



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

I Background Information:

A 510(k) Number

K242021

B Applicant

Thermo Fisher Scientific

C Proprietary and Established Names

The Sensititre 20 - 24 hour *Haemophilus influenzae*/*Streptococcus pneumoniae* (HP) MIC or Breakpoint Susceptibility System with Meropenem in the dilution range of 0.015 - 32 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
LTT	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

II Submission/Device Overview:

A Purpose for Submission:

To obtain substantial equivalence determination for the Sensititre 20-24 hour *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System with Meropenem in the dilution range of 0.015-32µg/ml with updated FDA-recognized breakpoints for *Streptococcus* spp. and an expanded dilution range originally cleared in K965190.

Breakpoints for *Haemophilus influenzae* (also indicated for use with this device) remain unchanged.

B Measurand:

Meropenem in the dilution range of 0.015 – 32 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 *Haemophilus influenzae*/*Streptococcus pneumoniae* plates are *in vitro* diagnostic products for clinical susceptibility testing of *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Streptococcus* species..

B Indication(s) for Use:

The Sensititre 20 - 24 hour *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of fastidious isolates.

This 510(k) is for meropenem in the dilution range of 0.015 - 32 µg/ml for testing fastidious isolates on the Sensititre 20 - 24 hour *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System.

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

Streptococcus agalactiae

Streptococcus pneumoniae (penicillin-susceptible isolates only)

Streptococcus pyogenes

Streptococcus spp. Viridans Group

Haemophilus influenzae

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Bold text was used to indicate updates to the limitation to include Meropenem.

The evaluation of Tedizolid and Dalbavancin, with *Streptococcus* spp. (*Streptococcus pyogenes*, *S. agalactiae*, and *S. anginosus*), Delafloxacin with *Streptococcus pyogenes*, *S. agalactiae*, *S. anginosus*, *S. pneumoniae* and *H. influenzae*, Imipenem-relebactam with *H. influenzae*, Imipenem with *Streptococcus pneumoniae*, Ceftolozane-tazobactam with *H. influenzae*, Ceftriaxone **and Meropenem** with *Streptococcus pneumoniae*, *Streptococcus* spp. β-hemolytic Group (*Streptococcus pyogenes* and *S. agalactiae*), *Streptococcus* spp. Viridans Group, and the evaluation of Oritavancin with *Streptococcus* spp. (*Streptococcus pyogenes*, *S. agalactiae*, *S. dysgalactiae*, and *S. anginosus*) was performed using the AIM autoinoculator. The use of an

alternative inoculation system when testing Tedizolid, Dalbavancin, Delafloxacin, Oritavancin, Imipenem-relebactam, imipenem, Ceftriaxone, **Meropenem**, and Ceftolozane-tazobactam has not been evaluated.

Due to a lack of interpretive criteria other than susceptible for Meropenem, isolates of *S. pyogenes* yielding MIC results other than Susceptible should be submitted to a reference laboratory for further testing.

D Special Instrument Requirements:

Sensititre AIM Autoinoculator for device inoculation
Sensititre VIZION for plate reading

IV Device/System Characteristics:

A Device Description:

The device 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 20-24 hours and examined for bacterial growth.

B Principle of Operation:

The Sensititre *Haemophilus influenzae*/*Streptococcus pneumoniae* (HP) 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 reading device (VIZION) or by use of an automated reader (ARIS/OptiRead).

The digital reading device (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 OptiRead utilizes fluorescence technology to read the microbroth dilution plates after 20 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.

Streptococcus spp. plates can either be read automatically on an ARIS/Autoreader/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 20 - 24 hour *Haemophilus influenzae*/*Streptococcus pneumoniae* (HP) MIC or Breakpoint Susceptibility System with Imipenem in the dilution range of 0.015 - 4 µg/ml

B Predicate 510(k) Number(s):

