

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

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

**K052091**

**B. Purpose for Submission:**

Addition of the antibiotic Tigecycline at concentrations of 0.008 – 16 µg/mL to the Gram Positive and of 0.015 – 16 µg/mL to the Gram Negative Sensititre® Susceptibility System (18 – 24 hour susceptibility plates)

**C. Measurand:**

Tigecycline at 0.008 – 16 µg/mL for Gram Positive panels  
Tigecycline at 0.015 – 16 µg/mL for Gram Negative panels

**D. Type of Test:**

Antimicrobial Susceptibility Test (Quantitative and Qualitative) fluorescence technology, growth-based

**E. Applicant:**

Trek Diagnostic Systems, Inc.

**F. Proprietary and Established Names:**

Sensititre® 18 – 24 hour MIC Susceptibility plates

**G. Regulatory Information:**

1. Regulation section:  
21 CFR 866.640 - Antimicrobial Susceptibility Test Powder
2. Classification:  
Class II
3. Product Code:  
  
JWY – Manual Antimicrobial Susceptibility Test Systems  
LRG - Instrument for AutoReader & Interpretation of Overnight  
Antimicrobial Susceptibility Systems  
LTT – Panels, Test, Susceptibility, Antimicrobial
4. Panel:  
83 Microbiology

**H. Intended Use:**1. Intended use(s):

The Sensititre® MIC Susceptibility system is an *in vitro* diagnostic product for clinical susceptibility testing of Gram negative and Gram positive organisms.

2. Indication(s) for use:

This submission is for the addition of the antibiotic tigecycline at concentrations of 0.008 – 16 µg/mL to Gram Positive and of 0.015 – 16 µg/mL to Gram Negative Sensititre® 18 – 24 hour MIC Susceptibility plates.

3. Special condition for use statement(s):

Prescription Use Only

4. Special instrument Requirements:

Sensititre® AutoInoculator (with Doseheads)  
Sensititre® AutoReader or ARIS®  
Sensititre SensiTouch®

**I. Device Description:**

The Sensititre® susceptibility system is a microversion of the broth dilution method and can provide both *in vitro* qualitative and quantitative susceptibility results in a dried plate format. Each 96 well microdilution plate is dosed with antimicrobial agents at appropriate dilutions and then dried. Isolated colonies for testing are selected from the primary agar plates and emulsified in demineralized water. This solution is adjusted to a 0.5 McFarland standard using the Sensititre® Nephelometer. A further dilution is made into the Sensititre® cation adjusted Mueller-Hinton broth with TES (CAMHBT). The final inoculum in each well is  $1 \times 10^5$ . Inoculated panels are sealed with adhesive film to prevent evaporation, and then are incubated at 34 - 36° C for 18 – 24 hours. The contents of the wells are examined for bacterial growth manually using the Sensititre® SensiTouch, or by using the Sensititre® AutoReader automated reading system (instrumentation and software).

The Sensititre® AutoReader system (or the Sensititre® ARIS®) utilizes fluorescence technology to read 18 – 24 hour test plates, and to provide printed reports of susceptibility results. 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 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 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 fluorescing. The amount of fluorescence detected is directly related to the activity of bacterial surface enzymes and, therefore, to the presence of bacterial growth and resistance to the antibiotic. Result reading and reports generation can be automatically obtained from the software, or results can be manually interfaced to a Laboratory Information System (LIS). Additional susceptibility result interpretation is done using software driven rules derived from the CLSI standards. The Sensititre® microdilution plate results can also be manually read and recorded using the Sensititre® SensiTouch, or any other manual light box viewer.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
Dade Microscan 18 hour, West Sacramento, CA
2. Predicate K number(s):  
K033948
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	The Sensititre® MIC Susceptibility system is an <i>in vitro</i> diagnostic product for clinical susceptibility testing of Gram negative and Gram positive organisms.	same
Isolates	Isolated colonies from culture used	same
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	same
Reading algorithm	Results are determined from serial twofold dilutions of antimicrobial agents. MIC determined by observing the lowest antimicrobial concentration showing growth inhibition.	same
Type of Test	Automated or manual read	same

Differences		
Item	Device	Predicate
Inoculum preparation	Inoculum density equated to 0.5 McFarland standard	Inoculum density equated to 0.5 McFarland standard or Prompt™ system
Suspension adjustment	Non fastidious isolates should have an inoculum of $1 \times 10^5$ CFU/mL, except for <i>Proteus</i> spp., which has an initial dilution adjustment (range $5 \times 10^3$ - $5 \times 10^4$ )	Final inoculum concentration is $1 \times 10^5$ CFL/mL
Technology	The automated Sensititre® system utilizes fluorescent compounds to detect bacterial growth after overnight incubation. The presence of turbidity or a deposit of cells in the bottom of the wells, without the addition of fluorescent materials, may also indicate bacterial growth.	The automated Microscan® system utilizes the detection of bacterial growth after overnight incubation, without fluorescence production.
Incubation conditions	18 - 24 hours	>16 hours manual

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”; CLSI M7 (M100-S15)

“Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.”

5. Test Principle:

The system employs both visual growth based and /or fluorogenic detection of organism growth. The MIC is determined by comparing growth in wells containing serial two-fold dilutions of an antibiotic to the growth in “growth control wells” included in all panels, which contain no antibiotic. Some plate formats also include a “negative growth” well used for calibration of the AutoReader, which is not required for manual reading.

