

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

A. 510(k) Number:

k062783

B. Purpose for Submission:

To add additional organism groups to the antibiotics gemifloxacin, linezolid, and levofloxacin on the Sensititre® *Haemophilus influenzae* / *Streptococcus pneumoniae* (HP) MIC and Sensititre® Susceptibility Plates

C. Measurand:

Gemifloxacin

Linezolid

Levofloxacin

Range µg/mL

0.03 – 0.5

0.5 – 4

0.5 – 16

D. Type of Test:

Quantitative Antimicrobial Susceptibility Test (AST) growth based fluorescence

E. Applicant:

TREK Diagnostic Systems, Inc.

F. Proprietary and Established Names:

Sensititre® *Haemophilus influenzae* / *Streptococcus pneumoniae* (HP) MIC 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® *Haemophilus influenzae* / *Streptococcus pneumoniae* (HP) MIC Susceptibility plate is an *in vitro* diagnostic product for clinical susceptibility

testing of *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Streptococcus* species.

2. Indication(s) for use:

This application is for the addition of *Streptococcus* species (spp.) to gemifloxacin (0.03 – 0.5 ug/mL), linezolid (0.5 – 4 ug/mL), and levofloxacin (0.5 – 16 ug/mL) for use with the Sensititre® *Haemophilus influenzae*/*Streptococcus pneumoniae* (HP) MIC Susceptibility Plates.

3. Special conditions for use statement(s):

For prescription use only

4. Special instrument requirements:

Automated readings are performed on the Sensititre® AutoReader or Sensititre® 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. The medium required for testing *S. pneumoniae* is Sensititre® Mueller-Hinton (MH) broth with 2 – 5% lysed horse blood with a final organism density of 5×10^5 colony units (CFU/mL). This is then incubated in a non CO₂ incubator for 20 – 24 hour and read manually for growth or using the Sensititre® autoread.

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:

Similarities		
Item	Device	Predicate
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	Same

Similarities		
Item	Device	Predicate
Growth medium	Mueller – Hinton (MH) broth with 2 – 5% lysed horse blood	Same
Inoculation method	Direct equated to a 0.5 McFarland	Same
Differences		
Item	Device	Predicate
Type panel	Dried antibiotics	100 µl/well frozen
Incubation	20 - 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 24 hour *Streptococcus pneumoniae* plates. 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 is 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. Enzymatic action of the bacterial surface enzymes on the specific substrates, cleave this bond releasing the fluorophore, which is now capable of 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 or automatically for the detection of fluorescence.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

A reproducibility study was performed on 25 *Streptococcus* spp. These isolates were tested once for each antimicrobial at each of the three sites on

the automated and manual read methods demonstrating >95% reproducibility for both read methods.

b. *Linearity/assay reportable range:*

Not applicable

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

The recommended QC isolate, *S. pneumoniae* 49619 was tested daily with acceptable results. 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 manual and automated read methods. The mode is the same between the reference method and the two read methods.

An additional QC organism *S. pneumoniae* #5 was tested to provide on-scale results. The reference method was in range for every day tested.

Quality Control Table

Antimicrobial	ORGANISM	Conc ug/mL	Sensititre® Autoread	Sensititre® manual	Reference
Gemifloxacin	<i>S. pneumoniae</i> ATCC 49619 Exp. Range: 0.008 – 0.003 ug/ml	≤0.03	60	60	60
	<i>S. pneumoniae</i> #5 Exp. Range : 0.015 – 0.06 ug/ml	≤0.03	60	60	60
Linezolid	<i>S. pneumoniae</i> ATCC 49619 Exp. Range:0.5 – 2 µg/mL	1	57	58	52
		2	3	2	8
	<i>S. pneumoniae</i> #5 Exp. Range:0.5 – 2 µg/mL	0.5	11	5	7
		1	49	55	53
Levofloxacin	<i>S. pneumoniae</i> ATCC 49619 Exp. Range:0.5 – 2 µg/mL	≤0.5	60	60	60
	<i>S. pneumoniae</i> #5 Exp. Range:0.5 – 2 µg/mL	≤0.5	1	2	14
		1	58	58	46
		2	1		

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 and in-house source was performed using direct inoculum method and the mean result was 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 recommended broth dilution reference panel was prepared according to the CLSI recommendation. Clinical testing included both 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 and incubated in a non CO2 incubator for 20 – 24 hours. The comparison resulted in the following performance evaluations as reflected below.

Summary Table for *Streptococcus* spp. Other than *S. pneumoniae* (**Manual Read Method**)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#NS/ R	min	maj	vmj
^a Gemifloxacin	349	349	100	35	35	100	-	-	-	-	-	-
*Linezolid	349	349	100	344	344	100	349	100	1	0	0	0
Levofloxacin	349	349	100	153	153	100	349	100	3	0	0	0

EA-Essential Agreement

vmj – very major discrepancies

CA-Category Agreement

maj - major discrepancies

R-resistant isolates

min – minor discrepancies

^aOnly EA can be determined since there are no interpretative criteria.

*NS-Not susceptible, only susceptible category exists

Summary Table for *Streptococcus* spp. Other than *S. pneumoniae* (**AutoRead Method**)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#NS/ R	min	maj	vmj
^a Gemifloxacin	349	349	100	33	33	100	-	-	-	-	-	-
*Linezolid	349	347	99.4	343	343	100	347	99.4	3	0	0	0
Levofloxacin	349	349	100	141	141	100	349	100	3	0	0	0

EA-Essential Agreement

vmj – very major discrepancies

CA-Category Agreement

maj - major discrepancies

R-resistant isolates

min – minor discrepancies

^aOnly EA can be determined since there are no interpretative criteria.

*NS-Not susceptible, only susceptible category exists

EA is when there is 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 interpretative results, Sensitive, Intermediate, and Resistant (SIR) 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”.

The charts above demonstrated that the performance for *Streptococcus* spp. other than *S. pneumoniae* was acceptable for both methods of reading.

The growth rate for *Streptococcus* spp. is greater than 90%.

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:

Antibiotic	Organism	Interpretative Criteria
<i>Gemifloxacin</i>	<i>Streptococcus pneumoniae</i>	≤0.12 (S), 0.25 (I), ≥0.5 (R)
* <i>Linezolid</i>	<i>Streptococcus</i> spp. including <i>S. pneumoniae</i>	≤2 (S)
<i>Levofloxacin</i>	<i>Streptococcus</i> spp. including <i>S. pneumoniae</i>	≤2 (S), 4 (I), ≥8 (R)

* (CLSI Comment) For some organism/antimicrobial agent combinations, the absence or rare occurrence of resistant strains precludes defining any results categories other than “susceptible.” For strains yielding results suggestive of a “nonsusceptible” 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 CLSI/NCCLS reference dilution method.

N. Proposed Labeling:

The expected value range, interpretive criteria and QC for gram positive panels 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.