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

## I Background Information:

### A 510(k) Number

K252062

### B Applicant

Thermo Fisher Scientific

### C Proprietary and Established Names

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Colistin in the dilution range of 0.12-16 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 |
| LRG | Class II | 21 CFR 866.1640 - Antimicrobial susceptibility test powder | MI - Microbiology |
| LTT | Class II | 21 CFR 866.1640 - Antimicrobial susceptibility test powder | MI - Microbiology |

## II Submission/Device Overview:

### A Purpose for Submission:

To obtain substantial equivalence determination for The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Colistin in the dilution range of 0.12-16 µg/mL.

### B Measurand:

Colistin in the dilution range of 0.12 to 16 µg/mL

### C Type of Test:

Quantitative antimicrobial susceptibility test (AST) growth-based detection

## III Intended Use/Indications for Use:

### A Intended Use(s):

The Sensititre MIC and Breakpoint Susceptibility system is an *in vitro* diagnostic product for clinical susceptibility testing of non-fastidious Gram negative isolates, comprising of *Acinetobacter* species, Enterobacterales, *Pseudomonas aeruginosa*, and other non-Enterobacterales and of non-fastidious Gram positive isolates, comprising of *Staphylococcus* spp., *Enterococcus* spp., and beta-haemolytic Streptococci other than *S. pneumoniae*.

### B Indication(s) for Use:

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of non-fastidious isolates.

This 510(k) is for colistin in the dilution range of 0.12-16 µg/mL for testing non-fastidious gram-negative isolates on the Sensititre 18-24 hour MIC or Breakpoint Susceptibility System. Testing is indicated for *Acinetobacter baumannii* complex, Enterobacterales, and *Pseudomonas aeruginosa*, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC) webpage.

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Colistin in the dilution range of 0.12-16 µg/mL demonstrated acceptable performance with the following organisms:

*Acinetobacter baumannii* complex *(Acinetobacter baumannii)*

Enterobacterales (*Citrobacter freundii, Citrobacter koseri, Enterobacter cloacae* complex*, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae*)

*Pseudomonas aeruginosa*

### C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

The following limitation was applied to colistin testing in the appropriate section of the device labeling that references other drugs:

> *Studies of the following drugs were performed with the AIM Autoinoculator and read using the ARIS HiQ/OptiRead and Vizion. The use of an alternative inoculation system or alternative read methods has not been evaluated.*

Due to the insufficient number of resistant *A. baumannii, C. freundii, C. koseri, E. cloacae* complex, *E. coli*, and *P. aeruginosa* isolates evaluated, the following limitation was applied to colistin testing in the appropriate section of the device labeling that references other drugs:

> *The ability of the Sensititre system to detect resistance or non-susceptibility to antimicrobics as shown below is unknown because an insufficient number of resistant or non-susceptible strains were available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory.*

### D Special Instrument Requirements:

Sensititre AIM for device inoculation
Sensititire Vizion digital viewing device
Sensititre ARIS HiQ/OptiRead automated plate reader

## IV Device/System Characteristics:

### A Device Description:

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility Plate System is an antimicrobial susceptibility test. Each plate is dosed with dried, stabilized antimicrobial agents at appropriate dilutions. It is a micro-version of the classic broth dilution method and can provide both qualitative and quantitative susceptibility results. After inoculation, plates are sealed with an adhesive seal, incubated at 34-36°C for 18-24 hours and examined for bacterial growth.

### B Principle of Operation:

The Sensititre 18-24 hour MIC Susceptibility plates are multi-well plastic microtiter plates that contain doubled dilutions of antibacterial agents. Each plate includes antimicrobial agents at appropriate dilutions. Results can be read using the digital viewing device (Vizion) or by use of an automated plate reader (ARIS HiQ/OptiRead).

