

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

A. 510(k) Number:

k093865

B. Purpose for Submission:

The addition of telavancin to the Sensititre Susceptibility Plates.

C. Measurand:

Telavancin doubling dilution concentrations of 0.001 to 16 µg/mL are included in the Sensititre HP susceptibility plates and Sensititre 18-24 hours susceptibility plates.

D. Type of Test:

Quantitative Antimicrobial Susceptibility Test (AST), growth based fluorescence. The minimum inhibitory concentration (MIC) is determined manually based on visual detection of growth or by the aid of an AutoReader. 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.

E. Applicant:

Trek Diagnostic Systems.

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:

JWY – Manual reading of AST of >16 hours incubation
LRG – Automated readings of AST of >16 hours incubation

4. Panel:

Microbiology

H. Intended Use:

1. Intended use(s):

The Sensititre MIC and Breakpoint Susceptibility system is an *in vitro* diagnostic product for clinical susceptibility testing of non fastidious isolates.

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

MIC plates can either be read manually or automatically on the Sensititre Autoreader and can provide both qualitative and quantitative results.

2. Indication(s) for use:

This 510(k) is for the addition of telavancin in the dilution range of 0.001-2/μg/ml to the Sensititre HP MIC Susceptibility plate for testing *Streptococcus* spp. and the Sensititre 18 24 hour MIC panel in the dilution range of 0.03-16/μg/ml for testing Gram positive isolates. According to the FDA approved label, telavancin has been shown to be active against most isolates of the following the microorganisms *in vitro* and in clinical infections:

Facultative Gram-Positive Microorganisms:

Staphylococcus aureus (including methicillin-resistant isolates)

Streptococcus pyogenes

Enterococcus faecalis

Streptococcus agalactiae

Streptococcus anginosus group (includes *S. anginosus*, *S. intermedius*, and *S. constellatus*)

3. Special conditions for use statement(s):

Prescription use only.

4. Special instrument requirements:

The Sensititre Autoinoculator, The Sensititre AutoReader and the Sensititre manual viewer SensiTouch.

I. Device Description:

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

The Sensititre 18-24 hours MIC or breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of non fastidious isolates. It consists of a disposable plate containing dilutions of antimicrobials dried in individual wells. The test plate is inoculated with a standardized suspension of the organism to be tested. After the indicated hours of incubation, the plate is read for growth to determine the MIC either on an AutoReader or manually using the Sensititre manual viewer or SensiTouch.

A report is then generated that contains the MIC value and the interpretive category result (S,I,R) for each antibiotic contained on the card.

The MIC interpretive criteria for Telavancin are as follows:

Organism	Susceptibility Interpretive Criteria (MIC* in µg/mL):		
	S	I	R
<i>Staphylococcus aureus</i>	≤ 1	-	=
<i>Enterococcus faecalis</i> (vancomycin-susceptible isolates only)	≤ 1	-	=
<i>Streptococcus pyogenes</i> <i>Streptococcus agalactiae</i> <i>Streptococcus anginosus</i> group	≤ 0.12	-	=

*Currently there are no intermediate or resistant interpretive criteria for telavancin. The absence of resistant strains precludes defining any results categories other than "susceptible." For strains yielding results suggestive of a "non-susceptible" category, organism identification and antimicrobial susceptibility test results should be confirmed. Subsequently, the isolates should be saved and submitted to a reference laboratory that will confirm results using a reference dilution method.

S = Susceptible: Attainable levels in blood or tissue on usual usage, including oral administration when applicable.

I = Intermediate: The intermediate category implies clinical efficacy in body sites where the drugs are physiologically concentrated (e.g. quinolones and B-lactams in urine), or when a higher than normal dosage of drug can be used (e.g. B-lactams). The "intermediate" category also includes a "buffer zone" which should prevent small, uncontrolled, technical factors from causing major discrepancies in interpretations, especially for drugs with narrow pharmacotoxicity margins.

R = Resistant to usually achievable systemic concentrations.

J. Substantial Equivalence Information:

1. Predicate device name(s):

Microscan AST Panel for Gatifloxacin

2. Predicate K number(s):

k010159

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Determining quantitative and qualitative susceptibility to antimicrobial agents	Same
Inoculation and test organism	Isolated colonies from culture are used	Same
Technology	Automated based on fluorescence detection of growth. Manual based on turbidity	Turbidity detection of growth for manual. Patented fluorescent technology for automated.
Result reported	Report results either as quantitative MIC value or qualitative interpretation (S,I,R)	Same
Type of test	Automated or manual	Same

Differences		
Item	Device	Predicate
Antibiotic	Telavancin	Gatifloxacin
Incubation	18-24 hours	3.5-24 hours

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/ucm071462.pdf>

2. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, Approved Standard -8th Edition, Document M7-A8

3. Performance Standards for Antimicrobial Susceptibility Testing – 19th Informational Supplement, M100-S19.

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 non-fluorescent 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 (9 *S. aureus*, 5 *E. faecalis*, 1 *E. faecium*, 5 group A Streptococci, and 5 coagulase negative staphylococci) and 25 *Streptococcus* sp. (10 *S. pneumoniae*, 5 *S. viridans*, 6 group A Streptococci, and 4 group B Streptococci) were tested at each site. These were tested one time at each of the three sites using both reading methods.

