

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

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

k053243

**B. Purpose for Submission:**

For addition of gemifloxacin on the Sensititre® 18 – 24 hour MIC panel for testing appropriate gram positive and gram negative organisms

**C. Measurand:**

Gemifloxacin (0.002 - 16 µg/mL for gram positive organisms and 0.002 – 4 µg/mL for gram negative organisms)

**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 plates

**G. Regulatory Information:**

1. Regulation section:

866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

II

3. Product code:

JWY-manual readings of AST testing of >16 hour incubation

LRG Automated readings of AST of >16 hour incubation.

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 gemifloxacin in the dilution range of 0.002 - 16 µg/mL for testing gram positive and 0.002 – 4 µg/mL for testing gram negative isolates on the Sensititre® 18 – 24 hour MIC panel
3. Special conditions for use statement(s):  
For prescription use only
4. Special instrument requirements:  
Automated readings are performed on the Sensititre® AutoReader or ARIS®.

**I. Device Description:**

Sensititre® MIC Susceptibility plate MIC panels are multi-well plastic microtitre plates, precision dosed with dried, stabilized antimicrobics. This is a microversion of the classic broth dilution methods and can provide both qualitative and quantitative susceptibility results.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):  
Pasco MIC and MIC/ID Panels
2. Predicate 510(k) number(s):  
K033119
3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Intended use	an <i>in vitro</i> diagnostic product for clinical susceptibility testing of gram negative and gram positive organisms.	same
Inoculum	Prepared from colonies using the direct inoculation method	Prepared from colonies using the direct inoculation method
Inoculation method	Direct equated to a 0.5 McFarland	Direct equated to a 0.5 McFarland
<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Type panel	Dried antibiotics	100 µl/well frozen
Incubation	18-24 hours	16-24 hours
Technology	Fluorescence detection of growth	Turbidity detection of growth
Reading method	Visual growth and Auto read by instrumentation	Turbidity detection of growth

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA”; CLSI M7 (M100-S16) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.”

**L. Test Principle:**

The Sensititre® Autoread System utilizes fluorescence technology to read 18-24 hour plates. The technology involves the detection of bacterial growth which is determined by generating a fluorescent product from a non-fluorescent substrate. The non-fluorescent substrate is prepared by conjugating a fluorescent compound to the specific enzyme substrates with a bond which prevents fluorescence. The substrate is added to the inoculum broth and dispensed into the test plates at the same time as the test organism. 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.

**M. Performance Characteristics (if/when applicable):**

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility testing was performed on 25 gram positive isolates and 25 gram negative isolates appropriate for testing with gemifloxacin. These were tested 1 time at each of the three sites on each reading method. Both gram

negative isolates and gram positive isolates demonstrated >95% reproducibility using either the automated read method or the manual method of reading.

b. *Linearity/assay reportable range:*  
Not applicable

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*  
The recommended QC isolates were tested daily with acceptable results with the reference method. Quality control was also performed at all sites using both manual and autoread methods. The Sensititre® results demonstrated that the system can produce QC results in the recommended range for both the manual method of reading and the automated read method.

Quality Control Table for Gram Positive Isolates

<b>ORGANISM</b>	<b>Conc ug/mL</b>	<b>Sensititre® Autoread</b>	<b>Sensititre® manual</b>	<b>Reference</b>
<i>S. aureus</i> ATCC 29213	0.008			28
	0.015	26	42	32
Expected Range : 0.008 – 0.03 ug/ml	0.03	34	18	
<i>E. faecalis</i> ATCC 29212	0.016	2		
	0.03	56	23	53
Expected Range : 0.016 – 0.12 µg/mL	0.06	1	37	7

Although the modes for these two gram positive QC organisms are different for each read method, they are within the expected range.

Quality Control Table for Gram Negative Isolates

<b>ORGANISM</b>	<b>Conc ug/mL</b>	<b>Sensititre® Autoread</b>	<b>Sensititre® manual</b>	<b>Reference</b>
<i>E. coli</i> ATCC 25922	<0.004			1
	0.004	24	16	35
Expected Range : 0.004 – 0.016 µg/mL	0.008	37	45	24
<i>P. aeruginosa</i> ATCC 27853	0.25	37	43	8
	0.5	21	16	49
Expected Range : 0.25 – 1 µg/mL	1	3	2	5
	>1	1	1	

The modes of both autoread and manual read methods for both gram negative QC organisms are the same but different with the reference method however still within the expected range.

Nephelometer was used at each site to standardize the inoculum and it was calibrated each time it was switched on. Colony counts from QC ATCC source were performed using direct inoculum method and the mean results were within the minimum and maximum ranges.