K240445

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>Device:</u> <u>K242021</u>	<u>Predicate:</u> <u>K240445</u>
Device Trade Name	The Sensititre 20-24 hour <i>Haemophilus</i> / <i>Streptococcus pneumoniae</i> (HP) MIC or Breakpoint Susceptibility System with Meropenem in the dilution range of 0.015-32µg/mL	The Sensititre 20-24 hour <i>Haemophilus</i> / <i>Streptococcus pneumoniae</i> (HP) MIC or Breakpoint Susceptibility System with Imipenem in the dilution range of 0.015-4µg/mL
General Device Characteristic Similarities		
Intended Use	The Sensititre <i>Haemophilus influenzae</i> / <i>Streptococcus pneumoniae</i> plates are <i>in vitro</i> diagnostic products for clinical susceptibility testing of <i>Haemophilus influenzae</i> , <i>Streptococcus pneumoniae</i> and <i>Streptococcus species</i> .	Same
Test Panel	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	20-24 hours	Same
Reading Method	Results can be read using the ARIS HiQ/OptiRead or VIZION (digital viewing device)	Same
Test Organisms	<i>Haemophilus influenzae</i> ,	<i>Haemophilus influenzae</i>

	<i>Streptococcus agalactiae</i> , <i>Streptococcus pneumoniae</i> (pencillin-susceptible isolates only), <i>Streptococcus pyogenes</i> , and <i>Streptococcus</i> spp. Viridans Group	and <i>Streptococcus pneumoniae</i>
General Device Characteristic Differences		
Antibiotic and Dilution Range	Meropenem 0.015- 32µg/ml	Imipenem 0.015-4µg/ml

VI Standards/Guidance Documents Referenced:

CLSI M7-A11: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard – 11th Edition

CLSI M100: Performance Standards for Antimicrobial Susceptibility Testing – 33rd edition

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 20-24-hour *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System with Meropenem in the dilution range of 0.015-32 µg/ml was performed at three sites using a panel of seventeen (17) isolates of *Streptococcus* spp. (6 *Streptococcus pneumoniae*, 3 *Streptococcus agalactiae*, 1 *Streptococcus pyogenes*, and 7 *Streptococcus* spp. Viridans Group) for a total of 459 data points read automatically with the ARIS HiQ and visually using the digital reading device (VIZION). The Sensititre AIM inoculator was used for Sensititre 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. Best-case reproducibility was greater than 95% for *Streptococcus* spp. read using the autoread and VIZION methods, and the worst-case reproducibility was greater than 90% using both read methods. Results were considered to be acceptable.

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 quality control strain recommended by CLSI, namely *S. pneumoniae* ATCC 49619, was tested with meropenem at three sites. The QC strain was tested a minimum of 20 times per site and read automatically with the ARIS HiQ and visually using the digital reading device (VIZION). The QC strain was also tested with the reference method. The results demonstrate that the Sensititre *Haemophilus influenzae*/*Streptococcus pneumoniae* (HP) MIC Susceptibility plates with meropenem produced quality control results in the recommended range >95% of time (Table 1).

Table 1. QC Results for *S. pneumoniae* with Meropenem Compared to the Reference Method with the ARIS HiQ and the Digital Reading Device (VIZION)

QC Organism	Expected Range (µg/mL)	Concentration (µg/mL)	Reference	Sensititre ARIS HiQ (Autoread)	Sensititre Digital Reading Device (VIZION)
<i>S. pneumoniae</i> ATCC 49619	0.03 – 0.25 µg/mL	≤0.0015	0	0	0
		0.03	2	0	0
		0.06	66	81	80
		0.12	3	0	1
		0.25	0	1	1
		≥0.5	1	1	1

Inoculum Density: Inoculum density checks were performed for all QC, reproducibility and challenge isolates and clinical isolates tested.

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

Growth Failures: There were two growth failures for *S. pneumoniae*, one growth failure for *S. agalactiae*, one growth failure for *S. pyogenes* and seven growth failures for *Streptococcus* spp. Viridans Group.

6. Detection Limit:

Not applicable

7. Assay Cut-Off:

Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

Testing of the Sensititre *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC Susceptibility plates with Meropenem 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 only the AIM Autoinoculator and results were interpreted automatically with the ARIS HiQ and visually using the digital reading device (VIZION). Reference panels were inoculated according to recommendations in the M07 CLSI document and results were interpreted manually using a mirrored reader.

