510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K242659

B Applicant

Thermofisher Scientific

C Proprietary and Established Names

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Vancomycin in the dilution range of 0.25-128 ug/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 Vancomycin in the dilution range 0.25–128 µg/mL with updated FDA-recognized breakpoints for *Staphylococcus aureus* and Staphylococci other than *Staphylococcus aureus* and an expanded dilution range from 1–128 µg/mL cleared in K060783.

B Measurand:

Vancomycin in the dilution range 0.25 to 128 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 Enterobacteriaceae, *Pseudomonas aeruginosa*, and other non-Enterobacteriaceae and of non-fastidious Gram positive isolates, comprising of *Staphylococcus* spp., *Enterococcus* spp., and beta-hemolytic 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 vancomycin in the dilution range of 0.25-128 µg/ml for testing non-fastidious gram-positive isolates on The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System. Testing is indicated for *Staphylococcus* aureus, Staphylococci other than *Staphylococcus aureus*, and *Enterococcus* spp., as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC) webpage.

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Vancomycin in the dilution range of 0.25-128 µg/mL demonstrated acceptable performance with the following organisms:

Staphylococcus aureus (including MRSA)
Staphylococci other than *Staphylococcus aureus* (*S. epidermidis, S. haemolyticus, S. hominis, S. lugdunensis, S. saprophyticus)*
*Enterococcu*s spp. (*E. faecalis, E. faecium*)

It is for Prescription use.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

The following limitation was applied to vancomycin testing in the appropriate sections of the device labeling that reference 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 *S. aureus*, *S. epidermidis, S. haemolytics, S. hominis, S. lugdunensis*, and *S. saprophyticus* isolates evaluated, the following limitation was applied to vancomycin 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 plate reader/viewer
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):
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 K242659	Predicate K192729
Device Trade Name	The Sensititre 18-24 Hour MIC or Breakpoint Susceptibility System with Vancomycin in the dilution range of 0.25-128 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	Vancomycin 0.25-128 µg/mL	Lefamulin 0.008-16 µg/mL
Test Organisms	*Staphylococcus aureus* (including MRSA) Staphylococci other than *Staphylococcus aureus*	*Staphylococcus aureus* (methicillin-susceptible isolates)

	Enterococcus species	

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; 33rd Edition", (March 2023)

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 Vancomycin was performed at three sites using a panel of thirteen (13) gram-positive isolates from indicated species (4 *Staphylococcus aureus* (MSSA), 4 *Staphylococcus aureus* (MRSA), 1 *Staphylococcus epidermidis* (MSSE), 1 *Staphylococcus lugdunensis*, 1 *Staphylococcus haemolyticus*, 1 *Enterococcus faecium* (VSE), and 1 *Enterococcus faecalis* (VSE)). All isolates were tested in triplicate over three days 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 the 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 100%.

   In addition, two vancomycin-resistant isolates (1 *Enterococcus faecium* and 1 *Enterococcus faecalis*) were also tested and demonstrated resistant results with MIC values at ≥128 µg/mL.

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 *S. aureus* ATCC 29213 and *Enterococcus faecalis* ATCC 29212 were tested at four 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 Susceptibility plates with vancomycin produced quality control results within the recommended range >95% of the time (**Table 1**).

Table 1. Quality Control Results for *S. aureus* and *E. faecalis* with Vancomycin with the Reference Method, ARIS HiQ/OptiRead, and Vizion

QC Organism	Expected Range (µg/mL)	Concentration (µg/mL)	Reference	ARIS HiQ/ OptiRead	Vizion
Staphylococcus aureus ATCC 29213	0.5-2 µg/mL	≤0.25	-	-	-
		0.5	73	2	2
		1	11	98	101
		2	-	1	1
		≥4	-	-	-
Enterococcus faecalis ATCC 29212	1-4 µg/mL	≤0.5	-	-	-
		1	1	1	-
		2	86	83	63
		4	-	19	43
		≥8	-	1	1

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 2 growth failures for *Staphylococcus aureus*. There were no growth failures for Staphylococci other than *Staphylococcus aureus* or *Enterococcus spp.*

ARIS HiQ/OptiRead Invalid (No fluorescence): There was one invalid for Staphylococci other than *Staphylococcus aureus* (*S. lugdunensis*) and seven invalids for *Enterococcus* spp. (2 *E. faecalis*, 5 *E. faecium*) that did not produce adequate fluorescence by the ARIS HiQ/OptiRead.

To address the high invalid rate for *Enterococcus* spp., the following general precaution statement was included in the device labeling:

> *The Autoread method is designed such that an autoread result is considered invalid when an isolate fails to produce adequate fluorescence in the positive control at the*

time of reading. If this occurs, it is recommended that the user manually confirm all results using a visual method. Prior to reporting any results, ensure that adequate growth is present in all control wells. If growth is not present in one or more control wells, the sample should be repeated.

