

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

**A. 510(k) Number:**

K142338

**B. Purpose for Submission:**

Addition of Tedizolid to the Sensititre HP MIC susceptibility plate for testing *Streptococcus* species

**C. Measurand:**

Tedizolid in the dilution range 0.002- 4µg/mL

**D. Type of Test:**

Quantitative Antimicrobial Susceptibility Test (AST) growth based

**E. Applicant:**

ThermoFisher Scientific

**F. Proprietary and Established Names:**

Sensititre *Haemophilus/S. pneumoniae* (HP) MIC Susceptibility plate

**G. Regulatory Information:**

1. Regulation section:

866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

Class II

3. Product code:

JWY- Manual Antimicrobial Susceptibility Test System

LRG- Instrument for Auto Reader and Instrumentation of Overnight Susceptibility Systems

LTT- Panels, Test, Susceptibility, Antimicrobial

4. Panel:

Microbiology

**H. Intended Use:**

1. 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.

2. Indication(s) for use:

The Sensititre HP MIC Susceptibility plate is *in vitro* diagnostic product for clinical susceptibility testing of fastidious isolates.

This 510(k) is for the newly approved Tedizolid for the dilution range of 0.002- 4µg/mL to the Sensititre HP MIC Susceptibility plate for testing *Streptococcus* spp.

The approved primary “Indications for Use” and clinical significance for *Streptococcus* spp. is for the following species:

*Streptococcus pyogenes*  
*Streptococcus agalactiae*  
*Streptococcus anginosus*

3. Special conditions for use statement(s):

For prescription use only

The ability of the Sensititre system to detect non-susceptible isolates to Tedizolid is unknown because non-susceptible isolates were not available at the time of the comparative testing. If such isolates are observed, they should be submitted to a reference lab.

4. Special instrument requirements:

The Sensititre Autoinoculator/AIM  
The Sensititre OptiRead System  
The Sensititre Vizion

**I. Device Description:**

The Sensititre 20-24 hour *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC Susceptibility plate is a micro-version of the classic broth dilution method and can provide

both qualitative and quantitative susceptibility test results in a dried microtitre plate format. Each micro-broth dilution plate is dosed with antimicrobial agents as specific concentrations and then dried.

The organism to be tested must be in pure culture and identified as *Streptococcus* spp. The medium for testing *Streptococcus* spp. is Sensititre Mueller-Hinton broth with 2-5% lysed horse blood with a final organism density of  $5 \times 10^5$  CFU/mL. A standardized suspension is prepared from colonies in pure growth and inoculated into the microtitre plate. After 20-24 hours of incubation, the microtitre plate is examined for growth to determine the MIC using either the Sensititre OptiRead or manually using the Vizion.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

MicroScan<sup>®</sup> MICroSTREP *plus* Panel

2. Predicate 510(k) number(s):

K021184

3. Comparison with predicate:

Table 1: Comparison with the Predicate Devices

Similarities		
Item	Device Sensititre <i>Haemophilus/Streptococcus pneumoniae</i> (HP) MIC Susceptibility Plates	Predicate MICroSTREP Plus Panel K021184
Intended Use	The Sensititre HP MIC Susceptibility is <i>in vitro</i> diagnostic product for clinical susceptibility testing	To determine bacterial antimicrobial agent susceptibility
Test Panel	The bacterial suspension in the appropriate broth is used to rehydrate the plate	Same
Test Organism	<i>Streptococcus</i> spp. ( <i>S. pyogenes</i> , <i>S. agalactiae</i> , <i>S. anginosus</i> )	<i>Streptococci</i> spp. other than <i>S. pneumoniae</i>
Incubation	20- 24 hours	Same
Results reported	Report results as Minimum Inhibitory Concentration (MIC) and interpretative criteria (S, NS)	MIC (SIR)

Differences		
Item	Device	Predicate
Antibiotic	Tedizolid	Clindamycin
Reading Method	Automated method by detection of fluorescence. Manual method by visual read of growth	Organism turbidity growth visually or by MicroScan instrumentation

**K. Standard/Guidance Document Referenced (if applicable):**

1. The FDA guidance document: Guidance for Industry and FDA Staff- Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems
2. CLSI M100-S24: Performance Standards for Antimicrobial Susceptibility Testing; Twenty-fourth Informational Supplement (QC parameters only)
3. CLSI M7-A9: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard- Ninth Edition

**L. Test Principle:**

The Sensititre 20-24 hour *Haemophilus influenzae*/*Streptococcus pneumoniae* MIC Susceptibility plates are multi-well plastic microtitre plates that contain doubling dilution of antibacterial agents. Each plate includes antimicrobial agents at appropriate dilutions. Results can be read manually by visual reading of growth or automatically on an autoreader via fluorescence.

