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

K191914

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 non-fastidious Gram-positive and Gram-negative 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 non-fastidious Gram-positive and Gram-negative 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 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 and non-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** K191914 (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 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** K191914 (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 was conducted using a Gram-positive non-fastidious panel that included 25 isolates and a Gram-negative non-fastidious panel consisting of 25 isolates. The isolates tested are listed in **Table 1**.

Table 1. Non-Fastidious Isolates Evaluated in the Reproducibility Study

Organisms (# Tested)	
Gram-Positive Isolates	**Gram-Negative Isolates**
Staphylococcus aureus (9)	*Escherichia coli* (6)
Enterococcus faecalis (6)	*Klebsiella pneumoniae* (5)
Staphylococcus epidermidis (1)	*Enterobacter cloacae* (3)
Staphylococcus lugdunesis (1)	*Serratia marcescens* (3)
Staphylococcus haemolyticus (1)	*Acinetobacter* spp. (3)
Staphylococcus saprophyticus (1)	*Pseudomonas aeruginosa* (4)
Staphylococcus hominis (1)	*Aeromonas hydrophila* (1)
Enterococcus raffinosus (1)	
Enterococcus gallinarum (1)	
Enterococcus faecium (3)	

The Gram-positive isolates listed above were tested against the following antimicrobial agents: Chloramphenicol, Oxacillin, Penicillin, Vancomycin, Piperacillin/Tazobactam, Ciprofloxacin, Clindamycin, Tetracycline, Dalbavancin, Telavancin, Daptomycin, Linezolid, Tedizolid, Gentamicin, Erythromycin, Ceftaroline and Quinupristin/Dalfopristin. The antimicrobial agents were selected as representatives of the major antimicrobial classes.

The Gram-negative isolates listed above were tested against the following antimicrobial agents: Ampicillin, Ticarcillin, Piperacillin/Tazobactam, Chloramphenicol, Cefazolin, Cefepime, Ceftazidime, Ertapenem, Tetracycline, Levofloxacin, Gentamicin, and Trimethoprim/Sulfamethoxazole (TMP/SMX). 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.

Review of the reproducibility study data revealed two antibiotic/Gram-positive organism combinations that lacked a sufficient number of on-scale MIC results. The antibiotics included the following:

- Gram-positive reproducibility study – Clindamycin and Quinupristin/Dalfopristin

To resolve this issue, an additional modified reproducibility study was conducted which included the testing of 10 isolates (with known on-scale results), in triplicate with three different operators; performed on three different days; using three separate ARIS HiQ instruments.

In summary, despite a number of isolates with off-scale MIC results, the percent reproducibility for all antibiotic/organism combinations tested met the acceptance criteria of >95% based on the "best-case" percent calculation as described in the AST Special Controls Guidance Document.

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 and CLSI recommended QC strains for Gram-negative (*E. coli* ATCC 25922, *E. coli* ATCC 35218, and *P. aeruginosa* ATCC 27853) and Gram-positive (*S. aureus* ATCC 29213, *S. aureus* ATCC BAA-977, *E. faecalis* ATCC 29212, and *E. faecalis* ATCC 51299) organisms were tested at two sites using both the ARIS HiQ and legacy ARIS (ARIS 2X), used with the OptiRead instrument. Twenty replicates were conducted per site for each QC strain/antimicrobial combination. For all antimicrobial/QC organisms evaluated, at least one QC organism exhibited acceptable results (≥95% in-range results), except for Cefepime tested with *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853. This was attributed to not including the full CLSI/FDA recommended dilution range for QC testing with these two organisms.

   Results are summarized in **Tables 2 – 7** by QC strain, while QC results for macrolide-inducible resistance to clindamycin (D-test) and the Cefoxitin Screen are illustrated in **Table 8** and **Table 9**, respectively. Shading in the tables indicate the expected concentration range or expected result.

