Food and Drug Administration
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510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT

I Background Information:

A 510(k) Number

K191918

B Applicant

Thermo Fisher Scientific

C Proprietary and Established Names

Thermo Scientific Sensititre ARIS HiQ System

D Regulatory Information

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

II Submission/Device Overview:

A Purpose for Submission:

To demonstrate substantial equivalence of the Thermo Scientific Sensititre ARIS HiQ System to the predicate Sensititre ARIS Module, used in conjunction with the OptiRead, to read Sensititre (18-24 hour) susceptibility plates for fastidious Gram-positive microorganisms.

B Measurand:

Used in conjunction with the embedded OptiRead module and Sensititre SWIN Software System to automatically read Sensititre MIC and Breakpoint (BP) Susceptibility test panels and interpret the antimicrobial susceptibility test results for fastidious Gram-positive microorganisms.

C Type of Test:
Automated plate management system containing an incubator and embedded OptiRead module, which is an automated fluorescence-based detection instrument used to read Sensititre Susceptibility plates.

III Intended Use/Indications for Use:

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

B Indication(s) for Use:
The Thermo Scientific Sensititre ARIS HiQ System is part of the Sensititre AST system and is an automated plate management device containing an incubator and embedded OptiRead module. The Thermo Scientific Sensititre ARIS HiQ System is designed for use with the Thermo Scientific Sensititre SWIN Software System. The ARIS HiQ and the SWIN system work together to read Sensititre (18-24 hr) susceptibility plates, generating minimum inhibitory concentration (MIC) and interpreting breakpoint (BP) results for non-fastidious and fastidious microorganisms.

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

D Special Instrument Requirements:
The Thermo Scientific Sensititre ARIS HiQ System can only be used with version 3.4 of the Thermo Scientific Sensititre SWIN Software System.

IV Device/System Characteristics:

A Device Description:
The Thermo Scientific Sensititre ARIS HiQ System is an automated plate management device containing an incubator and an embedded OptiRead reader. In its current version, it is designed for use with Sensititre SWIN Software System (version 3.4). The ARIS HiQ system handles plate incubation and management. The ARIS HiQ and SWIN Software System work together to read and interpret up to 100 Sensititre plates, generating minimum inhibitory concentration (MIC) results and corresponding categorical interpretation based on breakpoints (BP) information within the SWIN software for non-fastidious Gram-negative, non-fastidious Gram-positive, and fastidious Gram-positive microorganisms.

B Principle of Operation:
The Thermo Scientific ARIS HiQ System is for use with Sensititre (18-24 hr) Susceptibility plates which are micro-versions of the classic broth dilution method for providing qualitative and quantitative susceptibility results in a dried plate format. Each plate (panel) contains a fluorogenic substrate to monitor growth and antimicrobial agents at specific two-fold dilutions to achieve drug concentrations over a specified range. When microbial metabolism and growth occurs, fluorescence is released from plate wells in amounts 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.

To use the ARIS HiQ, plates are inoculated with a standardized suspension of microorganism using the Sensititre AutoInoculator/AIM instrument, covered, and then loaded onto the ARIS HiQ for automated incubation and reading. After the incubation time indicated for each susceptibility panel, the microtiter plates are automatically moved by the robotic arm component of the ARIS HiQ to the embedded OptiRead module where the fluorescence count values are measured from each plate well. The fluorescence count values are transmitted to the SWIN software on an external PC for processing and interpretation of MIC and BP results. No result processing is performed within the ARIS HiQ.

C Instrument Description Information:

Modes of Operation	Yes	No
Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?	☒	☐
Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?	☐	☒
Software		
FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types.	☒	☐

1. Instrument Name:

   Thermo Scientific Sensititre ARIS HiQ System

2. Specimen Identification:
   Specimen (Sensititre plate)identification information should be manually entered into the SWIN Software, followed by scanning the plate barcode. If plates have not yet been loaded in the ARIS HiQ, plate identification information can be sent from the SWIN to the ARIS HiQ. If plates have been loaded in the ARIS HiQ, the SWIN Software will automatically send plate identification information to the ARIS HiQ.