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 Vancomycin 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 method 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 vancomycin testing in the appropriate sections 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 *Staphylococcus* spp. and *Enterococcus* spp.
- Inoculum: Inoculated per CLSI M07 guidelines
- Incubation: 34-36° C in a non-CO_2 incubator for 24 hours.

Inoculation and incubation procedure for *Staphylococcus* spp. and *Enterococcus* 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. 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 (24 hours for vancomycin).

A total of 590 gram-positive clinical isolates comprised of *S. aureus* (334 isolates), Staphylococci other than *Staphylococcus aureus* (76 *S. epidermidis*, 11 *S. haemolyticus*, 10 *S. hominis*, 26 *S. lugdunensis*, and 25 *S. saprophyticus* isolates), and *Enterococcus* spp. (66 *E. faecalis* and 42 *E. faecium* isolates), as well as 150 challenge isolates comprised of *S. aureus* (100 isolates), Staphylococci other than *Staphylococcus aureus* (7 *S. epidermidis*, 4 *S. haemolyticus*, 3 *S. hominis*, 6 *S. lugdunensis*, and 5 *S. saprophyticus* isolates), and *Enterococcus* spp. (19 *E. faecalis* and 6 *E. faecium* isolates), were evaluated with the ARIS HiQ/OptiRead and the results are provided in **Table 2.**

For *S. aureus* read using the ARIS HiQ/OptiRead, the combined clinical and challenge results (434 isolates) were acceptable at 98.9% and 99.3% for essential agreement (EA) and categorical agreement (CA), respectively. There were 2 minor errors, no major errors, and one very major error (1/1 = 100%). A limitation to address the unacceptable very major error rate is described below.

For Staphylococci other than *Staphylococcus aureus* read by the ARIS/HiQ/OptiRead, the combined clinical and challenge results (173 isolates) were acceptable at 98.3% and 99.4% for EA and CA, respectively. There was one major error (1/173 = 0.6%) and no minor or very major errors. Due to the insufficient number of resistant *S. aureus*, *S. epidermidis, S. haemolytics, S. hominis, lugdunensis*, and *S. saprophyticus* isolates evaluated, the following limitation was applied to vancomycin 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.*

For *Enterococcus* spp. read by the ARIS/HiQ/OptiRead, the combined clinical and challenge results (133 isolates) were acceptable at 97.0% for both EA and CA. There were 2 minor errors, no major errors, and 2 very major errors (2/35 = 5.7%), which is not acceptable. When evaluating by individual species, the very major errors were due to *E. faecalis* isolates (2/10 = 20%). A supplemental study was performed to address the unacceptable very major error rate and is described below.

Table 2. Vancomycin Performance of *S. aureus*, Staphylococci other than *Staphylococcus aureus,* and *Enterococcus* spp. 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
***S. aureus* [≤ 2 (S), 4-8 (I), ≥16 (R)]**													
Clinical	334	330	98.8	334	330	98.8	333	99.7	1	333	0	0	1
Challenge	100	99	99	100	99	99.0	98	98.0	0	99	2	0	0
Combined	434	429	98.9	434	429	98.9	431	99.3	1	432	2	0	1
Staphylococci other than *Staphylococcus aureus* [≤ 4 (S), 8-16 (I), ≥32 (R)]													
Clinical	148	146	98.7	146	144	98.6	148	100	0	148	0	0	0
Challenge	25	24	96.0	25	24	96.0	24	96.0	0	25	0	1	0
Combined	173	170	98.3	171	168	98.3	172	99.4	0	173	0	1	0

	Tot	EA No.	EA %	Eval Tot	Eval EA No.	Eval EA %	CA Tot	CA %	No. R	No.S	min	maj	vmj
***Enterococcus* spp. [≤ 4 (S), 8-16 (I), ≥32 (R)]**													
Clinical	108	106	98.2	81	79	97.5	106	98.2	28	80	1	0	1
Challenge	25	23	92.3	21	19	90.5	24	92.3	7	19	1	0	1
Combined	133	129	97.0	101	97	96.0	129	97.0	35	98	2	0	2

EA – Essential Agreement
CA – Categorical Agreement
S – Susceptible
Maj – Major Discrepancies
EVAL – Evaluable MICs
R – Resistant
min – Minor 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.