The Sensititre Vizion digital viewing device allows the panel image to be displayed on a touch screen directly from a video camera and allows the user to visually determine MIC results. The Sensititre OptiRead utilizes fluorescence technology to read the microbroth dilution plates after 18 to 24 hours incubation. The technology involves the detection of bacterial growth by monitoring the activity of specific surface enzymes produced by the test organism. Growth is determined by generating a fluorescent product from a fluorogenic substrate. The non-fluorescent substrate is prepared by conjugating a fluorescent compound to the specific enzyme substrates with a bond which prevents fluorescence. The enzymatic action of the bacterial surface enzymes on the bound non-fluorescent substrate cleaves the bond releasing fluorescence. The amount of fluorescence detected is directly related to the activity of bacterial growth. The MIC is determined by observing the lowest dilution of antimicrobial agent that inhibits growth of the organism. The non-fluorescent (fluorogenic) substrate can be added to the inoculum broth which is dispensed into the test plate at the same time as the test organism, or the plates can be prepared with the substrate already added to each micro-well.

Sensititre 18-24 hour MIC plates can either be read automatically on an ARIS HiQ/OptiRead using fluorescence or by visual reading of growth on the Vizion digital viewing device.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):

The Sensititre 18-24 Hour MIC or Breakpoint Susceptibility System with Lefamulin in the dilution range of 0.008-16 µg/mL

**B Predicate 510(k) Number(s):**
K192729

**C Comparison with Predicate(s):**

| **Device & Predicate Device(s):** | Device:<br>K252062 | Predicate:<br>K192729 |
|---|---|---|
| Device Trade Name | The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Colistin in the dilution range of 0.12-16 µg/mL | The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Lefamulin in the dilution range of 0.008-16 µg/mL |
| **General Device Characteristic Similarities** | | |
| Intended Use | The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of non-fastidious bacterial isolates. | Same |
| Test Panel | Each 96 well plate is precision dosed with selected antimicrobial agents and substrate for the fluorescent reads, then dried. The bacterial suspension in the appropriate broth is used to rehydrate the plate. | Same |
| Incubation | 18-24 hours | Same |
| Read Method | Results can be read using fluorescence with the ARIS HiQ/OptiRead or by visual reading of growth with the Vizion. | Same |
| **General Device Characteristic Differences** | | |
| Antibiotic and Dilution Range | Colistin<br>0.12-16 µg/mL | Lefamulin<br>0.008-16 µg/mL |
| Test organisms | *Acinetobacter baumannii* complex *(Acinetobacter baumannii*)<br><br>Enterobacterales (*Citrobacter freundii,* | *Staphylococcus aureus* (methicillin-susceptible isolates) |

| | | |
|---|---|---|
| | *Citrobacter koseri, Enterobacters cloacae* complex*, Echerichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae*)<br><br>*Pseudomonas aeruginosa* | |

## 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; 34th Edition", (March 2024)

Guidance for Industry and FDA: Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems, August 28, 2009

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:

A reproducibility study of The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Colistin was performed at three sites using a panel of eighteen (18) gram-negative isolates from species indicated for use with the device (5 *Escherichia coli*, 4 *Klebsiella pneumoniae*, 4 *Pseudomonas aeruginosa*, 2 *Enterobacter cloacae*, 2 *Acinetobacter baumannii*, and 1 *Citrobacter koseri)*. All isolates were tested in triplicate over three days for a total of 486 data points with each read method (i.e., automatically with the ARIS HiQ/OptiRead and visually with the Vizion). The Sensititre AIM Autoinoculator was used for Sensititre plate inoculation. The mode MIC value was determined, and the reproducibility was calculated based on MIC values falling within ±1 doubling dilution of the mode MIC value. The reproducibility studies for both the ARIS HiQ/OptiRead and Vizion read methods demonstrated acceptable performance of ≥95%.

In addition, five Enterobacterales isolates that are intrinsically resistant to colistin (3 *Serratia marcescens*, 1 *Proteus mirabilis*, and 1 *Providencia stuartii*) and one *Escherichia coli* isolate with an off-scale mode were also tested.

2. Linearity:

Not applicable.

3. Analytical Specificity/Interference:

   Not applicable.

4. Assay Reportable Range:

   Not applicable.