Table 2. Quality Control *E. coli* ATCC 25922	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Ampicillin Expected MIC Range: 2-8 µg/mL	1		
	2		
	4	39	40
	8		
	16	1	
Ceftazidime[a]	≤0.25	34	34

Table 2. Quality Control *E. coli* ATCC 25922	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Expected MIC Range 0.06-0.5 µg/mL	0.5	5	6
	1	1	
Chloramphenicol Expected MIC Range 2-8 µg/mL	1		
	2		
	4	38	40
	8	2	
	16		
Ertapenem Expected MIC Range 0.004-0.016 µg/mL	0.002		
	0.004		
	0.008	38	40
	0.016	1	
	≥0.03	1	
Cefazolin Expected MIC Range 1-4 µg/mL	≤1		
	2	39	40
	4	1	
	8		
Cefepime[b] Expected MIC Range 0.016-0.12 µg/mL	≤0.5	40	40
	1		
Gentamicin Expected MIC Range 0.25-1 µg/mL	0.12		
	0.25		
	0.5	32	32
	1	8	8
	2		
Levofloxacin Expected MIC Range 0.008-0.06 µg/mL	0.004		
	0.008		
	0.015	33	32
	0.03	7	8
	0.06		
	0.12		
Piperacillin/Tazobactam[c] Expected MIC Range 1/4-4/4 µg/mL	0.5		
	1		
	2	39	40
	4		
	8	1	
Trimethoprim/Sulfamethoxazole Expected MIC Range ≤0.5/9.5 µg/mL	≤0.25/4.75	40	40
	0.5/9.5		
	1/19		
Tetracycline Expected MIC Range 0.5-2 µg/mL	0.25		
	0.5		
	1	40	40
	2		
	4		
Ticarcillin Expected MIC Range 4-16 µg/mL	2		
	4		
	8	36	38
	16	3	1

Table 2. Quality Control *E. coli* ATCC 25922	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
	≥32	1	1

[a] The Gram-negative panel did not include the full CLSI/FDA recommended dilution range for QC testing of this drug with this organism. However, at least one other QC organism was tested using the full CLSI/FDA recommended dilution range for this drug and exhibited acceptable results (≥95% in-range results)

[b] The Gram-negative panel did not include the full CLSI/FDA recommended dilution range for QC testing of this drug with this organism

[c] Tazobactam concentration was fixed at 4 ug/mL

Table 3. Quality Control *E. coli* ATCC 35218	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Ampicillin Expected MIC Range >32 µg/mL	32		
	>32	40	40
Piperacillin/Tazobactam[a, b] Expected MIC Range 0.5/4-2/4 µg/mL	≤0.5	24	25
	1	16	14
	2		1
	4		

[a] The Gram-negative panel did not include the full CLSI/FDA recommended dilution range for QC testing of this drug with this organism. However, at least one other QC organism was tested using the full CLSI/FDA recommended dilution range for this drug and exhibited acceptable results (≥95% in-range results)

[b] Tazobactam concentration was fixed at 4 ug/mL

Table 4. Quality Control *P. aeruginosa* ATCC 27853	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Ceftazidime Expected MIC Range 1-4 µg/mL	0.5		
	1	37	34
	2	2	6
	4	1	
	≥8		
Ertapenem Expected MIC Range 2-8 µg/mL	≤1		
	2	12	14
	4	28	26
	8		
Cefepime[a] Expected MIC Range 0.5-4 µg/mL	≤0.5	9	8
	1	30	29
	2	1	3
	4		
	8		
	16		
Gentamicin Expected MIC Range 0.5-2 µg/mL	0.25		
	0.5		1
	1	40	39
	2		

Table 4. Quality Control *P. aeruginosa* ATCC 27853	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
	≥4		
Levofloxacin Expected MIC Range 0.5-4 µg/mL	0.25	1	1
	0.5	21	24
	1	18	15
	2		
	4		
	8		
Piperacillin/Tazobactam[b] Expected MIC Range 1/4-8/4 µg/mL	0.5		
	1		3
	2	32	30
	4	8	7
	8		
	16		
Trimethoprim/Sulfamethoxazole Expected MIC Range 8/152-32/608 µg/mL	≤4/76		
	8/152	11	10
	16/304	28	29
	32/608	1	1
	>32/608		
Tetracycline Expected MIC Range 8-32 µg/mL	4		
	8	36	34
	16	4	6
	32		
	≥32		
Ticarcillin Expected MIC Range 8-32 µg/mL	4		
	8		
	16	36	37
	32	4	3
	64		

[a] The Gram-negative panel did not include the full CLSI/FDA recommended dilution range for QC testing of this drug with this organism

