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

A. 510(k) Number:

K141000

B. Purpose for Submission:

To obtain a substantial equivalence determination by demonstrating acceptable performance of the Sensititre 18-24 hours MIC or Breakpoint Susceptibility Test System with the revised CLSI and FDA interpretive criteria (breakpoints) for Telavancin and non-fastidious Gram positive organisms, utilizing the 0.002% Polysorbate 80 for the reference method.

C. Measurand:

Telavancin in the dilution range of 0.0005-2 μg/mL

D. Type of Test:

Quantitative Antimicrobial Susceptibility Test (AST), growth based fluorescence.

E. Applicant:

Trek Diagnostic Systems, Inc.,

F. Proprietary and Established Names:

Sensititre Susceptibility Plates

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.1640 Antimicrobial Test Powder

2. Classification:

   Class II

3. Product code(s):

JWY – Manual Antimicrobial Susceptibility Test Systems

LRG – Instrument for Auto Reader & Interpretation of overnight suscept systems

LTT – Panels, Test, Susceptibility, Antimicrobial

LTW – Susceptibility Test Cards, 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 breakpoints for Telavancin, utilizing the 0.002% Polysorbate 80 for the reference method in the dilution range of 0.0005-2 µg/mL to the Sensititre® 18-24 hour MIC panel for testing non-fastidious Gram positive isolates.

The approved primary "Indications for Use" and clinical significance for non-fastidious Gram positive isolates:

Staphylococcus aureus (including methicillin-resistant isolates)
Enterococcus faecalis

3. Special conditions for use statement(s):

Prescription use only.

4. Special instrument requirements:

The Sensititre Autoinoculator, the Sensititre Optiread, the Sensititre Vizion and the Sensititre Nephelometer.

I. Device Description:

Each plate is dosed with antimicrobial agents at appropriate dilutions. Results can be read manually by visual reading of growth or automatically on an ARIS® / Autoreader® / OptiRead® using fluorescence. The Sensititre Autoreader/OptiRead® system utilizes fluorescence technology. 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 fluorophore is then said to be quenched. The plates are prepared with the substrate already added to the plate. Enzymatic action of the bacterial surface enzymes on the specific substrates cleaves this bond releasing the fluorophore, which is now capable of fluorescence. The amount of fluorescence detected is directly related to the activity of the bacterial surface enzymes and, therefore, to the bacterial growth.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Sensititre® HP MIC Susceptibility Plate Telavancin 0.001-2µg/mL and The Sensititre® 18-24 hour MIC Susceptibility System Susceptibility Test Panel for Telavancin 0.03-16 µg/mL

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

   k093865

3. Comparison with predicate:

Table 1. Similarities and Differences of the Sensititre 18-24 hour and the Predicate

Similarities		
Item	Device	Predicate
Intended Use	The Sensititre MIC or Breakpoint Susceptibility system is an *in vitro* diagnostic product for clinical susceptibility testing	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
Instrumentation	Each plate is dosed with	Same

Similarities		
Item	Device	Predicate
	antimicrobial agents at appropriate dilutions and inoculated with standardized organism suspension. Results can be read automatically on ARIS®/Autoreader®/OptiRead® using fluorescence or manually on the Vizion or a manual viewer, by visual reading of growth.	
Reading method	Fluorescence	Same

Differences		
Item	Device	Predicate
Antibiotic/Assay	Telavancin, New Breakpoints: *S. aureus* ≤0.12 *E. faecalis* ≤0.25	Telavancin, Old Breakpoints K093865: *S. aureus* ≤1 *E. faecalis* ≤1 *S. pyogenes* ≤0.12 S. agalactiae ≤0.12 *S. anginosus* group ≤0.12
Product Name	Sensititre™ 18-24 hour Susceptibility System	Sensititre™ 18-24 hour Susceptibility System Sensititre Haemophilus/Streptococcus pneumonia (HP) MIC Susceptibility Plates
Test Organism	Non-fastidious Gram positive isolates	Non-fastidious Gram positive isolates & Streptococcus spp.
Incubation	18-24 hours for non-fastidious	18-24 hours for non-fastidious and 20-24 hours for fastidious
Reference Method	CLSI (with 0.002% Polysorbate 80)	CLSI (without 0.002% Polysorbate 80)
Quality Control organisms and ranges for Telavancin	*S. aureus* ATCC 29213 (0.03-0.12 µg/mL) *E. faecalis* ATCC 29212 (0.03-0.12 µg/mL)	*Streptococcus pneumoniae* ATCC 49619 (0.004-0.006 µg/mL) *S. aureus ATCC 29213* (0.12-1 µg/mL)*E. faecalis* ATCC 29212 (0.12-0.5 µg/mL)
Telavancin Dilution range	0.0005-2 µg/mL	0.001 to 16 µg/mL The MIC testing and reporting result range is 0.001-2 µg/mL for *Streptococcus* spp. and 0.03-16 µg/mL for other Gram positive isolates.