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

   The CLSI-recommended quality control (QC) strain *P. aeruginosa* ATCC 27853 and CLSI supplemental QC strain *E. coli* NCTC 13846 were tested at three sites. The QC strains were tested a minimum of 20 times per site and read automatically with the ARIS HiQ/OptiRead and visually with the Vizion. The QC strains were also tested with the reference method. The results demonstrate that The Sensititre 18-24 hour MIC Susceptibility System with Colistin produced quality control results within the recommended range >95% of the time (**Table 1**).

**Table 1.** Quality Control Results *P. aeruginosa* and *E. coli* with Colistin with the Reference Method, ARIS HiQ/OptiRead, and Vizion

| QC Organism | Expected Range (µg/mL) | Concentration (µg/mL) | Reference | ARIS HiQ/ OptiRead | Vizion |
|---|---|---|---|---|---|
| *Pseudomonas aeruginosa* ATCC 27853 | 0.25-2 µg/mL | ≤0.12 | - | - | - |
| | | 0.25 | - | - | - |
| | | 0.5 | 51 | - | - |
| | | 1 | 33 | 101 | 109 |
| | | 2 | - | 12 | 4 |
| | | ≥4 | - | 1 | 1 |
| *Escherichia coli* NCTC 13846 | 1-8 µg/mL | ≤0.5 | - | - | - |
| | | 1 | 1 | - | - |
| | | 2 | 75 | - | - |
| | | 4 | 9 | 106 | 113 |
| | | 8 | - | 8 | 1 |
| | | ≥8 | - | 1 | 1 |

**Inoculum Density**: Inoculum density checks were performed for all QC, reproducibility, challenge, and clinical isolates tested. Only results from cultures with appropriate inoculum densities were reported.

**Purity Checks**: Purity checks were performed for all QC, reproducibility, challenge, and clinical isolates tested. Only results from pure cultures were reported.

**Growth Failure:** There were no growth failures.

**ARIS HiQ/OptiRead Invalids (No fluorescence):** There were no invalids that did not produce adequate fluorescence by the ARIS HiQ/OptiRead.

6. Detection Limit:

Not applicable.

7. Assay Cut-Off:

Not applicable.

## B Comparison Studies:

1. Method Comparison with Predicate Device:

Testing of The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System with Colistin was performed at three external sites. Results were compared to those obtained with the CLSI broth microdilution reference method. Sensititre panels were inoculated using only the AIM Autoinoculator and results were read automatically by the ARIS HiQ/OptiRead and visually by the Vizion. Reference panels were inoculated according to recommendations in the M07 CLSI document and results were read manually using a mirrored reader.

No inoculation system other than the AIM Autoinoculator and no read methods other than ARIS HiQ/OptiRead and Vizion was used in the comparative study. To address the inoculation method and read method limitation, the following limitation was applied to colistin testing in the appropriate section of the device labeling that references other drugs:

> *Studies of the following drugs were performed with the AIM Autoinoculator and read using the ARIS HiQ/OptiRead and Vizion. The use of an alternative inoculation system or alternative read methods has not been evaluated.*

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

- Media: per CLSI M07 guidelines for *Acinetobacter* spp., Enterobacterales and *Pseudomonas aeruginosa*
- Inoculum: Inoculated per CLSI M07 guidelines
- Incubation: 34-36°C in a non-$CO_2$ incubator for 20-24 hours (*Acinetobacter* spp.) or 16-20 hours (Enterobacterales and *Pseudomonas aeruginosa*)

Inoculation and incubation procedure for *Acinetobacter baumannii* complex, Enterobacterales, and *Pseudomonas aeruginosa*

- Media: cation-adjusted Mueller Hinton broth with TES buffer (CAMHBT)
- Inoculum: A suspension approximating a 0.5 McFarland standard was prepared in 5 mL sterile water. Ten (10) µL of the standardized suspension was transferred to 11 mL of CAMHBT. Susceptibility plates were inoculated with 50 µL of the final organism suspension using the Sensititre AIM Autoinoculator.
- Incubation: 34-36°C in a non-$CO_2$ incubator for 18-24 hours (20-24 hours for *Acinetobacter baumannii* complex)