[b] Tazobactam concentration was fixed at 4 ug/mL

Table 5. Quality Control *S. aureus* ATCC 29213	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Chloramphenicol Expected MIC Range 2-16 µg/mL	1		
	2		
	4	4	1
	8	36	39
	16		
	>16		
Ciprofloxacin Expected MIC Range 0.12-0.5 µg/mL	≤0.12		
	0.25	28	23
	0.5	12	17
	1		
Clindamycin[a] Expected MIC Range 0.06-0.25 µg/mL	≤0.12	40	40
	0.25		
	0.5		

Table 5. Quality Control *S. aureus* ATCC 29213	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Daptomycin Expected MIC Range 0.12-1 µg/mL	≤0.12	2	
	0.25	18	21
	0.5	20	19
	1		
	2		
Erythromycin Expected MIC Range 0.25-1 µg/mL	≤0.12	1	
	0.25	5	8
	0.5	34	32
	1		
	2		
Gentamicin Expected MIC Range 0.12-1 µg/mL	≤0.12		
	0.25	28	30
	0.5	12	10
	1		
	2		
Linezolid Expected MIC Range 1-4 µg/mL	0.5		
	1	2	2
	2	29	38
	4	9	
	>4		
Oxacillin[a] Expected MIC Range 0.12-0.5 µg/mL	≤0.25	4	4
	0.5	36	36
	1		
Penicillin Expected MIC Range 0.25-2 µg/mL	0.12		
	0.25		
	0.5	26	24
	1	13	14
	2	1	2
Streptomycin 1000 Expected MIC Range ≤1000 µg/mL	≤1000	40	40
	>1000		
Quinupristin/Dalfopristin[a] Expected MIC Range 0.25-1 µg/mL	≤1	40	40
	2		
Tetracycline[a] Expected MIC Range 0.12-1 µg/mL	≤0.12	7	2
	0.25	34	38
	0.5		
	1		
	2		
Vancomycin Expected MIC Range 0.5-2 µg/mL	≤0.5		
	1	39	39
	2	1	1
	4		
Ceftaroline Expected MIC Range 0.12-0.5µg/mL	0.06		
	0.12		
	0.25	40	40
	0.5		
	1		

Table 5. Quality Control *S. aureus* ATCC 29213	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Dalbavancin Expected MIC Range 0.03-0.12 µg/mL	0.015		
	0.03	11	5
	0.06	29	35
	0.12		
	0.25		
Tedizolid Expected MIC Range 0.12-1 µg/mL	0.12		
	0.25	37	30
	0.5	3	10
	1		
	2		

[a] The Gram-positive panel did not include the full CLSI/FDA recommended dilution range for QC testing of this drug with this organism. However, at least one other QC organism was tested using the full CLSI/FDA recommended dilution range for this drug and exhibited acceptable results (≥95% in-range results)

Table 6. Quality Control *E. faecalis* ATCC 29212	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Chloramphenicol Expected MIC Range 4-16 µg/mL	2		
	4	40	37
	8		3
	16		
	>16		
Ciprofloxacin Expected MIC Range 0.25-2 µg/mL	0.12		
	0.25		
	0.5	40	40
	1		
	2		
	4		
Clindamycin Expected MIC Range 4-16 µg/mL	2		
	4	1	
	8	27	31
	16	11	9
	>16		
Daptomycin Expected MIC Range 1-4 µg/mL	0.5		
	1	3	1
	2	33	37
	4	3	2
	≥8	1	
Erythromycin Expected MIC Range 1-4 µg/mL	0.5		
	1	14	12
	2	26	28
	4		
	8		
Gentamicin Expected MIC Range 4-16 µg/mL	2		
	4	3	
	8	31	34
	16	6	6

Table 6. Quality Control *E. faecalis* ATCC 29212	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
	>16		
Gentamicin 500 Expected MIC Range ≤ 500 µg/mL	≤ 500	40	40
	>500		
Oxacillin Expected MIC Range 8-32 µg/mL	4		
	8		2
	16	40	36
	32		2
	>32		
Penicillin Expected MIC Range 1-4 µg/mL	0.5		
	1		
	2	39	39
	4	1	1
	8		
Streptomycin 1000 Expected MIC Range ≤1000 µg/mL	≤1000	40	40
	>1000		
Quinupristin/Dalfopristin Expected MIC Range 2-8 µg/mL	1		
	2		
	4	40	40
	8		
	>8		
Tetracycline Expected MIC Range 8-32 µg/mL	2	1	1
	4		
	8	6	7
	16	33	32
	32		
	>32		
Vancomycin Expected MIC Range 1-4 µg/mL	0.5		
	1		
	2	38	34
	4	2	6
	8		
Ceftaroline Expected MIC Range 0.25-2 µg/mL	0.12		
	0.25		
	0.5	8	2
	1	32	38
	2		
	4		
Dalbavancin Expected MIC Range 0.03-0.12 µg/mL	0.015		
	0.03	7	9
	0.06	33	31
	0.12		
	0.25		
Tedizolid Expected MIC Range 0.25-1 µg/mL	0.12	1	
	0.25	36	28
	0.5	3	12
	1		

