

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

A. 510(k) Number:

k142151

B. Purpose for Submission:

Addition of Tedizolid to the Sensititre 18-24 hour susceptibility plates

C. Measurand:

Tedizolid 0.03- 4µg/mL

D. Type of Test:

Quantitative Antimicrobial Susceptibility Test (AST) growth based

E. Applicant:

ThermoFisher Scientific

F. Proprietary and Established Names:

Sensititre 18-24 hour Susceptibility plates

G. Regulatory Information:

1. Regulation section:

21 CFR 866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

Class II

3. Product code:

JWY- Manual Antimicrobial Test

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

LTT- Panels, Test, Susceptibility, Antimicrobial

4. Panel:

83. Microbiology

H. Intended Use:

1. Intended use(s):

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

2. 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 the newly approved Tedizolid in the dilution range of 0.03- 4µg/mL for testing non-fastidious gram positive organisms on the Sensititre 18-24hour MIC panel.

The approved primary “Indications for Use” and clinical significance for non-fastidious gram positive isolates:

Staphylococcus aureus (including methicillin-resistant [MRSA] and methicillin-susceptible [MSSA] isolates)

Enterococcus faecalis

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Sensititre OptiRead System for automatic read

Sensititre VIZION for manual visual read

The ability of the Sensititre system to detect non-susceptible or resistant isolates to tedizolid is unknown because neither non-susceptible nor resistant isolates were available at the time of the comparative testing. If such isolates are observed, they should be submitted to a reference lab.

I. Device Description:

The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System 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 at specific concentrations and then dried.

The organism to be tested must be in pure culture and identified as Gram negative. A standardized suspension is prepared from colonies in pure growth and inoculated into the

microtitre plate. After the indicated 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 Dried Gram-Negative and Gram-Positive MIC Combo Panels

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

k010159

3. Comparison with predicate:

Table 1: Comparison with the Predicate Device

Similarities		
Item	Device	Predicate
	Sensititre 18-24 hour Susceptibility plates <i>S. aureus</i> , <i>E. faecalis</i> Tedizolid	MicroScan [®] Dried Gram-Negative and Gram-Positive MIC Combo Panels K010159
Intended Use	The Sensititre MIC or Breakpoint Susceptibility system is an <i>in vitro</i> diagnostic product for clinical susceptibility testing	Same
Test organism	Non-fastidious gram positive isolates from culture	Same
Results reported	Report results as Minimum Inhibitory Concentration (MIC) and interpretative criteria (SIR)	Same
Type of Test	Automatic or Manual	Same

Differences		
Item	Device	Predicate
Incubation	18- 24 hours	16- 20 hours
Antibiotic	Tedizolid	Gatifloxacin
Reading method	Automated OptiRead by detection of fluorescence. Manual method by visual read of growth	Organism growth read visually or by MicroScan instrumentation

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

1. Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA5
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 18-24 MIC Susceptibility System test panels 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 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 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.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility study was performed using 25 strains of MSSA, MRSA and *Enterococcus faecalis*. 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 ± 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):*

Organisms recommended by both the FDA (CDER) and the CLSI, namely *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212 were 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. The following table represents the frequency of the results and all results were in acceptable range.

Table 2: Tedizolid QC results by Sensititre auto and manual reads

ORGANISM	Conc. (µg/mL)	Reference	Sensititre Auto Read (OptiRead)	Sensititre Manual (Vizion)
<i>S. aureus</i> ATCC29213 Expected Range 0.25- 1µg/mL	0.12			
	0.25	41	45	46
	0.5	17	15	12
	1	2		2
	2			
<i>E. faecalis</i> ATCC29212 Expected Range 0.25- 1µg/mL	0.12			
	0.25	38	58	30
	0.5	21	2	30
	1	1		
	2			

The inoculum density of the quality control organisms was determined each day of testing. A total of 97 inoculum density checks were performed; the average colony counts of each QC strain at each site 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 plate was prepared according to CLSI recommendation. Clinical testing was performed on 330 *Staphylococcus aureus*, 60 *Enterococcus faecalis* at three sites and Sensititre AIM autoinoculator was used as the inoculation method. For *Staphylococcus aureus* clinical isolates, there were 165 each for MRSA and MSSA. They were all fresh isolates. The no growth/insufficient fluorescent signal rate was 0.52% (2/390) in the automated read method; they all grew in the manual VIZION read method. The challenge set included 75 *Staphylococcus aureus* and 17 *Enterococcus faecalis*.

The performance of *Staphylococcus aureus* is shown in the tables below.

Table 3: Performance summary of *Staphylococcus aureus* - Manual Read (Vizion)

Tedizolid	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#R	min	maj	vmj
MRSA ($\leq 0.5, 1, \geq 2$)												
Clinical	165	165	100	165	165	100	165	100	0	0	0	0
Challenge	38	38	100	38	38	100	38	100	0	0	0	0
Total	203	203	100	203	203	100	203	100	0	0	0	0
MSSA ($\leq 0.5, 1, \geq 2$)												
Clinical	165	165	100	165	165	100	164	99.4	0	1	0	0
Challenge	37	37	100	37	37	100	37	100	0	0	0	0
Total	202	202	100	202	202	100	201	99.5	0	1	0	0
<i>S. aureus</i>	405	405	100	405	405	100	404	99.8	0	1	0	0