ARIS HiQ/OptiRead:

A total of 480 gram-negative clinical isolates comprised of *A. baumannii* complex (60 *A. baumannii* isolates), Enterobacterales (30 *C. freundii*, 45 *C. koseri*, 60 *E. cloacae* complex, 75 *E. coli*, 60 *K. aerogenes*, 25 *K. oxytoca*, 65 *K. pneumoniae* isolates), and *P. aeruginosa* (60 isolates), as well as 151 challenge isolates comprised of *A. baumannii* complex (24 *A. baumannii* isolates), Enterobacterales (6 *C. freundii*, 5 *C. koseri*, 20 *E. cloacae* complex, 25 *E. coli*, 12 *K. aerogenes*, 5 *K. oxytoca*, 26 *K. pneumoniae* isolates) and *P. aeruginosa* (28 isolates) were evaluated with the ARIS HiQ/OptiRead and the results are provided in **Table 2**.

This is a unique case where there is not a defined susceptible (S) interpretive category for colistin: therefore, the intermediate (I) category is treated as an S for performance analysis. In these situations where errors cannot be categorized as minor, adjustments are made to categorical errors by considering if the MIC values where the errors occur are in essential agreement with the reference method. Additionally, due to the lack of a susceptible interpretive category, all errors are considered potential errors.

For *A. baumannii* complex read using the ARIS HiQ/OptiRead, the combined clinical and challenge isolates (84 isolates) were acceptable at 96.4% and 98.8% for EA and CA, respectively. There were no potential major errors and one potential very major error (1/2 = 50%). Due to the lack of resistant isolates evaluated, the potential very major error is considered random, and 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 resistant isolates tested for A. baumannii.*

For Enterobacterales read using the ARIS HiQ/OptiRead, the combined clinical and challenge isolates (459 isolates) were acceptable at 97.8% and 98.7% for EA and CA, respectively. There were three potential major errors (3/440 = 0.7%) and three potential very major errors (3/19 = 15.8%). Two of the three potential major errors had an MIC value that was in essential agreement with the reference MIC value; therefore, the adjusted potential major error rate is 0.2% (1/440). One of the three potential very major errors had an MIC value that was in essential agreement with the reference MIC value; therefore, the adjusted potential very major error rate is 10.5% (2/19). When evaluating by individual species, one potential very major error was due to a *C. freundii* isolate (1/2 = 50%) and one potential very major error was due to an *E. cloacae* complex isolate (1/5 = 20%). Due to the lack of resistant *C. freundii* and *E. cloacae* complex isolates evaluated, the potential very major errors are considered random, and the following performance footnote will be added to the device labeling:

> *The 2 potential very major errors observed were considered a random error due to the limited number of resistant isolates tested for C. freundii and E. cloacae complex.*

For *P. aeruginosa* read using the ARIS HiQ/OptiRead, the combined clinical and challenge isolates (88 isolates) were acceptable at 95.5% and 98.9% for EA and CA, respectively. There was one potential major error (1/88 = 1.1%) and no potential very major errors.

**Table 2.** Colistin Performance of *A. baumannii* complex, Enterobacterales, and *P. aeruginosa* Read by ARIS HiQ/OptiRead