Table 6. Quality Control *E. faecalis* ATCC 29212	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
	2		

Table 7. Quality Control *E. faecalis* ATCC 51299	**Concentration (µg/mL)**	**Legacy ARIS**	**ARIS HiQ**
Gentamicin 500 Expected MIC Range >500 µg/mL	≤ 500	1	1
	>500	39	39
Streptomycin 1000 Expected MIC Range >1000 µg/mL	≤1000		
	>1000	40	40

Table 8. D-Test[a]	**Test Version**	**Result**	**Legacy ARIS**	**ARIS HiQ**
S. aureus ATCC BAA-977 Expected Result: Growth	D-Test 1[b]	No Growth		
		Growth	40	40
S. aureus ATCC 29213 Expected Result: No Growth	D-Test 1[b]	No Growth	40	40
		Growth		
S. aureus ATCC BAA-977 Expected Result: Growth	D-Test 2[c]	No Growth		1
		Growth	40	39
S. aureus ATCC 29213 Expected Result: No Growth	D-Test 2[c]	No Growth	40	40
		Growth		

[a] D-Test is conducted on *Staphylococcus* spp. that are resistant to Erythromycin (MIC's ≥ 8 ug/mL) and susceptible or intermediate to Clindamycin (MIC's ≤ 2 ug/mL) to determine if they exhibit inducible Clindamycin resistance
[b] D-Test 1: 4 ug/mL Erythromycin and 0.5 ug/mL Clindamycin are included in a single well
[c] D-Test 2: 8 ug/mL Erythromycin and 1.5 ug/mL Clindamycin are included in a single well

Table 9. Cefoxitin Screen[a]	**Result**	**Legacy ARIS**	**ARIS HiQ**
S. aureus ATCC 29213 Expected Result: No Growth	No Growth	40	40
	Growth		

[a] Cefoxitin Screen predicts the presence of *mecA*-mediated resistance in *S. aureus*. Cefoxitin Screen was performed at 6 ug/mL

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 by means of a method comparison study conducted at one internal site. The study was designed to evaluate the performance of the ARIS HiQ compared to the legacy ARIS and OptiRead instruments using Sensititre (18-24 hour) susceptibility plates. Specially prepared susceptibility plates containing serial dilutions of select antibiotics representing a range of antimicrobial agent classes were used in the study. Each microorganism suspension was prepared using the Sensititre Nephelometer. Each plate was inoculated with the prepared microorganism suspension using the Sensititre Autoinoculator, incubated for 18-24 hours at 35ºC on either the ARIS HiQ or legacy ARIS, and then read using the OptiRead. The MIC results obtained by the ARIS HiQ and legacy ARIS were then compared. 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.

   Method comparison testing was performed of a total of 75 Gram-negative non-fastidious challenge isolates to include (56) *Enterobacteriaceae* [*E. cloacae* (4), *E. coli* (8), *K. aerogenes* (5), *K. oxytoca* (4), *K. ozaenae* (1), *K. pneumoniae* (10), M. *morganni* (1), *P. mirabilis* (3), *P. vulgaris* (3), *P. rettgeri* (3), *P. stuartii* (2), *S. marsescens* (10), *P. agglomerans* (1), and *S. odorifera* (1)], (2) *A. hydrophila*, (6) *Acinetobacter* spp., and (11) *P. aeruginosa* isolates.

   In addition, method comparison testing was performed on a total of 75 Gram-positive non-fastidious challenge isolates including (29) *Enterococcus* spp. [*E. faecalis* (15), *E. faecium* (10), *E. durans* (2), *E. gallinarum* (1) and *E. raffinosus* (1)], (27) *S. aureus* and (19) coagulase-negative *Staphylococci* (CoNS) [*S. epidermidis* (12), *S. haemolyticus* (3), *S. warneri* (2), *S. saprophyticus* (1) and *S. capitis* (1)] isolates. The full Gram-positive challenge panel was evaluated with each antimicrobial/screen performed, except for the Cefoxitin Screen, which was only conducted with *S. aureus* isolates.