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

1. Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA
http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucmO71462.pdf

2. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, Approved Standard-9th Edition, Document M07-A9

3. Performance Standards for Antimicrobial Susceptibility Testing - 24th Informational Supplement, Ml00-S24.

L. Test Principle:

Sensititre susceptibility plates are multi-well plastic microtiter plates that contain doubling dilutions of antibacterial agents. Each plate is dosed with antimicrobial agents at appropriate dilutions. Results can be read manually by visual reading of growth or automatically on an Autoreader® using fluorescence. The Sensititre Autoreader system utilizes fluorescence technology which 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 substrate can be added to the inoculum broth and dispensed into the test plates at the same time as the test organism or the plates can be prepared with the substrate already added to the plate. The nonfluorescent substrate is prepared by conjugating a fluorescent compound to the specific enzyme substrates with a bond, which prevents fluorescence (i.e. the fluorophore is quenched in this state). Enzymatic action of the bacterial surface enzymes on the specific substrates cleaves this bond releasing the fluorophore which is now capable of fluorescence. The amount of fluorescence detected is directly related to the activity of the bacterial surface enzymes and, therefore, to bacterial growth.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

A reproducibility study was conducted at three study sites. Twenty five Gram positive isolates (13 *S. aureus, 12 E. faecalis*) were tested at each site on the Sensititre18-24 hour Susceptibility System only.

Results were read by the AutoReader (using the Optiread) and manually (using the Vizion).

Reproducibility was calculated as the percent of results for the combined sites which were within +/- one doubling dilution of the mode MIC value for all sites.

For the sake of reproducibility calculations, off-scale values are handled in two ways; "best case" and "worst case" scenarios. Best case calculation for reproducibility assumes the off-scale result is within one well from the mode MIC value. Worst case calculation for reproducibility assuming the off-scale result is greater than one well from the mode MIC value. There were no off-scale results in this study. So, only one value for overall reproducibility is reported for each reading method.

For manual read by the Vizion the overall reproducibility was 100% for both *S. aureus* and *E. faecalis*.

For the OptiRead the overall reproducibility was 100% for both *S. aureus* and *E. faecalis.*

b. Linearity/assay reportable range:

Not applicable

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

The FDA and CLSI recommended QC isolates were tested on every test occasion with the reference method and the Sensititre. The reference method QC results were in range for every day tested. The Sensititre Susceptibility plate was tested a sufficient number of times to demonstrate that the system can produce QC results in the recommended range.

Quality Control was performed at all sites during the studies using both the OptiRead and the manual reading method (Vizion). The mode of the MIC obtained by the Sensititre manual read was similar to that obtained by the Optiread. Summary of the results are shown in the table 2 below.

Table 2. Summary of Quality Control Results for Telavancin for non-fastidious organisms

ORGANISMS	Telavancin (µg/mL)	Reference	AutoReader	Manual Read
***S. aureus* ATCC 29213** **0.03-0.12µg/mL**	0.015			
	0.03	26	0	3
	0.06	34	58	57
	0.12	0	2	0
	0.25			

ORGANISMS	Telavancin (µg/mL)	Reference	AutoReader	Manual Read
E. faecalis **ATCC 29212** **0.03-0.12µg/mL**	0.015			
	0.03	13	0	1
	0.06	44	31	31
	0.12	3	29	28
	0.25			

Quality Control results for the Sensititre Susceptibility System using either reading methods demonstrated that the system could produce the expected quality control results.

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:

Performance was established through a clinical study which was conducted at three sites. Studies have been conducted with the Sensititre dried susceptibility plates containing Telavancin to test susceptibility Gram positive isolates (Sensititre 18-24 hour susceptibility plate). The CLSI microdilution reference methods with 0.002% Polysorbate 80 containing the same antimicrobial in the same dilutions were used for a comparison and evaluation of performance.

The inoculum was prepared using the Sensititre Nephelometer which was calibrated at the start of each test. Plates were inoculated and incubated at 35^{o} C. The reading was done on the Optiread and manually using the Vizion at 18-24 hours.

Clinical testing was performed on 313 Gram positive isolates (179 *S. aureus* and 134 *Enterococcus faecalis*). All were freshly collected clinical isolates. In addition, testing was performed on 75 Gram positive stock challenge isolates (40 *S. aureus* and 35 *Enterococcus faecalis*)

The clinical study included 89 Methicillin Susceptible *Staphylococcus aureus* (MSSA) and 90 Methicillin Resistant *Staphylococcus aure*us (MRSA); the challenge set was comprised of 20 MSSA and 20 MRSA resulting 109 MSSA and 110 MRSA.

The performance evaluations are shown in tables 3 and 4 below.

