 *K. aerogenes*, 25 *K. oxytoca*, 65 *K. pneumoniae*, 30 *M. morganii*, 40 *P. mirabilis*, 36 *P. rettgeri*, 34 *P. stuartii*, 36 *P. vulgaris*, and 30 *S. marcescens* isolates), and *P. aeruginosa* (60 isolates), as well as 193 challenge isolates comprised of *A. baumannii*, (24 isolates), Enterobacterales (6 *C. freundii*, 5 *C. koseri*, 20 *E. cloacae* complex, 25 *E. coli*, 12 *K. aerogenes*, 5 *K. oxytoca*, 26 *K. pneumoniae*, 3 *M. morganii*, 10 *P. mirabilis*, 7 *P. rettgeri*, 7 *P. stuartii*, 4 *P. vulgaris*, and 11 *S. marcescens* isolates) and *P. aeruginosa* (28 isolates) were evaluated with the ARIS HiQ/OptiRead and the results are provided in **Table 2**.

For *Acinetobacter* spp. read using the ARIS HiQ/OptiRead, the combined clinical and challenge isolates (84 isolates) were acceptable at 97.6% and 91.7% for EA and CA, respectively. There were seven minor errors and no major errors or very major errors.

For Enterobacterales read using the ARIS HiQ/OptiRead, the combined clinical and challenge isolates (707 isolates) were acceptable at 96.3% and 98.9% for EA and CA, respectively. There were seven minor errors, no major errors, and one very major error (1/31 = 3.2%). When evaluating by individual species, the one very major error was due to an *E. coli* isolate (1/2 = 50%). Due to the lack of resistant isolates evaluated, the very major error is considered random, and the following performance footnote was included in the device labeling:

> *The 1 very major error observed was considered a random error due to the limited number of resistant isolates tested for E. coli.*

For *P. aeruginosa* read using the ARIS HiQ/OptiRead, the combined clinical and challenge isolates (88 isolates) were acceptable at 96.6% and 95.5% for EA and CA, respectively. There were four minor errors and no major errors or very major errors.

Table 2. Amikacin Performance of *Acinetobacter* spp., Enterobacterales, and *P. aeruginosa* Read by ARIS HiQ/OptiRead

	Tot	EA No.	EA %	Eval Tot	Eval EA No.	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Acinetobacter* spp. [≤16 (S), 32 (I), ≥64 (R)]**													
Clinical	60	58	96.7	48	46	95.8	59	98.3	16	44	1	0	0
Challenge	24	24	100	24	24	100	18	75.0	8	10	6	0	0
Total	84	82	97.6	72	70	97.2	77	91.7	24	54	7	0	0
Enterobacterales [≤16 (S), 32 (I), ≥64 (R)]													
Clinical	566	546	96.5	547	527	96.3	561	99.1	18	546	4	0	1
Challenge	141	135	95.7	131	125	95.4	138	98.9	13	121	3	0	0
Total	707	681	96.3	678	652	96.2	699	98.9	31	667	7	0	1
***P. aeruginosa* [≤16 (S), 32 (I), ≥64 (R)]**													

	Tot	EA No.	EA %	Eval Tot	Eval EA No.	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
Clinical	60	58	96.7	59	57	96.6	59	98.3	2	57	1	0	0
Challenge	28	27	96.4	28	27	96.4	25	89.3	4	21	3	0	0
Total	88	85	96.6	87	84	96.6	84	95.5	6	78	4	0	0

EA – Essential Agreement
CA – Category Agreement
S – Susceptible
R – Resistant
EVAL – Evaluable MICs
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 or those in which an off-scale result is at least two doubling dilutions from the on-scale result. Category agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the Sensititre panel.

Vizion:

A total of 686 gram-negative clinical isolates comprised of *A. baumannii* (60 isolates), Enterobacterales (30 *C. freundii*, 45 *C. koseri*, 60 *E. cloacae* complex, 75 *E. coli*, 60 *K. aerogenes*, 25 *K. oxytoca*, 65 *K. pneumoniae*, 30 *M. morganii*, 40 *P. mirabilis*, 36 *P. rettgeri*, 34 *P. stuartii*, 36 *P. vulgaris*, and 30 *S. marcescens* isolates), and *P. aeruginosa* (60 isolates), as well as 193 challenge isolates comprised of *A. baumannii*, (24 isolates), Enterobacterales (6 *C. freundii*, 5 *C. koseri*, 20 *E. cloacae* complex, 25 *E. coli*, 12 *K. aerogenes*, 5 *K. oxytoca*, 26 *K. pneumoniae*, 3 *M. morganii*, 10 *P. mirabilis*, 7 *P. rettgeri*, 7 *P. stuartii*, 4 *P. vulgaris*, and 11 *S. marcescens* isolates) and *P. aeruginosa* (28 isolates) were evaluated with the Vizion and the results are provided in **Table 3**.