The Sensititre AutoReader /OptiRead System utilize fluorescence technology to read the micro-broth 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 non-fluorescent (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 the 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 pneumoniae* and *Streptococcus* spp. plates can either be read manually or automatically on the AutoReader /ARIS/OptiRead. *Haemophilus influenzae* can only be read manually on the Vizion or manual viewer.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

A reproducibility study was conducted at three study sites using 25 organisms consisting of *S. pyogenes*, *S. agalactiae*, and *S. dysgalactiae*. The Sensititre plates were inoculated by the Sensititre Autoinoculator/AIM. The organisms were tested one time at each of three sites for each reading method (Vizion for manual, OptiRead for automated read). The mode MIC value was determined and the reproducibility was calculated based on MICs falling within  $\pm 1$  dilution of the mode MIC value. The testing resulted in overall reproducibility results of greater than 95% for both Manual and Automated read methods. The results were acceptable.

b. *Linearity/assay reportable range:*

Not Applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

The organism recommended by both the FDA (CDER) and the CLSI, *S. pneumoniae* ATCC 49619 was tested against Tedizolid. Quality control was performed at all sites using the Sensititre Autoinoculator/AIM for inoculation, read by the manual (i.e. Vizion) and the automated (i.e. OptiRead) read methods. Table 2 below represents the frequency of the results and all results were in acceptable range.

Table 2: Tedizolid QC Table

ORGANISM	Conc. (µg/mL)	Reference	Sensititre- Read Method	
			OptiRead	Manual (Vizion)
<i>S. pneumoniae</i>	0.06	0	0	0
ATCC 49619	0.12	48	53	39
Expected Range	0.25	10	6	20
0.12- 0.5 µg/mL	0.5	2	1	1
	1	0	0	0

The inoculum density of the quality control organisms was determined each day of testing. A total of 46 inoculum density checks were performed; the average colony counts of the QC strain were within the recommended range.

d. *Detection limit:*

Not Applicable

e. *Analytical specificity:*

Not Applicable

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The CLSI recommended broth microdilution reference panel was prepared according to the CLSI recommendation. Clinical testing was performed at three sites on a total of 225 *Streptococcus* isolates. The isolates were comprised of 90 *Streptococcus pyogenes*, 90 *Streptococcus agalactiae*, and 45 *Streptococcus anginosus* at three sites and AIM auto-inoculator was used as the inoculation method. All clinical isolates were fresh and all grew. The challenge set included 25 *S. pyogenes*, 25 *S. agalactiae*, and nine *S. anginosus*; one challenge isolate did not grow and the overall growth rate was 99.6% (284/285) for both manual (VIZION) and automated (Optiread) reads. The performance of claimed *Streptococcus* spp. (i.e., *S. agalactiae*, *S. pyogenes*, and *S. anginosus*) was demonstrated in Tables 3-5 below:

Table 3: Performance summary of *Streptococcus* spp. Manual (VIZION)

Tedizolid	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	NS
<b><i>S. agalactiae</i> (<math>\leq 0.5, -, -</math>)</b>									
Clinical	90	90	100	90	90	100	90	100	0
Challenge	25	25	100	25	25	100	25	100	0
Total	<b>115</b>	<b>115</b>	<b>100</b>	<b>115</b>	<b>115</b>	<b>100</b>	<b>115</b>	<b>100</b>	<b>0</b>
<b><i>S. pyogenes</i> (<math>\leq 0.5, -, -</math>)</b>									
Clinical	90	90	100	90	90	100	90	100	0
Challenge	25	25	100	25	25	100	25	100	0
Total	<b>115</b>	<b>115</b>	<b>100</b>	<b>115</b>	<b>115</b>	<b>100</b>	<b>115</b>	<b>100</b>	<b>0</b>
<b><i>S. anginosus</i> (<math>\leq 0.25, -, -</math>)</b>									
Clinical	45	45	100	45	45	100	45	100	0
Challenge	9	9	100	9	9	100	9	100	0
Total	<b>54</b>	<b>54</b>	<b>100</b>	<b>54</b>	<b>54</b>	<b>100</b>	<b>54</b>	<b>100</b>	<b>0</b>

EA - Essential Agreement

CA - Category Agreement

NS- Not susceptible

EA is when there is agreement between the reference method and the Sensititre® panel within plus or minus one serial two-fold dilution of antibiotic. Category agreement (CA) is when the Sensititre panel result interpretation agrees exactly with the reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the Sensititre® and the reference and have on-scale EA. 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) Systems; Guidance for Industry and FDA".

