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

A. 510(k) Number:

k111429

B. Purpose for Submission:

To obtain a substantial equivalence determination for the addition of Ceftaroline to the Sensititre HP MIC Susceptibility Plate and the Sensititre Gram-positive MIC Susceptibility Plate.

C. Measurand:

Ceftaroline concentrations of 0.004 - 8 µg/mL for Sensititre® HP MIC Susceptibility Plate and 0.06 - 64 µg/mL for Sensititre® MIC or BP Susceptibility Test System

D. Type of Test:

Antimicrobial Susceptibility Test (AST) Growth Based Detection Method

E. Applicant:

Trek Diagnostic Systems.

F. Proprietary and Established Names:

Sensititre 18 – 24 hour Susceptibility MIC Plates

G. Regulatory Information:

1. Regulation section:

   866.1640 Antimicrobial Susceptibility Test (AST) Powder

2. Classification:

   II

3. Product code:

   JWY - Manual Antimicrobial Susceptibility Test Systems

LRG- Instrument for AutoReader & Interpretation of Overnight Susceptibility Systems

4. Panel:

   83, Microbiology

H. Intended Use:

1. Intended use(s):

   The Sensititre® HP MIC Susceptibility Plate with Ceftaroline (0.004 - 8 µg/mL) and the Sensititre® 18-24 hour MIC Susceptibility System Test Panel with Ceftaroline (0.06 - 64 µg/mL) is intended for use with the Sensititre® MIC or BP Susceptibility Test System.

2. Indication(s) for use:

   The Sensititre® HP MIC Susceptibility Plate with Ceftaroline (0.004 - 8 µg/mL) and the Sensititre® 18-24 hour MIC Susceptibility System Test Panel with Ceftaroline (0.06 - 64 µg/mL) is intended for use with the Sensititre® MIC or BP Susceptibility Test 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 the Ceftaroline in the dilution range of 0.004- 8 µg/mL to the Sensititre HP MIC Susceptibility plate for testing *Streptococcus* spp. and the Sensititre 18-24 hour MIC panel in the dilution range of 0.06 - 64 µg/mL for testing gram positive isolates. The organisms which may be used for Ceftaroline susceptibility testing in this panel are:

   Facultative Gram-Positive Microorganisms:

   Staphylococcus aureus (including methicillin-resistant isolates)
   Streptococcus pyogenes
   Streptococcus agalactiae
   Streptococcus pneumoniae

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   The Sensititre AutoReader

I. Device Description:

The Sensititre HP MIC Susceptibility plate is an *in vitro* diagnostic product for clinical susceptibility testing of fastidious isolates.

The Sensititre 18-24 hours MIC or breakpoint Susceptibility System is an *in vitro* diagnostic product for clinical susceptibility testing of non fastidious isolates. It consists of a disposable plate containing dilutions of antimicrobials dried in individual wells. The test plate is inoculated with a standardized suspension of the organism to be tested. After the indicated hours of incubation, the plate is read for growth to determine the MIC either on an AutoReader or manually using the VIZION.

The MIC interpretive criteria for ceftaroline are as follows:

Organism	Susceptibility Interpretive Criteria (MIC* in µg/mL):		
	S	I	R
Staphylococcus aureus (includes methicillin-resistant isolates)	≤ 1	_	_
Streptococcus agalactiae	≤ 0.03	_	_
Streptococcus pyogenes	≤ 0.015	_	_
Streptococcus pneumoniae	≤ 0.25	_	_

*Currently there are no intermediate or resistant interpretive criteria for Ceftaroline. The current absence of data on resistant isolates precludes defining any categories other than "Susceptible." Isolates yielding MIC results suggestive of a "Non-Susceptible" category should be retested, and if the result is confirmed, the isolate should be submitted to a reference laboratory for further testing.
S = Susceptible
I = Intermediate
R = Resistant

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Siemens' MicroScan Dried Gram-positive MIC panels

2. Predicate 510(k) number(s):

   k010159

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use		
Isolates	Isolated colonies from culture	Same
Incubation Temperature	35°	Same
Inoculation	Isolated colonies from culture used	Same
Result	MIC	MIC
Incubation Atmosphere	Aerobic	Aerobic
Type of Test	Automated or Manual	Same

Differences		
Item	Device	Predicate
Product Name		
Incubation	18-24 hours	16-20 hours
Antibiotic	Ceftaroline 0.004 - 8 µg/ml and 0.06-8 µg/ml	Gatifloxacin 0.004 - 32 µg/ml

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

Guidance for Industry and FDA- Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; August 28, 2009.

Clinical and Laboratory Standards Institute (CLSI) Methods for Dilution Antimicrobial Susceptibility Tests for Bacterial That Grow Aerobically, Approved Standard- 8th Edition, Document M07-A8

CLSI Performance Standards for Antimicrobial Susceptibility Testing Approved Standard-, 19th Informational Supplement, Document M100-S19

L. Test Principle:

Sensititre susceptibility plates are multi-well plastic microtiter plates that contain doubling dilutions of antibacterial agents. Each plate is dosed with antimicrobial agents at appropriate dilutions. Results can be read manually by visual reading of growth or automatically on an AutoReader using fluorescence. The Sensititre AutoReader system utilizes fluorescence technology which 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 (f1uorogenic) substrate. The substrate can be 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. The non-

fluorescent substrate is prepared by conjugating a fluorescent compound to the specific enzyme substrates with a bond, which prevents fluorescence (i.e. the fluorophore is quenched in this state). Enzymatic action of the bacterial surface enzymes on the specific substrates cleaves this bond releasing the fluorophore which is now capable of fluorescence. The amount of fluorescence detected is directly related to the activity of the bacterial surface enzymes and, therefore, to bacterial growth. The MIC is determined by observing the lowest dilution of the antimicrobial agent that inhibits growth of the organism.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

   Reproducibility studies were conducted at three study sites. One study evaluated 34 isolates of *S. aureus.* The other study evaluated 25 Streptococcus species (15 *S. pneumoniae*, 6 *S. pyogenes* and 4 *S. agalactiae*).

