



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

I Background Information:

A 510(k) Number

K241967

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 Ceftriaxone in the dilution range of 0.015 - 2 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* (HP) MIC or Breakpoint Susceptibility System with Ceftriaxone in the dilution range of 0.015 – 2 µg/mL with updated FDA-recognized breakpoints for *Streptococcus* spp. and an expanded dilution range from 0.06 – 2 µg/mL cleared in K062681.

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

B Measurand:

Ceftriaxone in the dilution range of 0.015 - 2 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 ceftriaxone in the dilution range of 0.015 - 2 µg/ml for testing fastidious isolates on the Sensititre 20 - 24 hour *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC or Breakpoint Susceptibility System.

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

Streptococcus pneumoniae

Streptococcus pyogenes

Streptococcus spp. Viridans Group

Haemophilus influenzae

Ceftriaxone has been shown to be active *in vitro* only against the following organisms of the FDA drug label:

Streptococcus agalactiae

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

Bold text was used to indicate updates to the limitations to include ceftriaxone.

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 *S. pneumoniae*, Ceftolozane-tazobactam with *H. influenzae*, and the evaluation

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

Due to a lack of interpretive criteria other than susceptible for ceftriaxone, 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 nonfluorescent 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>K241967</u>	<u>Predicate:</u> <u>K240445</u>
Device Trade Name	The Sensititre 20 - 24 hour <i>Haemophilus influenzae</i> / <i>Streptococcus pneumoniae</i> (HP) MIC or Breakpoint Susceptibility System with Ceftriaxone in the dilution range of 0.015 - 2 µg/ml.	The Sensititre 20 - 24 hour <i>Haemophilus influenzae</i> / <i>Streptococcus pneumoniae</i> (HP) MIC or Breakpoint Susceptibility System with Imipenem in the dilution range of 0.015 - 4 µg/ml.
General Device Characteristic Similarities		
Intended Use	The Sensititre <i>Haemophilus influenzae</i> / <i>Streptococcus pneumoniae</i> (HP) MIC Susceptibility plate is an <i>in vitro</i> diagnostic product 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
General Device Characteristic Differences		
Test Organisms	<i>Streptococcus pneumoniae</i> , <i>Streptococcus pyogenes</i> , <i>Streptococcus agalactiae</i> , <i>Streptococcus</i> spp. Viridans Group and <i>Haemophilus influenzae</i>	<i>Haemophilus influenzae</i> and <i>Streptococcus pneumoniae</i>
Antibiotic and Dilution Range	Ceftriaxone 0.015 - 2 µg/mL	Imipenem 0.015 - 4 µg/mL

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)

Class II Special Control Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA, August 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 Ceftriaxone in the dilution range of 0.015-2 µg/ml was performed at three sites using 16 *Streptococcus* isolates [*Streptococcus pneumoniae* (6), *Streptococcus pyogenes* (1), *Streptococcus agalactiae* (2), *Streptococcus anginosus* (1), *Streptococcus anginosus* group (1), *Streptococcus sanguinis* (3), *Streptococcus salivarius* (2)] for a total of four hundred thirty-two (432) data points read automatically with the ARIS HiQ (OptiRead) as well as using the digital viewing/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 method, and 94.9% for *Streptococcus* spp. read with VIZION, and the worst-case reproducibility was 94.7% for *Streptococcus* spp. read using the autoread method.

2. Linearity:
Not applicable

Analytical Specificity/Interference:
Not applicable

3. Assay Reportable Range:
Not applicable

4. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

The quality control strain recommended by CLSI, namely *S. pneumoniae* ATCC 49619, was tested with ceftriaxone 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 ceftriaxone produced quality control results in the recommended range of 0.03 – 0.12 µg/mL >95% of time (**Table 1**).

Table 1. QC Results for *S. pneumoniae* with Ceftriaxone 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
<i>S. pneumoniae</i> ATCC 49619	0.03-0.12 µg/mL	≤0.015			
		0.03	3		3
		0.06	63	77	66
		0.12	5	5	13
		≥0.25	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 Failure: There were two growth failures for *S. pneumoniae*, one growth failure for *S. pyogenes*, eight growth failures for *Streptococcus* spp. Viridans Group, and one growth failure for *S. agalactiae*.