3. Specimen Sampling and Handling:
   Sensititre plates inoculated with pure cultures can be loaded and unloaded from the ARIS HiQ in one of two ways: (1) individually, interacting with a rack mounted to the turntable at the front of the ARIS HiQ, or (2) in batches, using transportable microplate racks to simultaneously load, unload and handle up to ten microplates at a time.

4. Calibration:
   All calibrations and adjustments to the ARIS HiQ System are performed by Sensititre system-trained service engineers during installation and regular servicing. No adjustments or calibrations are required by the end user during day-to-day operations.

5. Quality Control:
   QC organisms were tested as appropriate for each drug and in accordance with CLSI recommendations. For results, see **Section VII.A.5**.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Sensititre Aris Module

B Predicate 510(k) Number(s):
K911419

C Comparison with Predicate(s):

Similarities		
Device & Predicate Device(s):	**ARIS HiQ** K191918 (Device)	**Sensititre ARIS Module** K911419 (Predicate)
Intended Use	Automated plate handling and incubator instrument, used in conjunction with a plate reader and external software to read read Sensititre (18-24 hour) susceptibility plates, generating minimum inhibitory concentration (MIC) and interpreting breakpoint (BP) results.	Same
Plate Compatibility	FDA cleared Sensititre susceptibility plates designed for automated reading	Same
Barcode Reading	• Linear barcode reading capability on microtiter plates • The entire plate inventory is read when plates are loaded/ unloaded	Same
Reader Unit	OptiRead	Same
Incubation Temperature	35ºC ±1ºC	Same
System Control & Software	Embedded processor running firmware	Same
Results Processing	Handled by established algorithms in SWIN system software	Same

Differences		
Device & Predicate Device(s):	**ARIS HiQ** K191918 (Device)	**Sensititre ARIS Module** K911419 (Predicate)
Plate Loading, Unloading & Handling	Plates are loaded, unloaded and handled in one of two ways: (1) Individually, on a plate rack mounted to a turntable; (2) In batches, using transportable plate racks to simultaneously load, unload and handle up to ten plates at a time.	Plates are loaded, unloaded, and handled individually on a fixed plate carousel.
Incubation Control	Five heater chimneys with a fan for each chimney to provide heated air circulation to the microplate racks.	Heated microplate carousel and a single heater chimney (no fan).
Reader Unit Implementation	OptiRead is fully integrated into the ARIS HiQ.	OptiRead is a separate instrument which plugs into the Sensititre ARIS module beneath the instrument.
User Interface	Touch screen display with icon driven graphical user interface.	Seven segment display with keypad.
SWIN interface/ communication	USB	RS-232
Plate Capacity	100	64
Automated Plate Organization	Shuffle function to automatically relocate plates within the instrument during incubation and to consolidate plates for removal	No automated plate relocation function

VI Standards/Guidance Documents Referenced:

- Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA, August 2009.
- CLSI M100-28th ed., Performance Standard for Antimicrobial Susceptibility Testing; Approved Standard, Twenty-eighth Edition, January 2018.
- CLSI M07, Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically; Approved Standard, Tenth Edition, January 2015.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A reproducibility study with fastidious Gram-positive cocci was conducted using 25 isolates of *Streptococcus* spp.: *Streptococcus pneumoniae* (ten isolates), Viridans Group S*treptococcus* spp. (five isolates), *Streptococcus pyogenes* (six isolates), and *Streptococcus agalactiae* (four isolates). Inocula were prepared using the Sensititre AutoInoculator.

The isolates were tested against the following antimicrobial agents: Amoxicillin/ Clavulanic acid, Cefepime, Cefotaxime, Ceftaroline, Chloramphenicol, Clindamycin, Daptomycin, Dalbavancin, Erythromycin, Levofloxacin, Linezolid, Meropenem, Penicillin, Trimethoprim/Sulfamethoxazole, Tedizolid, Telavancin, Tetracycline, and Vancomycin. The antimicrobial agents were selected as representatives of the major antimicrobial classes.

Testing was performed at one site over three days by three operators using Sensititre susceptibility plates on three separate ARIS HiQ instruments. Percent reproducibility was calculated as the number of isolates with MIC values falling within +/- one doubling dilution from the mode MIC value. Most of data points in the study were on-scale and within +/- one doubling dilution agreement as compared to the mode MIC.