- 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 dilution reference panel was prepared according to the CLSI recommendation. Clinical testing was performed on 90 gram positive isolates and 322 gram negative isolates at 3 sites which included fresh and stock clinical isolates and a set of challenge organisms. The broth reference panel for *Streptococcus* spp. was set up on MH supplemented with 2% to 5% lysed horse blood as recommended by CLSI. The comparison resulted in the following performance evaluations as reflected below.

Summary Table for **Gram Negative Panel (Automated Read Method)**

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
<i>Enterobacteriaceae</i>	301	298	99.0	270	267	98.9	285	94.7	65	16	0	0
<i>Acinetobacter</i>	21	20	95.2	17	16	94.1	21	100	5	0	0	0
<b>Combined</b>	<b>322</b>	<b>318</b>	<b>98.8</b>	<b>287</b>	<b>283</b>	<b>98.6</b>	<b>306</b>	<b>95.0</b>	<b>70</b>	<b>16</b>	<b>0</b>	<b>0</b>

Summary Table for **Gram Negative Panel (Manual Read Method)**

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
<i>Enterobacteriaceae</i>	301	299	99.3	270	268	99.3	290	96.3	65	11	0	0
<i>Acinetobacter</i>	21	21	100	17	17	100	21	100	5	0	0	0
<b>Combined</b>	<b>322</b>	<b>320</b>	<b>99.4</b>	<b>287</b>	<b>285</b>	<b>99.3</b>	<b>311</b>	<b>96.6</b>	<b>70</b>	<b>11</b>	<b>0</b>	<b>0</b>

**EA**-Essential Agreement  
**CA**-Category Agreement  
**R**-resistant isolates

**maj**-major discrepancies  
**vmj**-very major discrepancies  
**min**- minor discrepancies

EA is defined as 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”.

Autoread results for the gram negative isolates were very similar to the manual readings with no observable trending. Although there were 16 min errors with the automated read method as compared to 11 min errors with the manual read method, the min error rate for both read methods were acceptable and were all in essential agreement. No vmj errors and maj errors were encountered with this group.

Per the FDA approved label, the following gram positive organisms are secondary organisms and have been evaluated using essential agreement alone since there is no FDA or CLSI interpretive criteria. Furthermore, the following comments have been included in the FDA approved label in reference to the secondary organisms: “Gemifloxacin exhibits *in vitro* minimal inhibitory concentrations (MICs) of 0.25 µg/mL or less against most (>=90%) strains of the following microorganisms such as *Staphylococcus aureus* (methicillin-susceptible strains only), *Streptococcus pyogenes*, *Acinetobacter lwoffii*, *Klebsiella oxytoca*, and *Proteus vulgaris*; however, the safety and effectiveness of gemifloxacin in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled clinical trials.”

Summary Table for **Gram Positive Panel (Automated Read Method)**

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %
<i>S. aureus</i> (MSSA)	56	52	92.9	56	52	92.9
<i>Streptococcus spp.</i>	34	32	94.1	34	32	94.1
<b>Combined</b>	<b>90</b>	<b>84</b>	<b>93.3</b>	<b>90</b>	<b>84</b>	<b>93.3</b>

Summary Table for **Gram Positive Panel (Manual Read Method)**

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %
<i>S. aureus</i> (MSSA)	56	56	100	56	56	100
<i>Streptococcus spp.</i>	34	33	97.1	34	33	97.1
<b>Combined</b>	<b>90</b>	<b>89</b>	<b>98.9</b>	<b>90</b>	<b>89</b>	<b>98.9</b>

Although the manual read method has a better EA than the automated read method, both EA% are greater than 90 and are both acceptable.

Growth rate for gram positive isolates is greater than 95% and for gram negative isolates is greater than 95% as well.

- 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:  
*Enterobacteriaceae* ≤0.25(S), 0.5 (I), ≥1 (R)  
*Staphylococcus aureus (MSSA)* – See Comment  
*S. pyogenes* – See Comment

**Comment:** Gemifloxacin exhibits *in vitro* minimal inhibitory concentrations (MICs) of 0.25 µg/mL or less against most (>=90%) strains of the following microorganisms: *Staphylococcus aureus* (methicillin-susceptible strains only), *Streptococcus pyogenes*, *Acinetobacter lwoffii*, *Klebsiella oxytoca*, and *Proteus vulgaris*. However, the safety and effectiveness of gemifloxacin in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled clinical trials. (FDA approved label)

**N. Proposed Labeling:**

The Interpretative criteria, QC isolates and the expected ranges are the same as recommended by the 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.