6. Performance Characteristics (if/when applicable):7. Analytical performance:**a. *Precision/Reproducibility:***

Reproducibility was established using 25 Gram positive and 25 Gram negative isolates which were evaluated one time at each site, for site to site, and inter site studies. Two reading methods (automated overnight with the AutoReader® and manual reads with the SensiTouch®) were tested at all three sites, which demonstrated >95% reproducibility.

**b. *Linearity/assay reportable range***

Not applicable

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

FDA / CLSI recommended Quality Control strains were tested at the concentrations listed. The results demonstrated that the device system could produce QC results in the recommended range.

Quality Control was performed daily with the automated overnight reading and the manual overnight reading methods with the following results (see table below). There does appear to be a slight trend for the Auto Read overnight method to produce more susceptible results than the reference method for the Gram positive panel QC organisms, but still remain in the expected range an acceptable number of times. The *Enterococcus faecalis* ATCC 29212 strain seemed to drive this trend. This trend was not observed for the Sensititre® results for the Gram negative QC organism.

Quality control results demonstrated the ability of both read methods to produce acceptable results >95% of the time for all three QC organisms

Organism	Concentration µg/mL	Reference results	Sensititre® results	
			Manual	AutoReader
<b>Gram negative</b>				
E. coli ATCC 25922 0.03 – 0.25 µg/mL	<0.03			
	0.03	5		
	0.06	54	56	60
	0.12		4	
	0.25			
	>0.25	1		
	>16			

Organism	Concentration µg/mL	Reference results	Sensititre® results	
			Manual	AutoReader
<b>Gram positive</b>				
<i>S. aureus</i> ATCC 29213 Expected range 0.03 – 0.25 µg/mL	<0.03			
	0.03			
	0.06	11		17
	0.12	51	57	42
	0.25	1	6	4
	0.5			
	>16			
<i>E. faecalis</i> ATCC 29212 Expected range 0.03 – 0.12 µg/mL	<0.03	2		
	0.03	14		53
	0.06	47	53	8
	0.12		8	2
	0.25		2	
	0.5			
	>16			

Inoculum density control: The organism suspension density of the cation adjusted Mueller-Hinton broth was equivalent to a 0.5 McFarland standard using the Sensititre® Nephelometer, which was verified each day of testing.

**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 reference panels were prepared and tested as recommended by CLSI, including the addition of 2.5 - 5% lysed horse blood when testing *Streptococcus spp.*, and were used to compare with the Sensititre® panel results. Clinical testing was performed at three sites. The testing included fresh clinical isolates along with a challenge set of Gram positive isolates and Gram negative isolates with known results.

The study included 297 Gram positive Clinical isolates and 75 Gram positive Challenge isolates, with the following performance.

**Gram positive isolates**

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	NS
<b>Clinical</b>	297	289	97.3	297	289	97.3	297	100	0
<b>Challenge</b>	75	69	94.7	75	69	94.7	75	100	0
<b>Combined</b>	372	358	96.2	372	358	96.2	372	100	0

There were 246 Clinical and 58 Challenge isolates from a variety of *Enterobacteriaceae* with the following performance.

***Enterobacteriaceae* isolates**

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
<b>Clinical</b>	246	244	99.2	246	244	99.2	233	94.7	4	13	0	0
<b>Challenge</b>	58	54	93.1	58	54	93.1	57	98.2	1	1	0	0
<b>Combined</b>	304	298	98.0	304	298	98.0	290	95.4	5	14	0	0

**NS**-Non Susceptible

**EA**-Essential Agreement

**CA**-Category Agreement

**R**-resistant isolates

**maj**-major discrepancies

**vmj**-very major discrepancies

**min**- minor discrepancies

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 (Eval) are results that are within the test range and on scale.

The Sensititre® Auto Read and manual overnight reading methods were evaluated at all three sites; no apparent difference in the performance between the two reading methods was observed. The same trending for the Auto Read overnight method to produce more susceptible results than the reference method, which was previously discussed in the Gram positive panel QC results data, was also present; however, the performance was not affected.

The test device had a growth rate of >95%.

**i. Matrix comparison:**

Not applicable

**b. Clinical studies:**

**i. Clinical sensitivity:**

Not applicable

**ii. Clinical specificity:**

Not applicable

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

Not applicable

**c. Clinical cut-off:**

Not applicable

**d. Expected values/Reference range**

<b>Organism</b>	<b>S</b>	<b>I</b>	<b>R</b>
<i>Staphylococcus aureus</i> (including methicillin-resistant isolates)	$\leq 0.5$	*	*
<i>Streptococcus spp.</i> other than <i>S. pneumoniae</i>	$\leq 0.25$	*	*
<i>Enterococcus faecalis</i> (vancomycin-susceptible isolates only)	$\leq 0.25$	*	*
<i>Enterobacteriaceae</i> **	$\leq 2$	4	$\geq 8$

\*The current absence of resistant isolates precludes defining any results other than Susceptible.

**N. Proposed Labeling:**

The expected value range, interpretive criteria and QC are the same as recommended by FDA. All values will be included in the package insert.

**O. Conclusion:**

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