In summary, the percent reproducibility for all antimicrobial/microorganism combinations tested met the acceptance criteria of greater than 95% for "best-case" as described in the AST Special Controls Guidance Document or "worst-case" calculations. The reproducibility results were 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):

   Quality Control (QC) Testing
   The FDA/CLSI recommended QC strain for Gram-positive organisms (*S. pneumoniae* ATCC 49619) was tested using Sensititre susceptibility plates at two sites. Inocula were prepared using the Sensititre AutoInoculator. The QC organism was tested a minimum of 20 times per site for each antimicrobial using both the ARIS HiQ and the legacy ARIS (ARIS 2X, used with the OptiRead instrument). All QC results were within the expected range >95% of the time. Overall, QC performance was acceptable. Results are summarized in **Table 1.** Shading in the table indicate the expected concentration range.

Table 1. Quality Control Results Summary

QC Organism *S. pneumoniae* ATCC 49619	Conc. (µg/mL)	ARIS HiQ	Legacy ARIS
Amoxicillin/ Clavulanic acid Expected Range 0.03/0.015-0.12/0.06 µg/mL	0.015/0.008		
	0.03/0.015		
	0.06/0.03	31	36
	0.12/0.06	8	3
	0.25/0.12		
Cefepime Expected Range 0.03-0.25 µg/mL	0.015		
	0.03		1
	0.06	29	32
	0.12	10	6
	0.25		
	0.5		
Cefotaxime Expected Range 0.03-0.12 µg/mL	0.015		
	0.03		
	0.06	37	38
	0.12	2	1
	0.25		
Chloramphenicol Expected Range 2-8 µg/mL	1		
	2	2	4
	4	37	35
	8		
	>8		
Clindamycin Expected Range 0.03-0.12 µg/mL	0.015		
	0.03	3	3
	0.06	36	34
	0.12		2
	0.25		
Daptomycin Expected Range 0.06-0.5 µg/mL	0.03		
	0.06		
	0.12	12	16
	0.25	23	17
	0.5	2	1
	1	2	5
Erythromycin Expected Range 0.03-0.12 µg/mL	0.015		1
	0.03	30	28
	0.06	9	10
	0.12		
	0.25		
Levofloxacin Expected Range 0.5-2 µg/mL	0.25		
	0.5		
	1	39	39
	2		
	4		
Linezolid Expected Range 0.5-2 µg/mL	0.25		
	0.5		1
	1	39	36
	2		2
	>2		
	0.03		1

QC Organism *S. pneumoniae* ATCC 49619	Conc. (µg/mL)	ARIS HiQ	Legacy ARIS
Meropenem Expected Range 0.06-0.25 µg/mL	0.06	39	36
	0.12		2
	0.25		
	0.5		
Penicillin Expected Range 0.25-1 µg/mL	0.12		
	0.25	15	14
	0.5	24	25
	1		
	2		
Tetracycline Expected Range 0.12-0.5 µg/mL	0.06		
	0.12	25	24
	0.25	13	13
	0.5		
	≥1	1	2
Trimethoprim/ sulfamethoxazole Expected Range 0.12/2.38-1/19 µg/mL	0.06/1.19		
	0.12/2.38	1	2
	0.25/4.75	37	36
	0.5/9.5	1	1
	1/19		
	2/38		
Vancomycin Expected Range 0.12-0.5 µg/mL	0.06		
	0.12		2
	0.25	38	36
	0.5	1	
	1		1
Ceftaroline Expected Range 0.008-0.03 µg/mL	0.004		
	0.008		
	0.015	14	13
	0.03	24	26
	0.06	1	
Dalbavancin Expected Range 0.008-0.03 µg/mL	0.004		
	0.008	10	10
	0.015	22	27
	0.03	7	2
	0.06		
Telavancin Expected Range 0.004-0.015 µg/mL	0.002		
	0.004	4	3
	0.008	19	25
	0.015	14	8
	0.03	2	3
Tedizolid Expected Range 0.12-0.5µg/mL	0.06		1
	0.12	13	13
	0.25	25	23
	0.5		
	≥1	1	2