Table 4: Performance summary of *Streptococcus* spp. Automated (OptiRead)

Tedizolid	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	NS
<b><i>S. agalactiae</i> (<math>\leq 0.5, -, -</math>)</b>									
Clinical	90	90	100	90	90	100	90	100	0
Challenge	25	25	100	25	25	100	25	100	0
<b>Total</b>	<b>115</b>	<b>115</b>	<b>100</b>	<b>115</b>	<b>115</b>	<b>100</b>	<b>115</b>	<b>100</b>	<b>0</b>
<b><i>S. pyogenes</i> (<math>\leq 0.5, -, -</math>)</b>									
Clinical	90	89	98.9	90	89	98.9	90	100	0
Challenge	25	25	100	25	25	100	25	100	0
<b>Total</b>	<b>115</b>	<b>114</b>	<b>99.1</b>	<b>115</b>	<b>114</b>	<b>99.1</b>	<b>115</b>	<b>100</b>	<b>0</b>
<b><i>S. anginosus</i> (<math>\leq 0.25, -, -</math>)</b>									
Clinical	45	43	95.6	45	43	95.6	44	97.8	0
Challenge	9	9	100	9	9	100	9	100	0
<b>Total</b>	<b>54</b>	<b>52</b>	<b>96.3</b>	<b>54</b>	<b>52</b>	<b>96.3</b>	<b>53</b>	<b>98.1</b>	<b>0</b>

Table 5: Overall Performance Summary of *Streptococcus* spp (Clinical+ Challenge)

Tedizolid	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	NS
Manual (Vizion)	284	284	100	284	284	100	284	100	0
Automated (OptiRead)	284	281	98.9	284	281	98.9	283	99.6	0

Table 5 above demonstrated acceptable performance (EA and CA) for both manual and automated reads when comparing to the reference method as described in the FDA guidance document, "Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA".

Using the data provided by the sponsor in the diagonal table format as recommended in the AST Guidance, an analysis was conducted to evaluate MIC values trending in Tables 6 and 7 below:

Table 6: Trending (Clinical+ challenge) by manual read (VIZION)

Tedizolid	Total	$\geq 1$ dil. lower	Exact	$\geq 1$ dil. higher
<i>S. agalactiae</i>	115	13.0% (15/115)	44.3% (51/115)	42.6% (49/115)
<i>S. pyogenes</i>	115	17.4% (20/115)	47.8% (55/115)	34.8% (40/115)
<i>S. anginosus</i>	54	9.3% (5/54)	38.9% (21/54)	51.9% (28/54)
<b>Overall</b>	<b>284</b>	<b>14.1% (40/284)</b>	<b>44.7% (127/284)</b>	<b>41.2% (117/284)</b>

Table 7: Trending (Clinical+ challenge) by automated read (OptiRead)

Tedizolid	Total	≥1 dil. lower	Exact	≥1 dil. higher
<i>S. agalactiae</i>	115	13.9% (16/115)	47.8% (55/115)	38.3% (44/115)
<i>S. pyogenes</i>	115	8.7% (10/115)	57.4% (66/115)	33.9% (39/115)
<i>S. anginosus</i>	54	5.6% (3/54)	53.7% (29/54)	40.7% (22/54)
Overall	284	10.2% (29/284)	52.8% (150/284)	37.0% (105/284)

The data from Tables 6 and 7 demonstrated trending of one doubling dilution higher 41.2% (117/284) on manual read and 37.0% (105/284) on automated read when compared to the reference MIC values. The “exact” reading compared to the reference was 44.7% (127/284) for the manual and 52.8% (150/284) for the automated read. For manual read, the “exact” and one doubling dilution higher was alike at 44.7% and 41.2% respectively.

There were eight *Streptococcus agalactiae* and two *Streptococcus pyogenes* tested at the Tedizolid reference susceptible breakpoint of 0.5µg/mL. The Sensititre results tended to be one dilution lower (70%, 7/10) when compared to the reference on both the manual and automated read.

There were ten *Streptococcus anginosus* tested at the reference susceptible breakpoint of 0.25µg/mL; the Sensititre tended to be one dilution lower (40%, 4/10) by the manual read and (30%, 3/10) by the automated read when compared to the reference MIC values.

The following footnote was added to the “Interpretation of Results” section of the Technical Product Information:

Sensititre Tedizolid MIC values for *Streptococcus agalactiae*, *Streptococcus pyogenes* and *Streptococcus anginosus* tended to be one doubling dilution higher than the reference MIC values. At the reference Tedizolid susceptible breakpoint of 0.5µg/mL (*S. agalactiae*, *S. pyogenes*) or 0.25µg/mL (*S. anginosus*), Sensititre MIC values tended to be one doubling dilution lower.

b. *Matrix comparison:*

Not Applicable

3. Clinical studies:

a. *Clinical Sensitivity:*

Not Applicable

b. *Clinical specificity:*

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

The FDA interpretative criteria were used to evaluate all performance data:

Table 8: Tedizolid FDA interpretative criteria

Organism	Susceptibility Interpretive Criteria (MIC in µg/mL)		
	S	I	R
<i>Streptococcus agalactiae</i> and <i>Streptococcus pyogenes</i>	≤0.5	-	-
<i>Streptococcus anginosus</i> group (including <i>S. anginosus</i> , <i>S.</i> <i>intermedius</i> , and <i>S. constellatus</i> )	≤0.25	-	-

**N. Proposed Labeling:**

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

**O. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.