

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

A. 510(k) Number:

K111615

B. Purpose for Submission:

Addition of Ceftaroline to the Sensititre non-fastidious Gram-negative MIC Susceptibility Plate and the Sensititre HP Susceptibility Plate.

C. Measurand:

Ceftaroline concentration of 0.015-64 ug/mL for the Sensititre MIC or BP Susceptibility Test System, and 0.015-32 ug/mL for the Sensititre HP MIC Susceptibility Plate.

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 Susceptibility Test Powder

2. Classification:

Class II

3. Product code:

JWY – Manual Antimicrobial Test System

LRG – Instrument for Autoreader and Interpretation of Overnight Susceptibility Systems

4. Panel:

83; Microbiology

H. Intended Use:

1. Intended use(s):

The Sensititre HP MIC Susceptibility plate with Ceftaroline (0.015-32 ug/ml) and the Sensititre 18-24 hour MIC Susceptibility system Test panel with Ceftaroline (0.015-64ug/ml) are intended for use with the Sensititre MIC or BP Susceptibility System.

2. Indication(s) for use:

The Sensititre HP MIC Susceptibility plate with Ceftaroline (0.015-32 ug/ml) and the Sensititre 18-24 hour MIC Susceptibility system Test panel with Ceftaroline (0.015-64ug/ml) are intended for use with the Sensititre MIC or BP Susceptibility System.

The Sensititre HP MIC Susceptibility plate is an *in vitro* diagnostic product for clinical susceptibility testing of fastidious isolates. The Sensititre 18-24 hour MIC or Breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of non-fastidious isolates.

This 510(k) is for the addition of Ceftaroline in the dilution range of 0.015-32 ug/ml to the Sensititre HP MIC Susceptibility plate for testing *Haemophilus influenzae* and the Sensititre 18-24 hour MIC panel in the dilution range of 0.015-64 ug/ml for testing Gram negative isolates.

The approved primary “Indications for Use” and clinical significance of Ceftaroline is for:

Facultative Gram-negative Microorganisms:

Escherichia coli

Klebsiella pneumoniae

Klebsiella oxytoca

Haemophilus influenzae

In vitro data, without clinical correlation is provided for:
Facultative Gram-negative Microorganisms:

Citrobacter koseri
Citrobacter freundii
Enterobacter cloacae
Enterobacter aerogenes
Moraxella catarrhalis
Morganella morganii
Proteus mirabilis

Ceftaroline is not active against Gram negative bacteria producing extended spectrum beta-lactamases (ESBLs) from the TEM, SHV or CTX-M families, serine carbapenemases (such as KPC), class B metallo-beta-lactamases or class C (AmpC cephalosporinases).

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

Use Sensititre AutoInoculator for inoculation.

I. Device Description:

The Sensititre 18-24 hours MIC or Breakpoint 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. A standardized suspension is prepared from colonies in pure growth and inoculated into the microtitre plate. After the indicated hours of incubation, the microtitre plate is examined for growth to determine the MIC using either the AutoReader or manually using the VIZION.

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.
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	16-20 hours
2. Antibiotic	Ceftaroline 0.015-32µg/mL (fastidious Gram negative rods) Ceftaroline 0.015-64µg/mL (non-fastidious Gram negative rods)	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-S19 and M100-S20: Performance Standards for Antimicrobial Susceptibility Testing;
3. CLSI M7-A8: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically.

L. Test Principle:

Sensititre Susceptibility plates are multi-well plastic microtitre plates that contain doubling dilution of antibacterial agents. Each plate includes antimicrobial agents at appropriate dilutions. Results can be read manually by visual reading of growth or automatically on an Autoreader via fluorescence. The Sensititre AutoReader System utilizes fluorescence technology to read the microbroth 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 isolates of *H. influenzae* (fastidious) and 26 isolates of non-fastidious Gram negative rods (6 *E.coli*, 5 *K. pneumoniae*, 3 *E. cloacae*, 3 *E. aerogenes*, 3 *P. mirabilis*, 1 *M. morgani*, 1 *C. freundii*, and 1 *C. koseri*). The isolates were tested one time at each of three sites for each reading method (Manual -VIZION, AutoReader). The testing resulted in the overall “best-case” reproducibility results of greater than 95% for both the Manual and AutoReader 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 *E. coli* ATCC 25922, and *H. influenzae* ATCC 49247 were tested against Ceftriaxone. Quality control was performed at three sites using both Manual and AutoRead® methods. All results were in acceptable range demonstrating that the Sensititre Susceptibility System can consistently produce quality control results in the recommended range for Ceftriaxone, for both the Manual and AutoReader methods.

QC Table

ORGANISM	Conc. (µg/mL)	Reference	Sensititre AutoReader	Sensititre Manual-VIZION
<i>E.coli</i> ATCC 25922 <i>Expected Range :</i> <i>0.03-0.12µg/mL</i>	0.015	0	0	0
	0.03	10	5	5
	0.06	46	34	31
	0.12	4	21	24
	0.25	0	0	0
<i>H. influenzae</i> ATCC 49247 <i>Expected Range :</i> <i>0.03-0.12µg/mL</i>	0.015	0	N/A	0
	0.03	0	N/A	0
	0.06	55	N/A	8
	0.12	5	N/A	52
	0.25	0	N/A	0

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.

Performance testing was conducted at three sites using 306 non-fastidious Gram negative rods of the Enterobacteriaceae family (75 *E. coli*, 59 *K. pneumoniae*, 11 *K. oxytoca*, 26 *E. aerogenes*, 26 *E. cloacae*, 21 *C. freundii*, 16 *C. koseri*, 23 *M. morgani*, 49 *P. mirabilis*) and 348 fastidious Gram negative rods (348 *H. influenzae*) totaling 654 isolates tested. Of the 654 isolates, 551 were fresh clinical isolates and 103 were stock challenge strains.

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

Tables A - C demonstrate performance based on essential agreement and category agreement of both clinical and challenge isolates. The data is stratified into groups of non-fastidious and fastidious Gram negatives and method of plate read (Manual or AutoRead).

Table A. Non-Fastidious Gram Negatives/ Manual Read	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	253	253	100	215	215	100	246	97	65	7	0	0
Challenge	53	52	99	41	40	99	51	97	22	2	0	0
Combined	306	305	99	256	255	99	297	97	87	9	0	0

Table B. Non-Fastidious Gram Negatives/ AutoRead	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	253	252	99	214	214	100	246	97	65	7	0	0
Challenge	53	53	100	43	43	100	52	98	22	1	0	0
Combined	306	257	99	257	257	100	298	97	87	8	0	0

Table C. Fastidious Gram Negatives/ Manual Read	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	298	297	99.7	30	30	100	298	100	6	0	0	0
Challenge	50	50	100	2	2	100	50	100	0	0	0	0
Combined	248	348	99.7	32	32	100	348	100	6	0	0	0

EA = Essential Agreement
R = Resistant Isolates
maj = major discrepancies

CA = Category Agreement
min = minor 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. The minor discrepancies which occurred 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:

Ceftaroline Interpretive Criteria:

Enterobacteriaceae (Community Acquired Bacterial Pneumoniae and skin isolates: ≤ 0.5 (S), 1 (I), ≥ 2 (R))

H. influenzae (Community Acquired Bacterial Pneumoniae isolates only): ≤ 0.12 (S)

The appropriate Quality Control ranges, recommended QC organisms and drug interpretive criteria are included in the package insert.

The FDA interpretive criteria, as listed above, were used to evaluate performance all data.

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.