No inoculation system other than the AIM Autoinoculator was used in the comparative study. To address the inoculation method limitation, an existing method limitation was modified in the device labeling to include testing *Streptococcus pneumoniae*, *Streptococcus* spp. β -Hemolytic Group (*Streptococcus pyogenes* and *S. agalactiae*), and *Streptococcus* spp. Viridans Group with Meropenem (**modifications in bold font**):

The evaluation of Tedizolid and Dalbavancin, with Streptococcus spp. (Streptococcus pyogenes, S. agalactiae, and S. anginosus), Delafloxacin with Streptococcus pyogenes, S. agalactiae, S. anginosus, S. pneumoniae and H. influenzae, Imipenem-relebactam with H. influenzae, Imipenem with Streptococcus pneumoniae, Ceftolozane-tazobactam with H.influenzae, Ceftriaxone and Meropenem with Streptococcus pneumoniae, Streptococcus spp. β -hemolytic Group (Streptococcus pyogenes and S. agalactiae), Streptococcus spp. Viridans Group, and the evaluation of Oritavancin with Streptococcus spp. (Streptococcus pyogenes, S. agalactiae, S. dysgalactiae, and S. anginosus) was performed using the AIM autoinoculator. The use of an alternative inoculation system when testing Tedizolid, Dalbavancin, Delafloxacin, Oritavancin, Imipenem-relebactam, imipenem, Ceftriaxone, Meropenem, and Ceftolozane-tazobactam has not been evaluated.

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

- Media: per CLSI M07 guidelines for *Streptococcus* spp.
- Inoculum: Inoculated per CLSI M07 guidelines
- Incubation: 34 - 36°C in a non-CO₂ incubator for 20 to 24 hours.

Streptococcus spp

- Media: cation-adjusted Mueller Hinton broth with TES buffer (CAMHBT) and cation-adjusted Mueller Hinton broth with TES buffer and lysed horse blood (CAMHBT+LHB, CP-114)
- Inoculum: A suspension approximating a 0.5 McFarland standard was prepared with *Streptococcus* spp. in 5 mL CAMHBT. A volume of 50 μ L of the standardized suspension was added to 11 mL of HTM. Susceptibility panels were inoculated with 100 μ L of the final organism suspension using the Sensititre AIM.
- Incubation: 34 - 36°C in a non-CO₂ incubator for 20 to 24 hours.

A total of 416 *Streptococcus* clinical isolates and 188 challenge isolates were evaluated using the ARIS HiQ (OptiRead) in this study and the results are provided in **Table 2**. For *S. pneumoniae* read using the ARIS HiQ, the combined clinical and challenge results (229 isolates) were acceptable at 97.8% and 93.9% for EA and CA, respectively. There were 13 minor errors, and no

very major errors. There was 1 major error observed but the error rate was considered acceptable at 0.5% (1/187). For *Streptococcus* spp. β -hemolytic Group read using the ARIS HiQ (OptiRead), the combined clinical and challenge results (94 *S. pyogenes* and 111 *S. agalactiae* isolates) were acceptable at 94.1% and 99.5% for EA and CA, respectively. There were no potential major errors and one potential very major error (1/1 = 100%) for *S. pyogenes*. A limitation to address the unacceptable error rate is described below. For *Streptococcus* spp. Viridans Group read using the ARIS HiQ, the combined clinical and challenge results (170 isolates) were acceptable at 97.6% and 99.4% for EA and CA, respectively. There were no potential very major errors. There was 1 potential major error observed but the error rate was considered acceptable at 0.6% (1/161).

Table 2. Meropenem Performance of *S. pneumoniae*, *Streptococcus* spp. β -Hemolytic Group, and *Streptococcus* spp. Viridans Group Read by ARIS HiQ (Autoread)