| | Tot | EA No. | EA % | Eval Tot | Eval EA No. | Eval EA % | CA Tot | CA % | No. R | No. I | maj | vmj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***A. baumannii* complex [≤2 (I), ≥4 (R)]** | | | | | | | | | | | | |
| **Clinical** | 60 | 57 | 95.0 | 59 | 56 | 94.9 | 59 | 98.3 | 2 | 58 | 0 | 1 |
| **Challenge** | 24 | 24 | 100 | 23 | 23 | 100 | 24 | 100 | 0 | 24 | 0 | 0 |
| **Total** | 84 | 81 | 96.4 | 82 | 79 | 96.3 | 83 | 98.8 | 2 | 82 | 0 | 1 |
| **Enterobacterales [≤2 (I), ≥4 (R)]** | | | | | | | | | | | | |
| **Clinical** | 360 | 350 | 97.2 | 314 | 304 | 96.8 | 355 | 98.6 | 13 | 347 | 2 | 3 |
| **Challenge** | 99 | 99 | 100 | 93 | 93 | 100 | 98 | 99.0 | 6 | 93 | 1 | 0 |
| **Total** | 459 | 449 | 97.8 | 407 | 397 | 97.5 | 453 | 98.7 | 19 | 440 | 3 | 3 |
| ***P. aeruginosa* [≤2 (I), ≥4 (R)]** | | | | | | | | | | | | |
| **Clinical** | 60 | 58 | 96.7 | 60 | 58 | 96.7 | 60 | 100 | 0 | 60 | 0 | 0 |
| **Challenge** | 28 | 26 | 92.9 | 28 | 26 | 92.9 | 27 | 96.4 | 0 | 28 | 1 | 0 |
| **Total** | 88 | 84 | 95.5 | 88 | 84 | 95.5 | 87 | 98.9 | 0 | 88 | 1 | 0 |

EA – Essential Agreement
CA – Category Agreement
R – Resistant
I – Intermediate
Eval – Evaluable MICs
maj – Major 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.

Vizion:

A total of 480 gram-negative clinical isolates comprised of *A. baumannii* complex (60 *A. baumannii* isolates), Enterobacterales (30 *C. freundii*, 45 *C. koseri*, 60 *E. cloacae* complex, 75 *E. coli*, 60 *K. aerogenes*, 25 *K. oxytoca*, 65 *K. pneumoniae* isolates), and *P. aeruginosa* (60 isolates), as well as 151 challenge isolates comprised of *A. baumannii* complex (24 *A. baumannii* isolates), Enterobacterales (6 *C. freundii*, 5 *C. koseri*, 20 *E. cloacae* complex, 25 *E. coli*, 12 *K. aerogenes*, 5 *K. oxytoca*, 26 *K. pneumoniae* isolates) and *P. aeruginosa* (28 isolates) were evaluated with the Vizion and the results are provided in **Table 3**.

This is a unique case where there is not a defined susceptible (S) interpretive category for colistin: therefore, the intermediate (I) category is treated as an S for performance analysis. In these situations where errors cannot be categorized as minor, adjustments are made to categorical errors by considering if the MIC values where the errors occur are in essential agreement with the reference method. Additionally, due to the lack of a susceptible interpretive category, all errors are considered potential errors.

For *A. baumannii* complex read using the Vizion, the combined clinical and challenge isolates (84 isolates) were acceptable at 95.2% and 98.8% for EA and CA, respectively. There were no potential major errors and one potential very major error (1/2 = 50%). Due to the lack of resistant isolates evaluated, the potential very major error is considered random, and 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 resistant isolates tested for A. baumannii.*

For Enterobacterales read using the Vizion, the combined clinical and challenge isolates (459 isolates) were acceptable at 97.8% and 99.1% for EA and CA, respectively. There was one potential major error (1/440 = 0.7%) and three potential very major errors (3/19 = 15.8%). All three potential major errors had an MIC value that were in essential agreement with the reference MIC value; therefore, the adjusted potential major error rate is 0% (0/440) . Two of the three potential very major errors had an MIC value that was in essential agreement with the reference MIC value; therefore, the adjusted potential very major error rate is 5.3% (1/19). When evaluating by individual species, the one potential very major error was due to a *C. freundii* isolate (1/2 = 50%). Due to the lack of resistant *C. freundii* isolates evaluated, the potential very major errors are considered random, and the following performance footnote will be added to the device labeling:

*The 1 potential very major errors observed were considered a random error due to the limited number of resistant isolates tested for C. freundii.*

For *P. aeruginosa* read using the Vizion, the combined clinical and challenge isolates (88 isolates) were acceptable at 95.5% and 98.9% for EA and CA, respectively. There was one potential major error (1/88 = 1.1%) and no potential very major errors.