5. Detection Limit:
Not applicable

6. 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 ceftriaxone was performed at two external sites and one internal site. Results were compared to results obtained with the frozen CLSI broth microdilution reference panel containing ceftriaxone. Sensititre panels were inoculated using only the AIM Autoinoculator and results were interpreted using the ARIS HiQ (Optiread) and using the digital reading device (VIZION). Reference panels were inoculated according to recommendations in the CLSI M07 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*), *Streptococcus* spp. Viridans Group with Ceftriaxone (**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 S. pneumoniae, Ceftolozane-tazobactam with H. influenzae, and the evaluation of Oritavancin with Streptococcus spp. (Streptococcus pyogenes, S. agalactiae, S. dysgalactiae, and S. anginosus), Ceftriaxone with Streptococcus pneumoniae, Streptococcus spp. (Streptococcus pyogenes and S. agalactiae), Streptococcus spp. Viridans Group was performed using the AIM autoinoculator. The use of an alternative inoculation system when testing Tedizolid, Dalbavancin, Delafloxacin, Oritavancin Imipenem-Relebactam, Imipenem, Ceftriaxone 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 410 *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**. Using meningitis breakpoints for *S. pneumoniae* read using the ARIS HiQ, the combined clinical and challenge

results (226 isolates) were acceptable at 94.7% and 92.9% for EA and CA, respectively. There were 15 minor errors, one major (1/187 = 0.53%) and no very major errors. Using non-meningitis breakpoints for *S. pneumoniae* read using the ARIS HiQ (OptiRead), the combined clinical and challenge results (226 isolates) were acceptable at 94.7% and 96.0% for EA and CA, respectively. There were 8 minor errors, one major (1/211 = 0.47%) and no 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*. A limitation to address the unacceptable error rate is described below. For *Streptococcus* spp. Viridans Group read using the ARIS HiQ (OptiRead), the combined clinical and challenge results (167 isolates) were acceptable at 96.4% and 97.6% for EA and CA, respectively. There were 4 minor errors and no major or very major errors.

Table 2. Ceftriaxone 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> [≤ 0.5 (S), 1 (I), ≥ 2 (R)] meningitis breakpoints													
Clinical	154	151	98.1	152	149	96.5	98.0	95.5	6	138	6	1	0
Challenge	72	63	87.5	69	60	89.0	63	87.5	9	49	9	0	0
Total	226	214	94.7	221	209	94.6	210	92.9	15	187	15	1	0
<i>S. pneumoniae</i> [≤ 1 (S), 2 (I), ≥ 4 (R)] non-meningitis breakpoints													
Clinical	154	151	98.1	152	149	98.0	149	96.8	2	148	4	1	0
Challenge	72	63	87.5	69	60	87.0	68	94.4	3	63	4	0	0
Total	226	214	94.7	221	209	94.6	217	96.0	5	211	8	1	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	148	147	99.3	147	99.3	1	148	0	0	1
Challenge	57	56	98.3	57	56	98.3	57	100	0	57	0	0	0
Total	205	203	99.0	205	203	99.0	204	99.5	1	204	0	0	1
<i>Streptococcus</i> spp. Viridans Group^a [≤ 1 (S), 2 (I), ≥ 4 (R)]													
Clinical	108	107	99.1	108	107	99.1	107	99.1	0	108	1	0	0
Challenge	59	54	91.5	56	51	91.1	56	94.9	3	51	3	0	0
Total	167	161	96.4	164	158	96.3	163	97.6	3	159	4	0	0

^aIncluding the following species: *S. anginosus* (39), *S. anginosus* group (18), *S. constellatus* (12), *S. intermedius* (7), *S. mitis* (34), *S. oralis* (2), *S. salivarius* (19), *S. sanguinis* (18), and Viridans group streptococci (18).

EA – Essential Agreement
CA – Categorical Agreement
S – Susceptible
NS – Non-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 412 *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**. Using meningitis ceftriaxone breakpoints, for *S. pneumoniae* read using the digital viewing device (VIZION), the combined clinical and challenge results (227 isolates) were acceptable at 98.7% and 94.3% for EA and CA, respectively. There were 13 minor errors, and no major or very major errors. Using non-meningitis breakpoints for *S. pneumoniae* read using the digital viewing device (VIZION), the combined clinical and challenge results (227 isolates) were acceptable at 98.7% and 97.8% for EA and CA, respectively. There were 5 minor errors, and no major or very major errors. For *Streptococcus* spp. β -Hemolytic Group read using the digital viewing device (VIZION), 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 *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 ceftriaxone, 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 digital viewing device (VIZION), the combined clinical and challenge results (168 isolates) were acceptable at 99.4% and 97.6% for EA and CA, respectively. There were 4 minor errors and no major or very major errors.