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R/N S	No. S	min	maj	vmj
<i>S. pneumoniae</i> [≤ 0.25 (S), 0.5 (I), ≥ 1 (R)]													
Clinical	157	153	97.5	48	44	91.7	147	93.6	10	139	9	1	0
Challenge	72	71	98.6	37	36	97.3	68	94.4	10	48	4	0	0
Total	229	224	97.8	85	80	94.1	215	93.9	20	187	13	1	0
<i>S. pyogenes</i> and <i>S. agalactiae</i> (<i>Streptococcus</i> spp. β-Hemolytic Group) [≤ 0.5 (S)]													
Clinical	148	142	95.9	75	69	92.0	147	99.3	0	147	NA ^b	0	0
Challenge	57	51	89.5	38	32	84.2	57	89.5	1	57	NA	0	1
Total	205	193	94.1	113	101	89.4	204	99.5	1	93	NA	0	1
<i>Streptococcus</i> spp. Viridans Group^a [≤ 0.5 (S)]													
Clinical	111	109	98.2	81	79	97.5	110	99.1	0	111	NA	1	0
Challenge	59	57	96.6	52	50	96.2	59	100	9	50	NA	0	0
Total	170	166	97.6	133	129	97.0	169	99.4	9	161	NA	1	0

^aIncluding the following species: *S. anginosus* (39), *S. anginosus* group (18), *S. constellatus* (12), *S. intermedius* (8), *S. mitis* (34), *S. oralis* (2), *S. salivarius* (19), *S. sanguinis* (18), and *Streptococcus* spp. Viridans group (18).

^bNot applicable due to susceptible-only breakpoint

EA – Essential Agreement
CA – Categorical Agreement
S – Susceptible
NS – Non-susceptible

EVAL – Evaluable MICs
R – Resistant
min – Minor Discrepancies
vmj – Very Major Discrepancies
Maj – 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 418 *Streptococcus* clinical isolates and 188 challenge isolates were evaluated using the digital viewing device (VIZION) in this study and the results are provided in **Table 3**. For *S. pneumoniae* read using the VIZION, the combined clinical and challenge results (230 isolates) were acceptable at 97.8% and 95.2% for EA and CA, respectively. There were 11 minor errors, and no major or very major errors. For *Streptococcus* spp. β -hemolytic Group read using the ARIS HiQ (OptiRead), the combined clinical and challenge results (94 *S. pyogenes* and 111 *S. agalactiae* isolates) were acceptable at 99.0% and 99.5% for EA and CA, respectively. There were no potential major errors and one potential very major error (1/1 = 100%) for *S. pyogenes*. There were no potential major errors and one potential very major error (1/1 = 100%). For

Streptococcus pyogenes, there was 1 potential very major error using both the VIZION read method and autoread method (potential errors since no other category is defined other than “susceptible only”). Due to the lack of non-susceptible isolates evaluated, the following limitation will be added to the device labeling:

Due to a lack of interpretive criteria other than susceptible for meropenem, isolates of *S. pyogenes* yielding MIC results other than Susceptible should be submitted to a reference laboratory for further testing.

Due to the lack of non-susceptible isolates evaluated, the potential VMJ error is considered random the following performance footnote will be added to the device labeling:

The 1 potential very major error observed was considered a random error due to the limited number of non-susceptible isolates tested for *S. pyogenes*.

For *Streptococcus* spp. Viridans Group read using the VIZION, the combined clinical and challenge results (171 isolates) were acceptable at 97.1% and 99.4% for EA and CA, respectively. There was no potential major errors and 1 potential very major error observed (1/9 = 11.1%). For *Streptococcus* spp. Viridans Group, there was 1 potential very major error using the autoread method (potential errors since no other category is defined other than “susceptible only”). Due to the lack of non-susceptible isolates evaluated, the potential VMJ error is considered random and a performance footnote will be added to the device labeling:

The 1 potential very major error observed was considered a random error due to the limited number of non-susceptible isolates tested for *Streptococcus* spp. Viridans Group.

Table 3. Meropenem Performance of *S. pneumoniae*, *Streptococcus* spp. β -Hemolytic Group, and *Streptococcus* spp. Viridans Group Read by the Digital Viewing Device (VIZION).

