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

A. 510(k) Number:

K092445

B. Purpose for Submission:

Addition of Minocycline into the TREK Sensititre® 18-24 hour MIC or Breakpoint (BP) Susceptibility System for gram negative and gram positive organisms.

C. Measurand:

Minocycline 0.03 – 32 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™ 18-24 hour Susceptibility MIC 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:

   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 gram positive and gram negative organisms.

2. Indication(s) for use:

   This 510(k) is for addition of Minocycline in the dilution range of 0.03-32µg/mL for testing gram negative and gram positive isolates on the Sensititre® 18-24 hour Susceptibility system. The approved primary "Indications for Use" and clinical significance of Minocycline is for:

   Aerobic and facultative Gram-negative and Gram-positive microorganisms:

   E.coli
   Klebsiella spp.
   Enterobacter aerogenes
   Acinetobacter spp.
   Staphylococcus aureus

3. Special conditions for use statement(s):

   For prescription use only.

   Minocycline is not the drug of choice in the treatment of any type of staphylococcal infection.

4. Special instrument requirements:

   Use Sensititre AutoInoculator for inoculation

I. Device Description:

The Sensititre Susceptibility System is a micro-version of the classic broth dilutions method and can provide both qualitative and quantitative susceptibility results in a dried microtitre plate format. Each micro-broth dilution plate is dosed with antimicrobial agents at specific dilutions and then dried.

The organism to be tested must be in pure culture and identified as Gram negative or Gram positive. Colonies are then suspended in broth and brought to a turbidity of 0.5 McFarland, with the recommendation to use the Sensititre nephelometer. The organism suspension is diluted using Mueller-Hinton broth to a final inoculum concentration of 1 X 10^5 CFU/mL. A volume of 50µl of broth suspension is transferred to each well of the microtitre plate by the Sensititre AutoInoculator. After inoculation, plates are sealed with an adhesive seal, incubated at 34-36ºC for 18 to 24 hours and examined for bacterial growth. Antimicrobial susceptibility testing results may be read automatically using the Sensititre® AutoReader® or manually using the Sensititre® manual viewer or SensiTouch®.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Siemens' MicroScan®, Dried Gram-Negative and Gram-Positive MIC/Combo Panels

2. Predicate K number(s):

   K010159

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
1. Intended Use	The Sensititre® 18-24 MIC or Breakpoint Susceptibility system is an in vitro diagnostic product for clinical susceptibility testing of non-fastidious (gram negative and gram positive organisms)	Same
2. Isolates	Isolated colonies from culture used.	Same
3. Sample Preparation	Inoculum density of 0.5 McFarland Standard	Same
4. Technology	Automated based on fluorescence detection of growth. Manual based on turbidity.	Turbidity detection of growth for manual. Patented fluorescent technology for the automated.

Similarities		
Item	Device	Predicate
5. Result Reported	Report results as a minimum inhibitory concentration (MIC) and interpretive criteria (SIR)	Same
6. Type of Test	Automated and Manual	Same

Differences		
Item	Device	Predicate
1. Incubation	18-24 hours	3.5-24 hours
2. Antibiotic	Minocycline 0.03-32µg/mL	Gatifloxacin 0.004-32µg/mL

K. Standards/Guidance Documents referenced (if applicable):

1. Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA;
2. CLSI M100-S18 and M100-S19: Performance Standards for Antimicrobial Susceptibility Testing;
3. CLSI M7-A7 and M7-A8: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically.

L. Test Principle:

The Sensititre® AutoRead® System utilizes fluorescence technology to read the micro broth dilution plates after 18 to 24 hour 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 testing was performed using 25 Gram negative and 25 Gram positive isolates. The isolates were tested one time at each of three sites for each reading method (Manual, AutoRead®). The testing resulted in overall reproducibility results of greater than 95% for both the Manual and AutoRead® methods.

b. Linearity/assay reportable range:

Not Applicable

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

Isolates recommended by both the FDA(CDER) and the CLSI, namely S.aureus ATCC 29213, E.faecalis ATCC 29212, and E.coli ATCC 25922 were tested against Minocycline. Quality control was performed at all sites using both Manual and AutoRead® methods. All results were in acceptable range which demonstrates that the Sensititre Susceptibility System can consistently produce quality control results in the recommended range for Minocycline, for both the Manual and AutoRead® methods.