6. Detection Limit:

Not applicable

7. Assay Cut-Off:

   Not applicable

8. Accuracy (Instrument):

   Not applicable

9. Carry-Over:

   Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:
   The performance of the ARIS HiQ was evaluated in a method comparison study conducted at one internal site. The study compared the performance of the ARIS HiQ to legacy ARIS and OptiRead instruments using Sensititre (18-24 hour) susceptibility plates. Microorganism suspensions were prepared using the Sensititre Nephelometer, and each Sensititre susceptibility plate was inoculated with the prepared microorganism suspension using the Sensititre AutoInoculator. A purity check and colony count check of all organisms was performed on the final inocula. Only those cultures that were pure were evaluated.

   The performance criteria described in the "*Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems*" were used to evaluate the performance of the ARIS HiQ. Performance evaluations used current FDA-recognized susceptibility interpretative criteria (STIC) as described on the FDA STIC webpage (https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria).

   Testing was conducted on 75 challenge isolates of fastidious Gram-positive cocci. These included *Streptococcus pneumoniae* (25), Viridans Group *Streptococcus* spp. (18), and the following β-hemolytic Group *Streptococcus* spp.: *Streptococcus agalactiae* (11), *Streptococcus dysgalactiae* (7), and *Streptococcus pyogenes* (14). One isolate each of *S. dysgalactiae* and *S. pneumoniae* failed to grow for a growth rate of 97.3% (73/75).

   The EA and CA were greater than 90% for all microorganism group/antimicrobial combinations. The overall performance was acceptable for all antimicrobials tested. Results are summarized in **Table 2** below.

Table 2. Fastidious Challenge Isolate Performance (ARIS HiQ vs. Legacy ARIS/OptiRead)

Antimicrobial	Organism Group	Total	EA N	EA %	Eval EA Total	Eval EA N	Eval EA %	CA N	CA %	#R or NS	Min	Maj	Vmj
Amoxicillin/ clavulanic acid	*S. pneumoniae*	24	24	100	22	22	100	23	95.8	2	1	0	0
Cefepime	*S. pneumoniae*	24	24	100	24	24	100	23	95.8	1	1	0	0

Antimicrobial	Organism Group	Total	EA N	EA %	Eval EA Total	Eval EA N	Eval EA %	CA N	CA %	#R or NS	Min	Maj	Vmj
	β-hemolytic Group *Streptococcus* spp.	31	31	100	30	30	100	31	100	0	N/A	0	0
	Total	55	55	100	54	54	100	54	98.2	1	1	0	0
Cefotaxime	*S. pneumoniae*	24	24	100	23	23	100	22	91.7	4	2	0	0
	β-hemolytic Group *Streptococcus* spp.	31	31	100	18	18	100	31	100	0	N/A	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	15	15	100	17	94.4	3	1	0	0
	Total	73	73	100	56	56	100	70	95.9	7	3	0	0
Ceftaroline	*S. pneumoniae*	24	24	100	24	24	100	23	95.8	1	N/A	1[a]	0
	β-hemolytic Group *Streptococcus* spp.	25	25	100	25	25	100	25	100	0	N/A	0	0
	Total	49	49	100	49	49	100	48	98.0	1	N/A	1[a]	0
Chloramphenicol	*S. pneumoniae*	24	24	100	12	12	100	24	100	14	N/A	0	0
	β-hemolytic Group *Streptococcus* spp.	31	31	100	31	31	100	31	100	0	0	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	18	18	100	18	100	2	0	0	0
	Total	73	73	100	61	61	100	73	100	16	0	0	0
Clindamycin	*S. pneumoniae*	24	24	100	14	14	100	24	100	10	0	0	0
Daptomycin	β-hemolytic Group *Streptococcus* spp.	31	30	96.8	31	30	96.8	31	100	0	N/A	0	0
Dalbavancin	β-hemolytic Group *Streptococcus* spp.	31	31	100	31	31	100	31	100	0	N/A	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	16	16	100	18	100	2	N/A	0	0
	Total	49	49	100	47	47	100	49	100	2	N/A	0	0
Erythromycin	*S. pneumoniae*	24	24	100	8	8	100	24	100	15	0	0	0
	β-hemolytic Group *Streptococcus* spp.	31	30	96.8	26	25	96.2	31	100	5	0	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	7	7	100	18	100	9	0	0	0
	Total	73	72	98.6	41	40	97.6	73	100	29	0	0	0
Levofloxacin	*S. pneumoniae*	24	24	100	24	24	100	24	100	0	0	0	0
	β-hemolytic Group *Streptococcus* spp.	31	31	100	27	27	100	31	100	1	0	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	18	18	100	18	100	0	0	0	0
	Total	73	73	100	69	69	100	73	100	1	0	0	0
Linezolid	*S. pneumoniae*	24	24	100	21	21	100	24	100	3	N/A	0	0
	β-hemolytic Group *Streptococcus* spp.	31	31	100	31	31	100	31	100	0	N/A	0	0
	Total	55	55	100	52	52	100	55	100	3	N/A	0	0
Meropenem	*S. pneumoniae*	24	24	100	17	17	100	24	100	18	N/A	0	0