**Table 3.** Colistin Performance of *A. baumannii* complex, Enterobacterales, and *P. aeruginosa* Read by Vizion

| | Tot | EA No. | EA % | Eval Tot | Eval EA No. | Eval EA % | CA Tot | CA % | No. R | No. I | maj | vmj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***A. baumannii* complex [≤2 (I), ≥4 (R)]** | | | | | | | | | | | | |
| **Clinical** | 60 | 57 | 95.0 | 59 | 56 | 94.9 | 59 | 98.3 | 2 | 58 | 0 | 1 |
| **Challenge** | 24 | 23 | 95.8 | 23 | 22 | 95.7 | 24 | 100 | 0 | 24 | 0 | 0 |
| **Total** | 84 | 80 | 95.2 | 82 | 78 | 95.1 | 83 | 98.8 | 2 | 82 | 0 | 1 |
| **Enterobacterales [≤2 (I), ≥4 (R)]** | | | | | | | | | | | | |
| **Clinical** | 360 | 354 | 98.3 | 311 | 305 | 98.1 | 357 | 99.2 | 13 | 347 | 1 | 2 |
| **Challenge** | 99 | 99 | 100 | 94 | 94 | 100 | 98 | 99.0 | 6 | 93 | 0 | 1 |
| **Total** | 459 | 453 | 98.7 | 405 | 399 | 98.5 | 455 | 99.1 | 19 | 440 | 1 | 3 |
| ***P. aeruginosa* [≤2 (I), ≥4 (R)]** | | | | | | | | | | | | |
| **Clinical** | 60 | 59 | 98.3 | 60 | 59 | 98.3 | 60 | 100 | 0 | 60 | 0 | 0 |
| **Challenge** | 28 | 25 | 89.3 | 28 | 25 | 89.3 | 27 | 96.4 | 0 | 28 | 1 | 0 |
| **Total** | 88 | 84 | 95.5 | 88 | 84 | 95.5 | 87 | 98.9 | 0 | 88 | 1 | 0 |

EA – Essential Agreement
CA – Category Agreement
R – Resistant
I – Intermediate
Eval – Evaluable MICs
maj – Major 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.

Since there is not a defined susceptible interpretive category for colistin, the following general statement was included in the device labeling:

> *There is not a defined susceptible interpretive category for colistin due to limited clinical efficacy. Please refer to appliable clinical and laboratory guidelines for testing and reporting considerations.*

Due to the insufficient number of resistant *A. baumannii, C. freundii, C. koseri, E. cloacae* complex, *E. coli*, and *P. aeruginosa* isolates evaluated, the following limitation was applied to colistin testing in the appropriate section of the device labeling that references other drugs:

> *The ability of the Sensititre system to detect resistance or non-susceptibility to antimicrobics as shown below is unknown because an insufficient number of resistant or non-susceptible strains were available at the time of comparative testing. If such a strain is observed, it should be submitted to a reference laboratory.*

**MIC Trending**

A trending analysis was conducted using the combined data (clinical and challenge) obtained for both the ARIS HiQ/OptiRead and the Vizion for *A. baumannii* complex, Enterobacterales, and *P. aeruginosa*. 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.

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 *A. baumannii* complex, species within Enterobacterales, and *P. aeruginosa* with colistin using the ARIS HiQ/OptiRead and Vizion are summarized in **Table 4**. A trend toward higher MIC values was observed for *C. freundii* and *P. aeruginosa* using both the ARIS/HiQ/OptiRead and Vizion when compared to the CLSI broth microdilution reference method.

To address the MIC trending, the sponsor included the following footnotes in the performance tables:

> For ARIS HiQ/OptiRead:
> *Colistin MIC values tended to be in exact agreement or at least one doubling dilution higher when testing C. freundii* and *P. aeruginosa the ARIS HiQ/OptiRead compared to the CLSI broth microdilution reference method.*

For Vizion:
*Colistin MIC values tended to be in exact agreement or at least one doubling dilution higher when testing C. freundii* and *P. aeruginosa the Vizion compared to the CLSI broth microdilution reference method.*