   Performance was evaluated using current FDA-recognized susceptibility interpretative criteria (STIC) on the FDA STIC webpage (https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria). As previously noted, performance of the ARIS HiQ System was being evaluated in a comparative study against the legacy ARIS using Sensititre MIC panels processed by both systems and there was no reference method testing required. Therefore, many representative drugs and organisms were used to encompass the multiple test combinations. The FDA STIC webpage information was used to assess categorical agreement. For some given organism/antimicrobial agent combinations, CLSI M100 (29th edition) was also used for this evaluation.

A single *P. aeruginosa* isolate did not grow in the Sensititre susceptibility plate, so no results were obtained by either the ARIS HiQ or the legacy ARIS. In addition, the only *E. gallinarum* isolate included in the study did not grow on either the ARIS HiQ or the legacy ARIS. Accounting for these growth failures, the growth rate for the Gram-negative and Gram-positive challenge isolate panels were 98.7% (74/75) and 98.7% (74/75), respectively.

Performance evaluations are shown in **Table 10** and **Table 11** for the Gram-negative and Gram-positive challenge isolates.

Table 10. Non-Fastidious Gram-Negative Organisms (ARIS HiQ vs. Legacy ARIS/OptiRead)

Drug	Organism Group	Total	EA N	EA %	Eval. Total	Eval. EA N	Eval. EA %	CA N	CA %	#R or NS	min	maj	vmj
Ampicillin	*Aeromonas hydrophila*	2	2	100	0	0	0	2	100	2	0	0	0
	Enterobacteriaceae	56	56	100	7	7	100	53	94.6	51	3	0	0
Cefazolin	*Aeromonas hydrophila*	2	2	100	0	0	0	2	100	2	0	0	0
	Enterobacteriaceae	56	56	100	9	9	100	59	100	55	0	0	0
Cefepime	*Acinetobacter* spp.	6	6	100	2	2	100	6	100	4	0	0	0
	Aeromonas hydrophila	2	2	100	1	1	100	2	100	0	0	0	0
	Enterobacteriaceae	56	56	100	18	18	100	51	91.1	11	5	0	0
Ceftazidime	*Acinetobacter* spp.	6	6	100	1	1	100	6	100	5	0	0	0
	Aeromonas hydrophila	2	1	50	1	1	100	1	50	1	1	0	0
	Enterobacteriaceae	56	56	100	11	11	100	56	100	26	0	0	0
Chloramphenicol	*Acinetobacter* spp.	6	6	100	3	3	100	6	100	3	0	0	0
	Aeromonas hydrophila	2	2	100	1	1	100	2	100	0	0	0	0
	Enterobacteriaceae	56	56	100	40	40	100	54	96.4	23	2	0	0
Ertapenem	*Aeromonas hydrophila*	2	2	100	1	1	100	2	100	1	0	0	0
	Enterobacteriaceae	56	54	96.4	48	46	95.8	55	98.2	22	1	0	0
Gentamicin	*Acinetobacter* spp.	6	6	100	2	2	100	6	100	3	0	0	0
	Aeromonas hydrophila	2	2	100	2	2	100	2	100	0	0	0	0
	Enterobacteriaceae	56	55	98.2	40	39	97.5	55	98.2	15	1	0	0
Levofloxacin	*Acinetobacter* spp.	6	6	100	5	5	100	6	100	1	0	0	0
	Aeromonas hydrophila	2	2	100	2	2	100	2	100	0	0	0	0
	Enterobacteriaceae	56	56	100	40	40	100	54	96.4	24	2	0	0
Piperacillin/ Tazobactam	*Acinetobacter* spp.	6	6	100	2	2	100	6	100	3	0	0	0
	Aeromonas hydrophila	2	2	100	1	1	100	2	100	1	0	0	0
	Enterobacteriaceae	56	56	100	30	30	100	54	96.4	19	2	0	0

