

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

A. 510(k) Number:

k040846

B. Purpose for Submission

Addition of ertapenem to the Sensititre® Haemophilus/Streptococcus pneumoniae (HP) MIC Susceptibility Plates

C. Analyte:

Ertapenem (0.008 - 16 ug/mL) AST

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/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/Streptococcus pneumoniae (HP) MIC plates are *in vitro* diagnostic product for clinical susceptibility testing of *Haemophilus influenzae* and *Streptococcus pneumoniae*.
2. Indication(s) for use:
This will include ertapenem in the dilution range of 0.008 - 16 ug/mL to the Sensititre® Haemophilus/Streptococcus pneumoniae (HP) MIC susceptibility plate for testing *Haemophilus influenzae* and *Streptococcus pneumoniae* isolates.
3. Special condition for use statement(s):
H. influenzae is a manual read only.

Prescription use only
4. Special instrument Requirements:

Automated readings are performed for *S. pneumoniae* only on the Sensititre® AutoReader or ARIS®.

I. Device Description:

Sensititre® Haemophilus/Streptococcus pneumoniae (HP) Susceptibility plates 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. *H. influenzae* inoculum is prepared in Haemophilus Test medium and *S. pneumoniae* inoculum is prepared in 2 – 5% lysed horse blood. After inoculation, plates are sealed with an adhesive seal, incubated at 34 -36°C for 20 – 24 hours and examined for bacterial growth.

AST results may be read automatically using the Sensititre® AutoReader® or Sensititre® ARIS® or manually using the Sensititre manual viewer or SensiTouch®.

J. Substantial Equivalence Information:

1. Predicate device name(s):
MicroScan® MICroSTREP *plus*™ Panel
2. Predicate K number(s):
K021037
3. Comparison with predicate:

Item	Device	Predicate
	<i>Similarities</i>	
Intended use	an <i>in vitro</i> diagnostic product for clinical susceptibility testing of <i>Haemophilus influenzae</i> and <i>Streptococcus pneumoniae</i> .	an <i>in vitro</i> diagnostic product for clinical susceptibility testing of streptococci including <i>Streptococcus pneumoniae</i> .
Type panel	Dried antibiotics	Same
Inoculation method	Direct equated to a 0.5 McFarland	Same
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
	<i>Differences</i>	
Reading method	Visual growth and Auto read by instrumentation	Visual growth only
Technology	Fluorescence detection of growth	Growth based

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

“Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”; NCCLS M7 (M100-S14)
“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.

The manual reading is based solely in visualization of growth as turbidity.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility testing was performed on 25 gram-positive isolates appropriate for testing with ertapenem. These were tested 1 time at each of the three sites on each reading method. This demonstrated >95% reproducibility using either the automated read method or the manual read method.

b. *Linearity/assay reportable range:*

Not applicable

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

The recommended QC isolates were tested daily with acceptable results with the reference method. Quality control was performed at all sites. For the QC organism, *S. pneumoniae* ATCC 49619, both the manual read method and the Autoread method were used. The Sensititre® results demonstrated that the system can produce QC results in the recommended range for both the manual read and the automated read methods. For the QC organism, *H. influenzae* ATCC 49766, only the manual read method was used.

ORGANISM	Conc ug/mL	Reference	Sensititre® Autoread	Sensititre® manual
<i>S. pneumoniae</i> ATCC 49619 Expected Range: 0.03 – 0.25 µg/mL	<0.03		1	
	0.03		1	
	0.06	28	6	5
	0.12	38	58	61
<i>H. influenzae</i> ATCC 49766 Expected Range: 0.016 – 0.06 µg/mL	<0.016	1		
	0.016	11		3
	0.03	46		52
	0.06	2		5

Nephelometer was used at each site to standardize the inoculum and it was calibrated each time it was switched on. Colony counts were also performed at each site to demonstrate that colony counts were in the expected range in most occasions.

- 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:*
Broth reference panels prepared according to the recommendations of the NCCLS standards were used to compare to the Sensititre® panel results. Testing was performed at 3 sites and included fresh and stock clinical isolates and a set of challenge organisms.

The following are the comparative results for the manual read method for *H. influenzae*.

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	Min	maj	vmj
Clinical	303	300	99%	277	274	99%	303	100%	0	N/A	0	0
Challenge	53	53	100%	47	47	100%	53	100%	0	N/A	0	0
Combined	356	353	99%	324	321	99%	356	100%	0	N/A	0	0

NA – No intermediate range therefore no minor errors possible

There were no vmj errors or maj errors in the *H. influenzae* study. The overall EA% of 99.0 and CA% of 100.0 are both very good. Since only susceptible category exists for *H. influenzae*, NCCLS recommends repeating of results that are not susceptible.

The percent no growth rate for the *H. influenzae* group is 0%.

The following are the comparative results for the manual read method for *S. pneumoniae*.

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	309	309	100%	297	297	100%	283	92%	1	26	0	0
Challenge	53	53	100%	52	52	100%	48	91%	1	5	0	0
Combined	362	362	100%	349	349	100%	331	91%	2	31	0	0

The following are the comparative results for the Automated Read method.

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	Min	maj	vmj
Clinical	309	309	100%	293	293	100%	290	94%	1	19	0	0
Challenge	53	53	100%	52	52	100%	50	94%	1	3	0	0
Combined	362	362	100%	345	345	100%	340	94%	2	22	0	0

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

maj-major discrepancies

vmj-very major discrepancies

min- minor discrepancies

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 result interpretation agrees exactly with the reference panel result interpretation. 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 *S. pneumoniae* were very similar to the manual readings with no observable trending. Although the number of resistant isolates tested was not that many, there was sufficient number of evaluable isolates tested. There were 31 min errors for the manual read method and 22 min errors for the autoread method. All min errors were in essential agreement. No vmj errors and maj errors were encountered in this group. The overall EA% of 100.0 and eval EA% of 100.0 for the manual read and overall EA% of 100.0 and eval EA% of 100.0 for the Autoread methods were both very good.

The percent no growth in the manual read method was 0% and the Autoread method was 0%.

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:

H. influenzae ≤ 0.5

S. pneumoniae ≤ 1 (S), 2(I), ≥ 4 (R)

The Interpretative criteria, QC isolates and the expected ranges are the same as recommended by the NCCLS. All values will be included in the package insert.

N. Conclusion:

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