QC Table

ORGANISM	**Conc. (µg/mL)**	**Reference**	**Sensititre® AutoRead**	**Sensititre® Manual**
S.aureus ATCC 29213	0.06	6	7	3
Expected Range :	0.12	51	41	41
0 .06-0.5µg/mL	0.25	3	10	14
	0.5	0	2	2
E.faecalis ATCC 29212	1	4	38	6
Expected Range :	2	50	21	51
1-4µg/mL	4	6	1	3
E.coli ATCC 29212	0.25	37	9	7
Expected Range :	0.5	16	33	31
0.25-1µg/mL	1	7	18	22

The Sensititre® nephelometer was used at each site to standardize the inoculum. Each time this nephelometer was turned on it underwent calibration.

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 micro-broth dilution panel was prepared according to the CLSI recommendation and used as the reference method.

Clinical testing was performed at three sites using 255 Gram negative and 179 Gram positives totaling 434 isolates tested. Of the 434 isolates, 356 were fresh clinical isolates and 78 were stock challenge strains.

The growth rate for both the Manual and AutoRead® methods was greater than 90%.

Tables A-D demonstrate performance based on essential agreement and category agreement of both clinical and challenge isolates. The data is stratified by isolate Gram reaction and method of plate read (Manual or AutoRead®).

Table A. Gram Negatives/ Manual Read	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	206	205	99.5	187	187	100	200	97.1	11	6	0	0
Challenge	49	49	100	44	44	100	49	100	8	0	0	0
Combined	255	254	99.6	231	231	100	249	97.6	19	6	0	0

Table B. Gram Negatives/ AutoRead®	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	206	204	99	188	187	99.5	204	99	11	2	0	0
Challenge	49	49	100	44	44	100	49	100	8	0	0	0
Combined	255	253	99.2	232	231	99.6	253	99.2	19	2	0	0

Table C. Gram Positives/ Manual Read	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	150	149	99.3	150	149	99.3	149	99.3	0	1	0	0
Challenge	29	29	100	29	29	100	29	100	0	0	0	0
Combined	179	178	99.4	179	178	99.4	178	99.4	0	1	0	0

Table D. Gram Positives/ AutoRead®	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	150	149	99.3	150	149	99.3	150	100	0	0	0	0
Challenge	29	29	100	29	29	100	29	100	0	0	0	0
Combined	179	178	99.4	179	178	99.4	179	100	0	0	0	0

EA = Essential Agreement
CA = Category Agreement
R = Resistant Isolates
min = minor discrepancies
maj = major discrepancies
vmj = very major discrepancies

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within plus/minus one dilution. Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of Sensititre® panel within plus or minus one serial two-fold dilution of the antibiotic. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the Sensititre® panel result.

In each instance, both the percent Category Agreement (CA) and percent Essential Agreement (EA) consistently fall above 90%, and are therefore acceptable as described in the "Class II Special Controls guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA, August 2009". A comparative evaluation of performance data of the Manual and AutoRead methods revealed very little difference. No very major or major discrepancies occurred. A total of nine minor discrepancies occurred and all fell within Essential Agreement of the reference method result.

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:

   Minocycline Interpretive Criteria: <4 (S), 8 (I), >16 (R)

   The FDA interpretive criteria, as listed above, were used to evaluate performance all data. The appropriate Quality Control ranges, recommended QC organisms and drug interpretive criteria are included in the package insert.

N. Proposed Labeling:

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

O. Conclusion:

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