Table 10. Non-Fastidious Gram-Negative Organisms (ARIS HiQ vs. Legacy ARIS/OptiRead)													
Drug	**Organism Group**	**Total**	**EA N**	**EA %**	**Eval. Total**	**Eval. EA N**	**Eval. EA %**	**CA N**	**CA %**	**#R or NS**	**min**	**maj**	**vmj**
	P. aeruginosa	10	10	100	9	9	100	10	100	1	0	0	0
TMP/SMX	*Acinetobacter* spp.	6	6	100	3	3	100	6	100	2	0	0	0
	Aeromonas hydrophila	2	2	100	0	0	0	2	100	0	0	0	0
	Enterobacteriaceae	56	56	100	9	9	100	56	100	25	0	0	0
Tetracycline	*Acinetobacter* spp.	6	6	100	5	5	100	6	100	1	0	0	0
	Aeromonas hydrophila	2	2	100	2	2	100	2	100	0	0	0	0
	Enterobacteriaceae	56	56	100	36	36	100	52	92.9	26	4	0	0
Ticaracillin	*Acinetobacter* spp.	6	6	100	1	1	100	6	100	5	0	0	0
	Aeromonas hydrophila	2	2	100	0	0	0	2	100	2	0	0	0
	Enterobacteriaceae	56	56	100	13	13	100	55	98.2	43	1	0	0
	P. aeruginosa	10	10	100	4	4	100	10	100	9	0	0	0

Table 11. Non-Fastidious Gram-Positive Organisms (ARIS HiQ vs. Legacy ARIS/OptiRead)													
Drug	**Organism Group**	**Total**	**EA N**	**EA %**	**Eval. Total**	**Eval. EA N**	**Eval. EA %**	**CA N**	**CA %**	**#R or NS**	**min**	**maj**	**vmj**
Ceftaroline	*S. aureus*	27	27	100	27	27	100	26	96.3	0	1	0	0
Chloramphenicol	*Enterococcus* spp.	28	28	100	22	22	100	28	100	5	0	0	0
	S. aureus	27	27	100	22	22	100	26	96.3	5	1	0	0
	CoNS	19	19	100	17	17	100	19	100	2	0	0	0
Ciprofloxacin	*Enterococcus* spp.	28	28	100	19	19	100	27	96.4	9	1	0	0
	S. aureus	27	27	100	18	18	100	27	100	9	0	0	0
	CoNS	19	19	100	15	15	100	19	100	0	0	0	0
Clindamycin	*S. aureus*	27	27	100	0	0	0	27	100	3	0	0	0
	CoNS	19	19	100	1	1	100	19	100	5	0	0	0
Dalbavancin	*S. aureus*	27	26	96.3	27	26	96.3	27	100	0	0	0	0
Daptomycin	*E. faecalis*	15	15	100	15	15	100	15	100	0	0	0	0
	S. aureus	27	26	96.3	25	24	96.0	27	100	0	0	0	0
	CoNS	19	19	100	17	17	100	19	100	0	0	0	0
Erythromycin	*Enterococcus* spp.	28	28	100	8	8	100	27	96.4	17	1	0	0
	S. aureus	27	26	96.3	10	9	90	25	92.6	17	2	0	0
	CoNS	19	19	100	1	1	100	19	100	7	0	0	0
Gentamicin	*S. aureus*	27	26	96.3	23	22	95.7	27	100	2	0	0	0
	CoNS	19	19	100	2	2	100	18	94.7	5	1	0	0