EA - Essential Agreement

maj – major discrepancies

CA - Category Agreement

vmj- very major discrepancies

R- resistant isolates

min- minor discrepancies

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 *Staphylococcus aureus* - Automated Read (OptiRead)

Tedizolid	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#R	min	maj	vmj
MRSA ($\leq 0.5, 1, \geq 2$)												
Clinical	165	164	99.4	165	164	99.4	165	100	0	0	0	0
Challenge	38	38	100	38	38	100	38	100	0	0	0	0
Total	203	202	99.5	203	202	99.5	203	100	0	0	0	0
MSSA ($\leq 0.5, 1, \geq 2$)												
Clinical	163	163	100	163	163	100	162	99.4	0	1	0	0
Challenge	37	37	100	37	37	100	37	100	0	0	0	0
Total	200	200	100	200	200	100	199	99.5	0	1	0	0
<i>S. aureus</i>	403	402	99.8	403	402	99.8	402	99.8	0	1	0	0

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".

Using the data provided by the sponsor in the diagonal table format recommended in the AST Guidance, an analysis was conducted to check for trending in MIC values.

MRSA

A trending was observed at the susceptible breakpoint (BP) of 0.5µg/mL on the automated reading method. There were a total of 26 isolates at this susceptible BP by the automated read, and 20 were one to two doubling dilutions lower than the reference method, a rate of 76.9% (20/26). Nineteen were within EA. Using the manual read with VIZION, there were eight (8) results that were one dilution lower than results obtained with the reference method, a rate of 29.6% (8/27). They all were within EA. No isolates were at the non-susceptible (i.e. intermediate or resistant) range in the comparative study.

MSSA

At the BP of 0.5µg/mL, there were 23 results (50%, 23/46) that were one doubling dilution lower than results obtained with the automated reading method and seven results (13.7%, 7/51) that were lower with the manual VIZION method. There was one result in the intermediate range that was also one doubling dilution lower. There were no results in the resistant range.

At the susceptible (0.5µg/mL) BP, the following is footnoted in the “Performance Characteristics of Sensititre Panels Read at 18- 24 hours on Optiread” section of the Addendum to Technical Product Information:

“*Staphylococcus aureus* (MRSA and MSSA) MIC values tended to be one doubling dilution lower at the susceptible (0.5µg/mL) breakpoints”

The performance of *Enterococcus faecalis* is shown below.

Table 5: Performance summary of *Enterococcus faecalis* (≤0.5,--, --) Manual (Vizion)

Tedizolid	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#NS
Clinical	60	60	100	60	60	100	60	100	0
Challenge	17	17	100	17	17	100	17	100	0
Total	77	77	100	77	77	100	77	100	0

EA - Essential Agreement

CA - Category Agreement

NS- Not susceptible

Table 6: Performance summary of *Enterococcus faecalis* (≤0.5,--, --) automated (Optiread)

Tedizolid	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#NS
Clinical	60	59	98.3	60	59	98.3	60	100	0
Challenge	17	17	100	17	17	100	17	100	0
Total	77	76	98.7	77	76	98.7	77	100	0

Table 7: Trending comparison between VIZON and OptiRead for *Enterococcus faecalis* (clinical +challenge)

Tedizolid	Total	≥1 dil. lower	Exact	≥1 dil. higher
Manual (Vizion)	77	3.9% (3/77)	63.6% (49/77)	32.5% (25/77)
Automated (Optiread)	77	37.7% (29/77)	55.8% (43/77)	6.5% (5/77)

Enterococcus faecalis

The clinical data demonstrated a trending of one dilution higher 32.5% (25/77) on the manual read. However, it was one doubling dilution lower 37.7% (29/77) on the automated read. The “exact” reading compared to the reference was similar, 63.6% (49/77) for the manual and 55.8% (43/77) for the automated.

There were a total of ten isolates with results at the BP of 0.5µg/mL. There was one result that was one doubling lower than the reference on the manual read. However, six results (60%, 6/10) were one doubling lower in the automated read. In general, results were one doubling dilution lower on the automated read.

The following is footnoted in “Performance Characteristics of Sensititre Panels Read at 18-24 hours” section of the Addendum to Technical Product Information:

“Sensititre Tedizolid MIC values for *Enterococcus faecalis* tended to be one doubling dilution higher than the reference MIC values on the manual VIZION read.”

“On the Optiread read, Sensititre Tedizolid MIC values tended to be one doubling dilution lower than the reference MIC values for *Enterococcus faecalis*.”

Table 8: Performance of *Staphylococcus aureus* and *Enterococcus faecalis* combined

Tedizolid	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#R	min	maj	vmj
Manual												
<i>S. aureus</i>	405	405	100	405	405	100	404	99.8	0	1	0	0
<i>E. faecalis</i>	77	77	100	77	77	100	77	100	0	NA	NA	NA
Total	482	482	100	482	482	100	481	99.8	0	1	0	0
Automated												
<i>S. aureus</i>	403	402	99.8	403	402	99.8	402	99.8	0	1	0	0
<i>E. faecalis</i>	77	76	98.7	77	76	98.7	77	100	0	NA	NA	NA
Total	480	478	99.6	480	478	99.6	479	99.8	0	1	0	0

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:

Tedizolid Interpretative Criteria:

S. aureus (MRSA, MSSA) ≤ 0.5 (S), 1(I), ≥ 2 (R)

E. faecalis ≤ 0.5 (S), --, --

The FDA interpretative criteria, as listed above, were used to evaluate all performance data.

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.