**Table 4.** Colistin Trending Analysis for *A. baumannii* complex, Enterobacterales, and *P. aeruginosa* with ARIS HiQ/OptiRead and Vizion

| Read Method | Organism | Total Evaluable for Trending | ≥ 1 Dilution Lower No. (%) | Exact No. (%) | ≥ 1 Dilution Higher No. (%) | Percent Difference (95% CI) | Trending Noted |
|---|---|---|---|---|---|---|---|
| ARIS HiQ/ OptiRead | *A. baumannii* | 82 | 20, (24.4) | 44 | 18, (22.0) | -2% (-15% to 10%) | No |
| | *C. freundii* | 35 | 4, (11.4) | 15 | 16, (45.7) | 34% (13% to 52%) | Yes, high |
| | *C. koseri* | 49 | 10, (20.4) | 22 | 17, (34.7) | 14% (-3% to 31%) | No |
| | *E. cloacae* complex | 77 | 14, (18.2) | 54 | 9, (11.7) | -6% (-18% to 5%) | No |
| | *E. coli* | 100 | 29, (29.0) | 59 | 12, (12.0) | -17% (-28% to -6%) | No |
| | *K. aerogenes* | 71 | 17, (23.9) | 46 | 5, (7.0) | -17% (-29% to -5%) | No |
| | *K. oxytoca* | 29 | 7, (24.1) | 16 | 6, (20.7) | -3% (-24% to 18%) | No |
| | *K. pneumoniae* | 91 | 22, (24.2) | 52 | 17, (18.7) | -5% (-17% to 6%) | No |
| | *P. aeruginosa* | 88 | 4, (4.6) | 29 | 55, (62.5) | 58% (46% to 68%) | Yes, high |
| Vizion | *A. baumannii* | 82 | 14, (17.1) | 39 | 29, (35.4) | 18% (5% to 31%) | No |
| | *C. freundii* | 35 | 4, (11.4) | 16 | 15, (42.9) | 31% (11% to 49%) | Yes, high |
| | *C. koseri* | 49 | 11, (22.5) | 21 | 17, (34.7) | 12% -6% to 29%) | No |
| | *E. cloacae* complex | 76 | 13, (17.1) | 58 | 5, (6.6) | -11% (-21% to 0%) | No |
| | *E. coli* | 100 | 32, (32.0) | 64 | 4, (4.0) | -28% (-38% to -18%) | No |
| | *K. aerogenes* | 71 | 21, (29.6) | 48 | 2, (2.8) | -27% (-38% to -15%) | No |
| | *K. oxytoca* | 29 | 10, (34.5) | 15 | 4, (12.8) | -21% (-41% to 2%) | No |
| | *K. pneumoniae* | 90 | 27, (30.0) | 52 | 11, (12.2) | -18% (-29% to -6%) | No |
| | *P. aeruginosa* | 88 | 0, (0.0) | 22 | 66, (75.0) | 75% (68% to 83%) | Yes, high |

**Testing/Reporting MICs for Species Not Listed in the Indications for Use**
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 species not listed in the Indications for Use:

*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 5**: FDA-Recognized Interpretive Criteria for Colistin

| | Minimum Inhibitory Concentrations (µg/mL)[a] | | |
|---|---|---|---|
| **Organisms** | **Susceptible*** | **Intermediate** | **Resistant** |
| *Acinetobacter baumannii* complex | - | ≤2 | ≥4 |
| Enterobacterales | - | ≤2 | ≥4 |
| *Pseudomonas aeruginosa* | - | ≤2 | ≥4 |

[a]According to FDA STIC Webpage, https://www.fda.gov/drugs/development-resources/fda-recognized-antimicrobial-susceptibility-test-interpretive-criteria

*There is not a defined susceptible interpretive category for colistin

**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 included a predetermined change control plan (PCCP) with a breakpoint change protocol that was reviewed and accepted by FDA in submission K231994 cleared on August 25, 2023. This 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 protocol outlined the specific procedures and acceptance criteria that Thermo Fisher Scientific intends to use to evaluate The Sensititre 18–24 hour MIC or Breakpoint Susceptibility System with Colistin when revised breakpoints for colistin 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 colistin 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.