For *Acinetobacter* spp. read using the Vizion, the combined clinical and challenge isolates (84 isolates) were acceptable at 95.2% for both EA and CA. There were four minor errors and no major errors or very major errors.

For Enterobacterales read using the Vizion, the combined clinical and challenge isolates (707 isolates) were acceptable at 95.6% and 98.7% for EA and CA, respectively. There were eight minor errors, no major errors, and one very major error (1/31 = 3.2%). When evaluating by individual species, the one very major error was due to an *E. coli* isolate (1/2 = 50%). Due to the lack of resistant isolates evaluated, the very major error is considered random, and the following performance footnote was included in the device labeling:

> *The 1 very major error observed was considered a random error due to the limited number of resistant isolates tested for E. coli.*

For *P. aeruginosa* read using the Vizion, the combined clinical and challenge isolates (88 isolates) were acceptable at 97.7% for both EA and CA. There were two minor errors and no major errors or very major errors.

Table 3. Amikacin Performance of *Acinetobacter* spp., Enterobacterales, and *P. aeruginosa* Read by Vizion

	Tot	EA No.	EA %	Eval Tot	Eval EA No.	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
***Acinetobacter* spp., [≤16 (S), 32 (I), ≥64 (R)]**													
Clinical	60	56	93.3	48	44	91.7	59	98.3	16	44	1	0	0
Challenge	24	24	100	24	24	100	21	87.5	8	10	3	0	0
Total	84	80	95.2	72	68	94.4	80	95.2	24	54	4	0	0
Enterobacterales [≤16 (S), 32 (I), ≥64 (R)]													
Clinical	566	540	95.4	547	521	95.3	561	99.1	18	546	4	0	1
Challenge	141	136	96.5	131	126	96.2	137	97.2	13	121	4	0	0
Total	707	676	95.6	678	647	95.4	698	98.7	31	667	8	0	1
***P. aeruginosa* [≤16 (S), 32 (I), ≥64 (R)]**													
Clinical	60	59	98.3	59	58	98.3	59	98.3	2	57	1	0	0
Challenge	28	27	96.4	28	27	96.4	27	96.4	4	21	3	0	0
Total	88	86	97.7	87	85	97.7	86	97.7	6	78	2	0	0

EA – Essential Agreement
CA – Category Agreement
S – Susceptible
R – Resistant

EVAL – Evaluable MICs
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 or those in which an off-scale result is at least two doubling dilutions from the on-scale result. Category agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the Sensititre panel.

Due to the insufficient number of *C. freundii*, *C. koseri*, *E. cloacae* complex, *E. coli*, *K. aerogenes*, *K. oxytoca*, *M. morganii*, *P. vulgaris*, and *S. marcescens* resistant isolates evaluated, the following limitation was applied to amikacin testing in the appropriate section of the device labeling that references other drugs:

> *The ability of the Sensititre system to detect resistance or non-susceptibility to antimicrobics as shown below is unknown because an insufficient number of resistant or non-susceptible strains were available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory.*

MIC Trending

A trending analysis was conducted using the combined data (clinical and challenge) obtained for both the ARIS HiQ/OptiRead and the Vizion for *Acinetobacter* spp., Enterobacterales, and *P. aeruginosa*. 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.

Species 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 shows higher or lower MIC values compared to the reference is addressed in the labeling.

Evaluation of results for *A. baumannii*., species within Enterobacterales, and *P. aeruginosa* with amikacin using the ARIS HiQ/OptiRead and Vizion are summarized in **Table 4**. A trend toward

lower MIC values was observed for *P. mirabilis*, *P. stuartii*, and *P. vulgaris* using the ARIS/HiQ/OptiRead when compared to the CLSI broth microdilution reference method. A trend toward lower MIC values was observed for *P. mirabilis*, *P. stuartii*, and *P. vulgaris* using the Vizion when compared to the CLSI broth microdilution reference method.

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

For ARIS HiQ/OptiRead:
Amikacin MIC values tended to be in exact agreement or at least one doubling dilution lower when testing P. mirabilis, P. stuartii, and P. vulgaris with the ARIS HiQ/OptiRead compared to the CLSI broth microdilution reference method.

For Vizion:
Amikacin MIC values tended to be in exact agreement or at least one doubling dilution lower when testing P. mirabilis, P. stuartii, and P. vulgaris with the Vizion compared to the CLSI broth microdilution reference method.