Table 3. Trek Telavancin Summary Table for non-fastidious organisms (AutoReader)

	EA TOT	EA N	EA%	Eval EA Tot	Eval EAN	Eval EA%	CA N	CA%	No. NS	CA Err # (%)
MSSA										
Clinical	89	88	98.9	89	88	98.9	89	100	0	0 (0)
Challenge	20	20	100	20	20	100	20	100	0	0 (0)
MRSA										
Clinical	90	89	98.9	89	89	100	90	100	2	0 (0)
Challenge	20	20	100	20	20	100	20	100	0	0 (0)
***S. aureus* (MRSA + MSSA)**										
Clinical	179	177	98.9	178	177	99.4	179	100	2	0 (0)
Challenge	40	40	100	40	40	100	40	100	0	0 (0)
Combined	219	217	99.1	218	217	99.5	219	100	2	0 (0)
Enterococcus faecalis										
Clinical	134	134	100	126	126	100	134	100	14	0 (0)
Challenge	35	35	100	31	31	100	35	100	6	0 (0)
Combined	169	169	100	157	157	100	169	100	20	0 (0)

Table 4. Trek Telavancin Summary Table for non-fastidious organisms (Manual Read Method)

	EA TOT	EA N	EA%	Eval EA Tot	Eval EA N	Eval EA%	CA N	CA%	No. NS	CA Err # (%)
MSSA										
Clinical	89	89	100	89	89	100	89	100	0	0 (0)
Challenge	20	20	100	20	20	100	20	100	0	0 (0)
MRSA										
Clinical	90	90	100	90	90	100	90	100	2	0 (0)
Challenge	20	20	100	20	20	100	20	100	0	0 (0)
***S. aureus* (MRSA + MSSA)**										
Clinical	179	179	100	179	179	100	179	100	2	0 (0)
Challenge	40	40	100	40	40	100	40	100	0	0 (0)
Combined	219	219	100	219	219	100	219	100	2	0 (0)
Enterococcus faecalis										
Clinical	134	132	98.5	125	123	98.4	134	100	14	0 (0)
Challenge	35	35	100	31	31	100	35	100	6	0 (0)
Combined	169	167	98.8	15	154	98.7	169	100	20	0 (0)

EA-Essential Agreement CA-Category Agreement NS-not susceptible

No minor, major or very major errors were calculated because there are no intermediate or resistance interpretative criteria for Telavancin

Essential agreement (EA) is when the Sensititre panels agree with the reference test panel results exactly or within one doubling dilution of the reference method. 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 I1 Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA".

Auto-read results were very similar to the manual readings. Currently, there are no intermediate or resistance interpretive criteria for Telavancin. Two *S. aureus* and 20 *E. faecalis* were noted to have MIC outside the susceptibility category. There were no minor, major or very major errors using both the Manual Read and the AutoRead methods.

Table 5. Performance of Sensititre Panels read manually on the Vizion and on the Optiread

ORGANISMS	**Number of isolates tested**	**% EA**	**% CA**
Optiread			
S. aureus	219	99.1	100
E. faecalis	169	100	100
Manual Read Method-Vizion			
S. aureus	219	100	100
E. faecalis	169	98.8	100

EA and CA for all organisms were greater than 90%.

Using the data provided by the sponsor in the diagonal table format recommended in the AST Guidance, an analysis was conducted to check for any trending in MIC values. Of 219 clinical and challenge *S. aureus* isolates tested, 219 yielded on-scale MIC values. The data demonstrated that there was a significant upward trend in the MIC of the Sensititre® 18-24 hour Susceptibility System compared to the reference method. Analysis of this data demonstrated that 27.8% (61/219) of the Sensititre were equal to the reference method, 71.2% (156/219) of the Sensititre were higher by one doubling dilution. There was only 0.9% (2/219) of Sensititre Telavancin results that were one doubling dilution lower than the reference method.

This significant trending and the potential for occurrence of major errors(s) for Telavancin when testing *S.aureus* particularly if this occurs with isolates with MIC values around the breakpoint was addressed in labeling. The following footnote was recommended to be included in the addendum to technical product information:

“Sensititre Telavancin MIC values for non-fastidious gram positive organisms tended to be one doubling dilution higher than the reference MIC value at concentrations below the susceptible

breakpoint. None of the plus one well MICs caused a categorical error as they were all at least one doubling dilution below the breakpoint".

Growth Rate:

The growth rate for the manual and automated read methods was greater than 90%; this meets the acceptance criteria of ≤10% non-growth of organisms tested.

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:

Table 6. Interpretive Criteria and QC Ranges for Telavancin

Antibiotic - Concentration reviewed	**Interpretive Criteria (µg/mL)**		
Telavancin 0.0005-2 µg/mL	**FDA (S, I, R)**	**CLSI (S,I,R)**	**Trek (S, I, R)**
S. aureus	≤0.12, -, -	≤0.12, -, -	≤0.12, -, -
E. faecalis	≤0.25, -, -	≤0.25, -, -	≤0.25, -, -
QC organism	Expected Range		
S. aureus ATCC 29213	0.03-0.12	0.03-0.12	0.03-0.12
E. faecalis ATCC 29212	0.03-0.12	0.03-0.12	0.03-0.12

Currently, there are no intermediate or resistance interpretative criteria for Telavancin.

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.