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R/NS	No. S	min	maj	vmj
<i>S. pneumoniae</i> [≤ 0.25 (S), 0.5 (I), ≥ 1 (R)]													
Clinical	158	156	98.7	46	44	95.7	152	95.2	10	140	6	0	0
Challenge	72	69	95.8	39	36	92.3	67	93.1	10	48	5	0	0
Total	230	225	97.8	85	80	94.1	219	95.2	20	188	11	0	0
<i>S. pyogenes</i> and <i>S. agalactiae</i> (<i>Streptococcus</i> spp. β-Hemolytic Group) [≤ 0.5 (S)]													
Clinical	148	147	99.3	73	72	98.6	147	99.3	1	147	NA	0	1
Challenge	57	56	98.2	38	37	97.4	57	100	0	57	NA	0	0
Total	205	203	99.0	111	109	98.2	204	99.5	1	204	NA	0	1
<i>Streptococcus</i> spp. Viridans Group^a [≤ 0.5 (S)]													
Clinical	112	108	96.4	81	77	95.1	112	100	0	112	NA	0	0
Challenge	59	58	98.3	52	51	98.1	58	98.3	9	50	NA	0	1
Total	171	166	97.1	133	128	96.2	170	99.4	9	162	NA	0	1

^aIncluding the following species: *S. anginosus* (39), *S. anginosus* group (18), *S. constellatus* (12), *S. intermedius* (8), *S. mitis* (34), *S. oralis* (2), *S. salivarius* (19), *S. sanguinis* (18), and *Streptococcus* spp. Viridans group (18).

^bNot applicable due to susceptible-only breakpoint

EA – Essential Agreement
CA – Categorical Agreement
S – Susceptible
NS – Non-Susceptible

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.

Trending

A trending analysis was conducted using the combined data (clinical and challenge) obtained for both the ARIS HiQ (OptiRead) and the digital viewing device (VIZION) for *S. pneumoniae*, *Streptococcus* spp. β -Hemolytic Group, and *Streptococcus* spp. Viridans 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.

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.

A trend toward higher MIC values was observed for *S. agalactiae* and *S. pyogenes* using the autoread method (ARIS HiQ) when compared to the CLSI broth microdilution reference method, as summarized in **Table 4**. The following statement is included as a footnote to the performance table in the device labeling to address the observed trending:

“Meropenem MIC values tended to be in exact agreement or at least one doubling dilution higher when testing *S. agalactiae* and *S. pyogenes* with the autoread method compared to the CLSI broth microdilution reference method.”

Evaluation of results for *Streptococcus* spp. and meropenem using the digital viewing device (VIZION) did not indicate trending for these organisms. (**Table 5**).

Table 4. Trending Analysis for *S. pneumoniae*, *Streptococcus* spp. β -Hemolytic Group, and *Streptococcus* spp. Viridans Group with Meropenem Read by the Sensititre ARIS HiQ (Autoread)

Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
<i>S. pneumoniae</i>	95	13 (13.7%)	61 (64.2%)	21 (22.1%)	8.4 (-2.6% to 19.3%)	No
<i>Streptococcus</i> spp. β -Hemolytic Group	172	8 (4.7%)	40 (23.3%)	124 (72.1%)	67.4% (59.1% to 74.0%)	Yes
<i>Streptococcus</i> spp. Viridans Group	139	34 (24.5%)	89 (64.0%)	16 (11.5%)	-12.0 (-21.8 to -3.9%)	No

Table 5. Trending Analysis for *S. pneumoniae*, *Streptococcus* spp. β -Hemolytic Group, and *Streptococcus* spp. Viridans Group with Meropenem Read by the Digital Viewing Device (VIZION)

Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
<i>S. pneumoniae</i>	95	9 (9.5%)	61 (64.2%)	25 (26.3%)	16.8% (6.0% to 27.5%)	No
<i>Streptococcus</i> spp. β -Hemolytic Group	114	8 (7.0%)	76 (66.7%)	30 (26.3%)	19.3% (9.8% to 28.7%)	No
<i>Streptococcus</i> spp. Viridans Group	143	28 (19.6%)	85 (59.4%)	30 (21.0%)	1.4% (-7.9 to 10.7%)	No

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-Identified Interpretive Criteria for Meropenem

Organism	Interpretive Criteria ^a for Meropenem		
	Susceptible	Intermediate	Resistant
<i>Streptococcus pneumoniae</i>	≤0.25	0.5	≥1
<i>Streptococcus</i> spp β- Hemolytic Group	≤0.5	-	-
<i>Streptococcus</i> spp Viridans Group	≤0.5	-	-

^aAccording to the [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 intends to use to evaluate the Sensititre 20–24-hour *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System with Meropenem when revised breakpoints for Meropenem 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 Meropenem 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.