Results were read on the AutoReader and manually using the SensiTouch. Reference method plates were read visually in accordance with CLSI M-7 standard. 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 SensiTouch, the overall reproducibility was 100% for Gram positive organism and 97% for *Streptococcus* sp.

For the AutoReader, the overall reproducibility was 100% for Gram positive organism and 99% for *Streptococcus* sp.

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. 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 AutoReader and the manual reading method (SensiTouch). The mode of the MIC obtained by the Sensititre manual read was similar to that obtained by the AutoReader. Results obtained by Sensititre for *S. aureus* and *E. faecalis* trended towards the low end of the acceptable MIC range and were generally one dilution lower than was obtained with the reference method. Summary of the results are shown in the table below.

Quality Control Results for Telavancin

Organism	Concentration (µg/mL)	Reference	Telavancin	
			AutoReader	SensiTouch (manual)
<i>S. aureus</i> ATCC 29213 Acceptable MIC range: 0.12-1 µg/mL	0.06	0	0	0
	0.12	4	54	54
	0.25	52	6	6
	0.5	2	0	0
	1	2	0	0
	2	0	0	0

<i>E. faecalis</i> ATCC 29212 Acceptable MIC range: 0.12-0.5 µg/mL	0.06	0	0	0
	0.12	16	54	59
	0.25	42	6	1
	0.5	2	0	0
	1	0	0	0
<i>S. pneumoniae</i> ATCC 49619 Acceptable MIC range: 0.004-0.006 µg/mL	0.002	0	0	0
	0.004	0	0	0
	0.008	0	1	1
	0.015	50	58	57
	0.03	10	1	2
	0.06	0	0	0

At least one Quality control organism was in control in the reference on all days. Quality Control results for the Sensititre Susceptibility System using either reading methods demonstrated that the system could produce the expected quality control results.

Inoculum density control for QC organisms ranged between a minimum of 1.0×10^5 CFU/mL and a maximum of 5.5×10^5 CFU/mL. These colony count values were the result of 33 density evaluation tests with *S. aureus*, 30 tests with *E. faecalis* and five tests with *S. pneumoniae*. All were in the expected range.

If the non-fastidious Sensititre plate is utilized for testing it does not require lysed horse blood in its testing. Therefore, *S. pneumoniae* ATCC 49619 can not be used as the QC organism for the *Streptococcus* spp. The recommended QC organism for this non-fastidious Sensititre plate is *S. aureus* ATCC 29213.

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 of *Streptococcus* spp. (Sensititre *Streptococcus* spp. HP MIC panel) and gram positive isolates (Sensititre 18-24 hour susceptibility plate). The CLSI microdilution reference methods containing the same antimicrobial in the same dilutions were used for a comparison and evaluation of performance.

The inoculum was prepared using a Nephelometer which was calibrated at the start of each test. Plates were inoculated and incubated at 34-36° C (in CO₂ incubator for *S. pneumoniae*). The reading was done on the AutoReader and manually using the SensiTouch at 20-24 hours.

Clinical testing was performed on 666 Gram positive isolates (263 *Staphylococcus* spp., 70 *Enterococcus* spp. and 333 *Streptococcus* spp.). All were freshly collected clinical isolates. In addition, testing was performed on 59 Gram positive CDC stock challenge isolates and 61 *Streptococcus* spp. CDC stock challenge isolates.

The growth rate for the manual and automated read methods was greater than 90%. The performance evaluations are shown in the table below.

Summary Table (AutoReader)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#NS
AutoReader									
<i>Streptococcus agalactiae</i> w LHB									
CLINICAL	76	76	100	76	76	100	76	100	0
CHALLENGE	11	11	100	11	11	100	11	100	0
COMBINED (CLINICAL AND CHALLENGE)	87	87	100	87	87	100	87	100	0
<i>Streptococcus pyogenes</i> w LHB									
CLINICAL	75	75	100	75	75	100	75	100	0
CHALLENGE	14	14	100	14	14	100	14	100	0
COMBINED (CLINICAL AND CHALLENGE)	89	89	100	89	89	100	89	100	0
<i>Streptococcus agalactiae</i> w MHB									
CLINICAL	44	43	97.7	39	39	100	44	100	0
CHALLENGE	5	5	100	5	5	100	5	100	0
COMBINED (CLINICAL AND CHALLENGE)	49	48	98.0	44	44	100	49	100	0
<i>Streptococcus pyogenes</i> w MHB									
CLINICAL	34	34	100	5	5	100	34	100	0
CHALLENGE	6	6	100	3	3	100	6	100	0
COMBINED (CLINICAL AND CHALLENGE)	40	40	100	8	8	100	40	100	0
<i>Streptococcus anginosus</i> w LHB									
CLINICAL	104	104	100	104	104	100	104	100	0
CHALLENGE	25	25	100	25	25	100	25	100	0
COMBINED (CLINICAL AND CHALLENGE)	129	129	100	129	129	100	129	100	0
<i>Staphylococcus aureus</i>									
CLINICAL	150	150	100	150	150	100	150	100	0
CHALLENGE	27	27	100	27	27	100	27	100	0
COMBINED (CLINICAL AND CHALLENGE)	177	177	100	177	177	100	177	100	0
<i>Enterococcus faecalis</i>									
CLINICAL	59	57	96.6	59	57	96.6	59	100	0
CHALLENGE	5	5	100	5	5	100	5	100	0
COMBINED (CLINICAL AND CHALLENGE)	64	62	96.9	64	62	96.9	62	100	0
<i>Staphylococcus spp.</i>									
CLINICAL	112	111	99.1	110	110	100	112	100	0
CHALLENGE	17	17	100	17	17	100	17	100	0
COMBINED (CLINICAL AND CHALLENGE)	129	128	99.2	127	127	100	127	100	0
<i>Enterococcus spp.</i>									
CLINICAL	11	11	100	8	8	100	8	100	0
CHALLENGE	10	10	100	9	9	100	9	100	0
COMBINED (CLINICAL AND CHALLENGE)	21	21	100	17	17	100	21	100	0