Antimicrobial	Organism Group	Total	EA N	EA %	Eval EA Total	Eval EA N	Eval EA %	CA N	CA %	#R or NS	Min	Maj	Vmj
	S. pyogenes	14	14	100	2	2	100	14	100	0	N/A	0	0
	Total	38	38	100	19	19	100	38	100	18	N/A	0	0
Penicillin	*S. pneumoniae*	24	24	100	19	19	100	24	100	16	0	0	0
	β-hemolytic Group *Streptococcus* spp.	31	31	100	14	14	100	31	100	0	N/A	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	13	13	100	18	100	5	0	0	0
	Total	73	73	100	46	46	100	73	100	21	0	0	0
Trimethoprim/ sulfamethoxazole	*S. pneumoniae*	24	24	100	4	4	100	23	95.8	20	1	0	0
Tedizolid	β-hemolytic Group *Streptococcus* spp.	31	31	100	31	31	100	31	100	0	N/A	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	16	16	100	18	100	2	N/A	0	0
	Total	49	49	100	47	47	100	49	100	2	N/A	0	0
Telavancin	β-hemolytic Group *Streptococcus* spp	31	31	100	31	31	100	31	100	0	N/A	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	16	16	100	18	100	2	N/A	0	0
	Total	49	49	100	47	47	100	49	100	2	N/A	0	0
Tetracycline	*S. pneumoniae*	24	24	100	10	10	100	24	100	14	0	0	0
	β-hemolytic Group *Streptococcus* spp	31	30	96.8	18	17	94.4	31	100	13	0	0	0
	Viridans Group *Streptococcus* spp.	18	18	100	11	11	100	17	94.4	7	1	0	0
	Total	73	72	98.6	39	38	97.4	72	98.6	34	1	0	0
Vancomycin	*S. pneumoniae*	24	24	100	21	21	100	24	100	3	N/A	0	0
	β-hemolytic Group *Streptococcus* spp	31	31	100	31	31	100	31	100	0	N/A	0	0
	Total	55	55	100	52	52	100	55	100	3	N/A	0	0

a. A single categorical very major error was observed for ceftaroline when testing *S. pneumoniae* (1/24). Based on the essential agreement and lack of an intermediate breakpoint for ceftaroline, the overall adjusted very major error rate for *S. pneumoniae* isolates was 0% (0/24).

N/A - Not applicable, as there are no intermediate breakpoints.

EA – Essential Agreement
CA – Category Agreement
Eval – Evaluable isolates
R – Resistant isolates
Min – minor discrepancies
Maj – major discrepancies
Vmj – very major discrepancies
NS - Non-susceptible isolates

Essential agreement (EA) is when the ARIS HiQ result is within plus or minus one doubling dilution of the legacy ARIS result. Category Agreement (CA) is when the ARIS HiQ result interpretation agrees exactly with the legacy ARIS result interpretation. Evaluable results are those that are on-scale for both the ARIS HiQ and legacy ARIS instruments.

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):

See comparison studies in **Section VII.B** above.

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

Not applicable

F Other Supportive Instrument Performance Characteristics Data:

Not applicable

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.