A total of 596 gram-positive clinical isolates comprised of *S. aureus* (333 isolates), Staphylococci other than *Staphylococcus aureus* (76 *S. epidermidis*, 11 *S. haemolyticus*, 10 *S. hominis*, 27 *S. lugdunensis*, and 25 *S. saprophyticus* isolates), and *Enterococcus* spp. (67 *E. faecalis* and 47 *E. faecium* isolates), as well as 150 challenge isolates comprised of *S. aureus* (100 isolates), Staphylococci other than *Staphylococcus aureus* (7 *S. epidermidis*, 4 *S. haemolyticus*, 3 *S. hominis*, 6 *S. lugdunensis*, and 5 *S. saprophyticus* isolates), and *Enterococcus* spp. (19 *E. faecalis* and 6 *E. faecium* isolates), were evaluated with the Vizion and the results are provided in **Table 3.**

For *S. aureus* read using the Vizion, the combined clinical and challenge results (433 isolates) were acceptable at 99.1% and 99.3% for EA and CA, respectively. There were 2 minor errors, no major errors, and one very major error (1/1 = 100%). For *S. aureus*, there was one very major error using both the ARIS HiQ/OptiRead and the Vizion. Due to the lack of resistant isolates evaluated, the very major error is considered random the following performance footnote will be added to the device labeling:

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

For Staphylococci other than *Staphylococcus aureus* read by the Vizion, the combined clinical and challenge results (174 isolates) were acceptable at 99.4% and 100% for EA and CA, respectively. There were no minor, major, or very major errors.

For *Enterococcus* spp. read by the Vizion, the combined clinical and challenge results (139 isolates) were acceptable at 99.3% for both EA and CA. There were no minor or major errors and 1 very major error (1/36 = 2.8%), which is not acceptable. When evaluating by individual species, the very major error was due to an *E. faecalis* isolate (1/10 = 10%).

Table 3. Vancomycin Performance of *S. aureus*, Staphylococci other than *Staphylococcus aureus,* and *Enterococcus* spp. read by Vizion

	Tot	EA No.	EA %	Eval Tot	Eval EA No.	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj

***S. aureus* [≤ 2 (S), 4-8 (I), ≥16 (R)]**													
Clinical	333	330	99.1	333	330	99.1	332	99.7	1	332	0	0	1
Challenge	100	99	99.0	100	99	99.0	98	98.0	0	99	2	0	0
Combined	433	429	99.1	433	429	99.1	430	99.3	1	431	2	0	1
Staphylococci other than *Staphylococcus aureus* [≤ 4 (S), 8-16 (I), ≥32 (R)]													
Clinical	149	148	99.3	147	146	99.3	149	100	0	149	0	0	0
Challenge	25	25	100	25	25	100	25	100	0	25	0	0	0
Combined	174	173	99.4	172	171	99.4	174	100	0	174	0	0	0
***Enterococcus* spp. [≤ 4 (S), 8-16 (I), ≥32 (R)]**													
Clinical	114	113	99.1	89	88	98.9	113	99.1	29	85	0	0	1
Challenge	25	25	100	18	18	100	24	100	7	17	0	0	0
Combined	139	138	99.3	108	107	99.1	138	99.3	36	103	0	0	1

EA – Essential Agreement
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S – Susceptible
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EVAL – Evaluable MICs
R – Resistant
min – Minor 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.

The VMJ rate for *Enterococcus* spp. read by ARIS HiQ/OptiRead and Vizion in the original study was unacceptable. To address this, additional *E. faecalis* challenge isolates (85, including 44 resistant) were tested and read by the ARIS/HiQ/OptiRead and Vizion in a supplemental study performed at one internal site.

The original clinical and challenge data were combined with the supplemental testing.
The final results demonstrated an acceptable very major error rate of 1.3% (1/80) with the Vizion and an improved very major error rate from 5.7% (2/35) to 2.5% (2/79) with the ARIS HiQ/OptiRead. These results were considered acceptable given the high overall EA and CA for *Enterococcus* spp., as well as no additional very major errors observed in the supplemental testing of *E. faecalis* (**Table 4**).

Table 4. Combined (Original and Supplemental) Vancomycin Performance of *Enterococcus* spp. Read by ARIS HiQ/OptiRead and Vizion

	Tot	**EA No.**	**EA %**	**Eval Tot**	**Eval EA No.**	**Eval EA %**	**CA Tot**	**CA %**	**No. R**	**No. S**	**min**	**maj**	**vmj**
***Enterococcus* spp. [≤ 4 (S), 8-16 (I), ≥32 (R)]**													
ARIS HiQ/OptiRead													
Clinical	108	106	98.2	81	79	97.5	106	98.2	28	80	1	0	1
Challenge	25	23	92.3	21	19	90.5	24	92.3	7	19	1	0	1
Supplemental	84	82	97.6	46	44	95.7	81	96.4	44	36	3	0	0
Total	217	211	97.2	147	141	95.9	210	96.8	79	134	5	0	2
Vizion													
Clinical	114	113	99.1	89	88	98.9	113	99.1	29	85	0	0	1
Challenge	25	25	100	18	18	100	24	100	7	17	0	0	0
Supplemental	85	84	98.8	45	44	97.8	85	100	44	37	0	0	0

	Tot	EA No.	EA %	Eval Tot	Eval EA No.	Eval EA %	CA Tot	CA %	No. R	No. S	min	maj	vmj
Total	224	222	99.1	153	151	98.7	223	99.6	80	140	0	0	1

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CA – Categorical Agreement
S – Susceptible
Maj – Major Discrepancies
EVAL – Evaluable MICs
R – Resistant
min – Minor 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.