Table 3. Ceftriaxone Performance of *S. pneumoniae*, *Streptococcus* spp. β -Hemolytic Group, and *Streptococcus* spp. Viridans Group Read by 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> [≤ 0.5 (S), 1 (I), ≥ 2 (R)] meningitis breakpoints													
Clinical	155	155	100	68	68	100	150	96.8	6	139	5	0	0
Challenge	72	69	93.3	45	42	93.3	64	88.9	9	49	8	0	0
Total	227	224	98.7	222	219	97.3	214	94.3	15	188	13	0	0
<i>S. pneumoniae</i> [≤ 1 (S), 2 (I), ≥ 4 (R)] non-meningitis breakpoints													
Clinical	155	155	100	153	153	100	153	98.7	2	149	2	0	0
Challenge	72	69	95.8	69	66	95.7	69	95.8	3	63	3	0	0
Total	227	224	98.7	222	219	98.6	222	97.8	5	212	5	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	148	147	99.3	147	99.3	1	147	0	0	1
Challenge	57	56	98.3	57	56	98.5	57	100	0	57	0	0	0
Total	205	203	99.0	205	203	99.0	204	99.5	1	204	0	0	1
<i>Streptococcus</i> spp. Viridans Group^a [≤ 1 (S), 2 (I), ≥ 4 (R)]													
Clinical	109	108	99.1	109	108	99.1	107	98.2	0	109	2	0	0

	Tot	EA N	EA %	Eval Tot	Eval EA N	Eval EA %	CA Tot	CA %	No. R/ NS	No.S	min	maj	vmj
Challenge	59	59	100	56	56	100	57	96.6	3	51	2	0	0
Total	168	167	99.4	165	164	96.3	163	97.6	3	160	4	0	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 Viridans group streptococci (18).

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min – Minor Discrepancies

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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.

Evaluation of results for *S. pneumoniae*, *Streptococcus* spp. β -Hemolytic Group and *Streptococcus* spp. Viridans Group and ceftriaxone using either the autoread method (ARIS HiQ) and the digital viewing device (VIZION) did not indicate trending for these organisms (Tables 4 and 5).

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

Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (95% CI)	Trending Noted
<i>S. pneumoniae</i>	221	16 (7.2%)	145 (65.6%)	60 (27.1%)	20% (13% to 27%)	No
β -Hemolytic <i>Streptococcus</i> spp.	205	14 (6.8%)	150 (73.2%)	41 (20.0%)	13% (7% to 20%)	No
<i>Streptococcus</i> spp. Viridans Group	164	46 (28.1)	90	28 (17.1)	-11% (-20 to -2%)	No

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

Organism	Total Evaluable for Trending	≥ 1 Dilution lower No. (%)	Exact No. (%)	≥ 1 Dilution Higher No. (%)	Percent Difference (95% CI)	Trending Noted
<i>S. pneumoniae</i>	222	53 (23.9%)	139 (62.6%)	30 (13.5%)	-10% (-18.0% to -3%)	No
<i>Streptococcus</i> spp. β -Hemolytic Group	205	11 (5.4%)	142 (69.3%)	29 (14.1%)	14% (7% to 21%)	No
<i>Streptococcus</i> spp. Viridans Group	165	30 (18.2)	97	38 (23.0)	5% (-4% to 14%)	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-Recognized Interpretive Criteria for Ceftriaxone

Organism	Interpretive Criteria ^a for Ceftriaxone		
	Susceptible	Intermediate	Resistant
<i>S. pneumoniae</i> (meningitis)	≤0.5	1	≥2
<i>S. pneumoniae</i> (non-meningitis)	≤1	2	≥4
<i>Streptococcus</i> spp. β- Hemolytic Group	≤0.5	-	-
<i>Streptococcus</i> spp. Viridans Group	≤1	2	≥4
<i>Haemophilus influenzae</i>	≤0.25	-	-

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