Table 11. Non-Fastidious Gram-Positive Organisms (ARIS HiQ vs. Legacy ARIS/OptiRead)													
Drug	**Organism Group**	**Total**	**EA N**	**EA %**	**Eval. Total**	**Eval. EA N**	**Eval. EA %**	**CA N**	**CA %**	**#R or NS**	**min**	**maj**	**vmj**
Linezolid	*Enterococcus* spp.	28	28	100	25	25	100	28	100	0	0	0	0
	S. aureus	27	27	100	27	27	100	27	100	0	0	0	0
	CoNS	19	19	100	4	4	100	19	100	0	0	0	0
Oxacillin	*S. aureus*	27	27	100	15	15	100	27	100	11	0	0	0
	CoNS	19	19	100	8	8	100	19	100	13	0	0	0
Penicillin	*Enterococcus* spp.	28	28	100	17	17	100	28	100	10	0	0	0
	S. aureus	27	27	100	4	4	100	27	100	21	0	0	0
	CoNS	19	19	100	8	8	100	18	94.7	16	0	0	1[e]
Quinupristin / Dalfopristin	*Enterococcus* spp.	28	28	100	17	17	100	26	92.9	18	2	0	0
	S. aureus	27	27	100	0	0	0	27	100	0	0	0	0
	CoNS	19	19	100	0	0	0	19	100	0	0	0	0
Tedizolid	*E. faecalis*	15	15	100	15	15	100	15	100	0	0	0	0
	S. aureus	27	27	100	27	27	100	27	100	0	0	0	0
Telavancin	*E. faecalis*	15	15	100	12	12	100	15	100	3	0	0	0
	S. aureus	27	27	100	27	27	100	27	100	0	0	0	0
Tetracycline	*Enterococcus* spp.	28	28	100	11	11	100	28	100	22	0	0	0
	S. aureus	27	27	100	7	7	100	27	100	5	0	0	0
	CoNS	19	19	100	11	11	100	19	100	2	0	0	0
Vancomycin	*Enterococcus* spp.	28	28	100	14	14	100	28	100	11	0	0	0
	S. aureus	27	27	100	26	26	100	27	100	0	0	0	0
	CoNS	19	19	100	16	16	100	18	94.7	0	1	0	0
D-Test 1[a]	*Enterococcus* spp.	28	NA					28	100	19	NA	0	0
	S. aureus	27						16	96.3	16		1[f]	0
	CoNS	19						19	100	6		0	0
D-Test 2[b]	*Enterococcus* spp.	28	NA					28	100	18	NA	0	0
	S. aureus	27						27	100	17		0	0
	CoNS	19						19	100	6		0	0
Cefoxitin Screen[c]	*S. aureus*	27	NA					27	100	11	NA	0	0
HLAR Screen: Gentamycin 500 ug/mL	*Enterococcus* spp.	28	NA					28	100	12	NA	0	0
	S. aureus	27						27	100	0		0	0
	CoNS	19						19	100	1		0	0

Table 11. Non-Fastidious Gram-Positive Organisms (ARIS HiQ vs. Legacy ARIS/OptiRead)													
Drug	**Organism Group**	**Total**	**EA N**	**EA %**	**Eval. Total**	**Eval. EA N**	**Eval. EA %**	**CA N**	**CA %**	**#R or NS**	**min**	**maj**	**vmj**
HLAR Screen: Streptomycin 1000 ug/mL[d]	*Enterococcus* spp.	28	NA					28	100	12	NA	0	0

a. Erythromycin – 4 ug/mL; Clindamycin – 0.5 ug/mL
b. Erythromycin – 8 ug/mL; Clindamycin – 1.5 ug/mL
c. Cefoxitin – 6 ug/mL
d. 27 *S. aureus* isolates and 19 coagulase-negative *Staphylococci* (CoNS) challenge isolates were also tested but performance was not included because this test is only cleared for use with *Enterococcus* spp.
e. The categorical very major error rate for penicillin when testing coagulase-negative *Staphylococci* (CoNS) challenge isolates is 6.3% (1/16). Based on the essential agreement and lack of an intermediate breakpoint for penicillin, the overall adjusted very major error rate for coagulase-negative staphylococci challenge isolates is 0% (0/16)
f. A single major error was obtained for D-test 1 with *S. aureus*. This result was considered a random error occurrence and is acceptable

NA – Not applicable, as these are qualitative tests

EA – Essential Agreement
CA – Category Agreement
EVAL – Evaluable isolates
R – Resistant isolates
NS – Non-Susceptible isolates

min – minor errors
maj – major errors
vmj – very major errors

Essential Agreement (EA) is when the ARIS HiQ result agrees exactly or is within 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 EA is when the MIC result for the ARIS HiQ and the legacy ARIS are on-scale.

The %EA is acceptable when compared to the reference method as described in the FDA guidance document, "*Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) System; Guidance for Industry and FDA"*.

Overall, the MIC results of the ARIS HiQ and the legacy ARIS were very similar, for all antimicrobials tested. The %EA and %CA for all microorganism group/antimicrobial combinations were greater than 90%, except for *A. hydrophila* challenged with Ceftazidime, for which only two isolates were evaluated.

Resistance Markers
Resistance markers for indicated Gram-negative non-fastidious isolates were provided in the submission. They consisted of the Extended Spectrum β-lactamase (ESBL) gene CTX-M-1 and the carbapenemase genes KPC and NDM.

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.