EA-Essential Agreement

CA-Category Agreement

NS-not susceptible

Summary Table (Manual Read Method-SensiTouch)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#NS
Manual Read Method-SensiTouch									
<i>Streptococcus agalactiae</i> w LHB									
CLINICAL	76	76	100	76	76	100	76	100	0
CHALLENGE	11	11	100	11	11	100	11	100	0
COMBINED (CLINICAL AND CHALLENGE)	87	87	100	87	87	100	87	100	0
<i>Streptococcus pyogenes</i> w LHB									
CLINICAL	75	75	100	75	75	100	75	100	0
CHALLENGE	14	14	100	14	14	100	14	100	0
COMBINED (CLINICAL AND CHALLENGE)	89	89	100	89	89	100	89	100	0
<i>Streptococcus agalactiae</i> w MHB									
CLINICAL	44	43	97.7	39	39	100	44	100	0
CHALLENGE	5	5	100	5	5	100	5	100	0
COMBINED (CLINICAL AND CHALLENGE)	49	48	98.0	44	44	100	49	100	0
<i>Streptococcus pyogenes</i> w MHB									
CLINICAL	34	34	100	6	6	100	34	100	0
CHALLENGE	6	6	100	1	1	100	6	100	0
COMBINED (CLINICAL AND CHALLENGE)	40	40	100	7	7	100	40	100	0
<i>Streptococcus anginosus</i> w LHB									
CLINICAL	104	104	100	104	104	100	104	100	0
CHALLENGE	25	25	100	25	25	100	25	100	0
COMBINED (CLINICAL AND CHALLENGE)	129	129	100	129	129	100	129	100	0
<i>Staphylococcus aureus</i>									
CLINICAL	150	150	100	150	150	100	150	100	0
CHALLENGE	27	27	100	27	27	100	27	100	0
COMBINED (CLINICAL AND CHALLENGE)	177	177	100	177	177	100	177	100	0
<i>Enterococcus faecalis</i>									
CLINICAL	59	57	96.6	59	57	96.6	59	100	0
CHALLENGE	5	5	100	5	5	100	5	100	0
COMBINED (CLINICAL AND CHALLENGE)	64	62	96.9	64	62	96.9	62	100	0
<i>Staphylococcus spp.</i>									
CLINICAL	113	113	100	112	112	100	113	100	0
CHALLENGE	17	17	100	17	17	100	17	100	0
COMBINED (CLINICAL AND CHALLENGE)	130	130	100	129	129	100	130	100	0
<i>Enterococcus spp.</i>									
CLINICAL	11	11	100	8	8	100	8	100	0
CHALLENGE	10	10	100	9	9	100	9	100	0
COMBINED (CLINICAL AND CHALLENGE)	21	21	100	17	17	100	21	100	0

EA-Essential Agreement

CA-Category Agreement

NS-not susceptible

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 II 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. No isolates in this study were noted to have MICs outside the susceptible category. Therefore, there were no minor, major or very major errors. As summarized in the table below, the combined (clinical + challenge) EA and CA for all organisms were greater than 90%.

	Number of isolates tested	EA	CA
	AutoReader		
Gram Positive Organisms (MHB)	480	99%	100%
Gram Positive Organisms (MHB w LHB)	305	100%	100%
	Manual Read Method-SensiTouch		
Gram Positive Organisms (MHB)	481	99.4%	100%
Gram Positive Organisms (MHB w LHB)	305	100%	100%

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:

$\leq 1 \mu\text{g/mL}$ (S) for *Staphylococcus aureus* and *Enterococcus faecalis*
(vancomycin-susceptible isolates only)

$\leq 0.12 \mu\text{g/mL}$ (S) for *Streptococcus pyogenes*, *Streptococcus agalactiae*, and
Streptococcus anginosus group

Currently, there are no intermediate (I) or resistance (R) interpretive criteria for telavancin.

N. Proposed Labeling:

The expected value range, interpretive criteria and QC are included in the package insert. The labeling is sufficient and 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.