Table 4. Amikacin Trending Analysis for *Acinetobacter* spp., Enterobacterales, and *P. aeruginosa* with ARIS HiQ/OptiRead and Vizion

Read Method	Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (95% CI)	Trending Noted
ARIS HiQ/ OptiRead	*A. baumannii*	72	20, (27.8)	36	16, (22.2)	-6% (-19% to 9%)	No
	C. freundii	35	7, (20.0)	22	6, (17.1)	-3% (-21% to 16%)	No
	C. koseri	50	19, (38.0)	24	7, (14.0)	-24% (-40% to -7%)	No
	E. cloacae complex	79	16, (20.3)	59	4, (5.1)	-15% (-26% to -25%)	No
	E. coli	99	20, (20.2)	65	14, (14.1)	-6% (-17% to 5%)	No
	K. aerogenes	72	19, (26.4)	46	7, (9.7)	-17% (-29% to -4%)	No
	K. oxytoca	30	6, (20.0)	23	1, (3.3)	-17% (-34% to 0%)	No
	K. pneumoniae	76	9, (11.8)	49	18, (23.7)	12% (0% to 24%)	No
	M. morganii	33	11, (33.3)	18	4, (12.4)	-21% (-40% to -1%)	No
	P. mirabilis	48	20, (41.7)	23	5, (10.4)	-31% (-46% go -14%)	Yes, low
	P. rettgeri	41	15, (36.6)	22	4, (9.8)	-27% (-43% to -9%)	No
	P. stuartii	39	17, (43.6)	17	5, (12.8)	-31% (-48% to -11%)	Yes, low
	P. vulgaris	40	23, (57.5)	17	0, (0.0)	-57% (-71% to -40%)	Yes, low
	S. marcescens	41	8, (19.5)	27	6, (14.4)	-5% (-21% to 12%)	No
	P. aeruginosa	87	25, (28.7)	58	4, (4.6)	-24% (-35% to -13%)	No
	A. baumannii	72	14, (19.4)	39	19, (26.4)	7%	No

Read Method	Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (95% CI)	Trending Noted
						(-7% to 20%)	
Vizion	*C. freundii*	35	4, (11.4)	20	11, (31.4)	20% (1% to 38%)	No
	C. koseri	50	15, (30.0)	21	14, (28.0)	-2% (-19% to 15%)	No
	E. cloacae complex	79	8, (10.1)	61	10, (12.7)	3% (-8% to 13%)	No
	E. coli	99	17, (17.2)	57	25, (25.3)	8% (-8% to 19%)	No
	K. aerogenes	72	14, (19.4)	46	12, (16.7)	-3% (-15% to 10%)	No
	K. oxytoca	30	5, (16.7)	19	6, (20.0)	3% (-17% to 23%)	No
	K. pneumoniae	76	6, (7.9)	48	22, (29.0)	21% (9% to 33%)	No
	M. morganii	33	4, (12.1)	24	5, (15.2)	3% (-14% to 20%)	No
	P. mirabilis	48	20, (41.7)	23	5, (10.4)	-31% (-46% to -14%)	Yes, low
	P. rettgeri	41	13, (31.7)	21	7, (17.1)	-15% (-32% to 4%)	No
	P. stuartii	39	17, (43.6)	18	4, (10.3)	-33% (-50% to -14%)	Yes, low
	P. vulgaris	40	19, (47.5)	21	0, (0.0)	-48% (-63% to -31%)	Yes, low
	S. marcescens	41	5, (12.2)	24	12, (29.3)	17% (-1% to 34%)	No
	P. aeruginosa	87	6, (6.9)	66	15, (17.2)	10% (1% to 20%)	No

Testing/Reporting MICs for Species Not Listed in the Indications for Use
For this review, the interpretive 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 included in the Warnings and Precautions section of the device labeling to address testing and reporting of non-indicated species:

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.

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:

Table 5: FDA-Recognized Interpretive Criteria for Amikacin

	Minimum Inhibitory Concentrations (µg/mL)[a]		
Organisms	**Susceptible**	**Intermediate**	**Resistant**
Acinetobacter spp.	≤16	32	≥64
Enterobacterales	≤16	32	≥64
Pseudomonas aeruginosa	≤16	32	≥64

[a]According to FDA STIC Webpage, https://www.fda.gov/drugs/development-resources/fda-recognized-antimicrobial-susceptibility-test-interpretive-criteria

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 predetermined change control plan (PCCP) with a breakpoint change protocol that was reviewed and accepted by FDA in submission K231994 cleared on August 25, 2023. 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 Fisher Scientific intends to use to evaluate The Sensititre 18–24 hour MIC or Breakpoint Susceptibility

System with Amikacin when revised breakpoints for amikacin are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, Thermo Fisher Scientific will update the amikacin 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.