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 *S. aureus*, Staphylococci other than *Staphylococcus aureus*, and *Enterococcus* spp. 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.

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 *S. aureus*, Staphylococci other than *Staphylococcus aureus*, and *Enterococcus* spp. with vancomycin using the ARIS HiQ/OptiRead and the Vizion are summarized in **Table 5**. A trend toward higher MIC values was observed for *S. aureus*, *S. epidermidis*, *S. lugdunensis*, *S. saprophyticus*, and *E. faecium* using the ARIS HiQ/OptiRead. A trend toward higher MIC values was observed for *S. aureus, S. epidermidis, S. lugdunensis, S. saprophyticus, E. faecalis*, and *E. faecium* using the Vizion when compared to the CLSI broth microdilution reference method.

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

For ARIS HiQ/OptiRead:
Vancomycin MIC values tended to be in exact agreement or at least one doubling dilution higher when testing S. aureus, S. epidermidis, S. lugdunensis, S. saprophyticus, and *E. faecium with the ARIS HiQ/OptiRead compared to the CLSI reference broth microdilution method.*

For Vizion:
Vancomycin MIC values tended to be in exact agreement or at least one doubling dilution higher when testing S. aureus, S. epidermidis, S. lugdunensis, S. saprophyticus, E. faecalis, and *E. faecium with the Vizion compared to the CLSI reference broth microdilution method.*

Table 5. Vancomycin trending Analysis for *Staphylococcus aureus,* Staphylococci other than *Staphylococcus aureus,* and *Enterococcus* spp. 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	*S. aureus*	434	2, (0.5)	109	323, (74.4)	74%, (69% to 78%)	Yes, high
	S. epidermidis	82	1, (1.2)	54	27, (32.9)	32%, (21% to 42%)	Yes, high
	S. haemolyticus	14	0, (0)	13	1, (7.1)	7%, (-15% to 31%)	No
	S. hominis	13	0, (0)	11	2, (15.4)	15%, (-10% to 42%)	No
	S. lugdunensis	32	0, (0)	11	21, (65.6)	66%, (45% to 80%)	Yes, high
	S. saprophyticus	30	0, (0)	19	11, (36.7)	37%, (18% to 54%)	Yes, high
	E. faecalis	125	11, (8.8)	79	35, (28)	19%, (10% to 28%)	No
	E. faecium	29	2, (6.9)	13	14, (48.3)	41%, (19% to 59%)	Yes, high
Vizion	*S. aureus*	433	2, (0.5)	107	324, (74.8)	74%, (70% to 78%)	Yes, high
	S. epidermidis	82	1, (1.2)	50	31, (37.8)	37%, (25% to 47%)	Yes, high
	S. haemolyticus	14	0, (0)	11	3, (21.4)	21%, (4% to 48%)	No
	S. hominis	13	0, (0)	10	3, (23.1)	23%, (-4% to 50%)	No
	S. lugdunensis	33	0, (0)	9	24, (72.7)	73%, (53% to 85%)	Yes, high
	S. saprophyticus	30	0, (0)	18	12, (40)	40%, (21% to 58%)	Yes, high
	E. faecalis	126	3, (2.38)	77	46, (36.5)	34%, (25% to 61%)	Yes, high
	E. faecium	32	0, (0)	18	14, (43.8)	44%, (25% to 61%)	Yes, high

Testing/Reporting MICs for Non-indicated Species.
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 6: FDA-Recognized Interpretive Criteria for Vancomycin

	Minimum Inhibitory Concentrations (µg/mL)[a]		
Organisms	**Susceptible**	**Intermediate**	**Resistant**
Staphylococcus aureus	≤2	4-8	≥16
Staphylococci other than *Staphylococcus aureus*	≤4	8-16	≥32
Enterococcus spp.	≤4	8-16	≥32

[a]According to 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 incorporated by reference a breakpoint change

protocol that was reviewed and accepted by FDA in submission K231994 cleared on August 25, 2023. This referenced 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 referenced 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 Vancomycin when revised breakpoints for vancomycin 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 vancomycin 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.