   Reproducibility was calculated as the percent of results for the combined sites which were within +/- one doubling dilution of the mode MIC value for all sites. Each reproducibility organism was tested once on the TREK Test panel. Panels were read on the AutoReader and manually on the VIZION.

   All the MIC values obtained were on-scale except for three instances with *S. aureus* and two instances with *Streptococcus* species where ceftaroline gave "off-scale" results. For reproducibility calculations, off-scale values are handled in two ways; "best case" and "worst case" scenarios. Best case calculation for reproducibility assumes the off-scale result is within one well from the mode MIC value. Worst case calculation for reproducibility assuming the off-scale result is greater than one well from the mode MIC value.

   The overall best case and worst case reproducibility values for VIZION and AutoRead for each organism group are shown below.

   S. aureus

Read Method	% Reproducible (Best case-all sites)	% Reproducible (Worst case-all sites)
VIZION	100	97.1
AutoReader	100	97.1

Streptococci

Read Method	% Reproducible (Best case-all sites)	% Reproducible (Worst case-all sites)
VIZION	98.7	93.3
AutoReader	98.7	92.0

b. *Linearity/assay reportable range:*

Not applicable

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

The recommended Quality Control (QC) isolates were tested a sufficient number of times with acceptable results with the reference method. The ceftaroline panel test results demonstrate that the system can produce QC results in the recommended range.

Ceftaroline QC data from three combined sites is shown below. Each isolate was tested 20 times at each site.

QC Organism	MIC range (μg/mL)	MIC value (μg/mL)	Broth Micro Dilution Reference Frequency	AutoReader	Manual Read
S. aureus ATCC 29213	0.12-0.5	0.06	0	0	0
		0.12	50	0	4
		0.25	50	60	54
		0.5	1	0	2
		1	0	0	0
S. pneumoniae ATCC 49619	0.008-0.03	0.004	0	0	0
		0.008	41	10	10
		0.015	18	39	32
		0.03	1	11	12
		0.06	0	0	0

All QC values were in the expected range.

Inoculum density checks showed acceptable results for QC organisms, as well as a select number of challenge and clinical isolates. All results were within the expected range.

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 Sensititre HP MIC Susceptibility Plate with Ceftaroline (0.004 - 8 µg/mL) and the Sensititre® 18-24 hour MIC Susceptibility System Test Panel with Ceftaroline (0.06 - 64 µg/mL) results were compared to the respective reference method as recommended in the CLSI standard M7-A6. Testing of the reference method and the Sensititre panels was performed at the same time. Sensititre ceftaroline panel and CLSI reference broth microdilution results were compared based on the guidelines provided in the AST Guidance Document. The % Essential Agreement (EA) and % Category Agreement (CA) results are acceptable.

A total of 456 fresh clinical isolates were evaluated at three clinical study sties. There were 142 *Staphylococcus aureus,* 76 *Streptococcus pyogenes,* 86 *Streptococcus agalactiae,* and 152 *Streptococcus pneumoniae* isolates.

A total of 77 stock challenge isolates were also included and were tested at one site. There were 27 *Staphylococcus aureus,* 13 *Streptococcus pyogenes,* 12 *Streptococcus agalactiae,* and 25 *Streptococcus pneumoniae* challenge isolates.

Combined results from clinical and challenge studies demonstrated an overall EA of 99.4% (529/532) and an overall CA of 99.6% (531/532) for AutoReader and an overall EA of 100% and an overall CA of 99.6% (531/532) for manual read (VIZION).

According the approved drug label for ceftaroline, only a susceptible interpretive category is defined. There are no intermediate or resistance interpretive categories. In this study, there were three cases in which Sensititre ceftaroline panel results gave a categorical interpretation that was not in agreement with the reference broth dilution MIC (Reference interpretation was “susceptible” while the Sensititre ceftaroline panel interpretation was “non-susceptible). Three isolates (2 *S. aureus* and 1 *S. pneumoniae*) were noted to have MIC values outside the susceptible category for ceftaroline by the Sensititre method but those were susceptible by the reference method.

Labeling will recommend that isolates yielding test results suggestive of a "Non-

Susceptible" category should be retested, and if the result is confirmed, the isolate should be submitted to a reference laboratory for further testing.

The performance evaluation summary of essential and category agreement results for challenge and clinical strains is shown in the following tables.

AutoReader

Clinical data

Organism group	Total Tested	#EA	%EA Total	Total Evaluable	#EA of Evaluable	%EA Evaluable	#CA	%CA	#NS	#vmj	#maj	#min
S. aureus	142	142	100.0%	141	141	100.0%	141	99.3%	2	0	1	0
S. pyogenes	76	76	100.0%	18	18	100.0%	76	100.0%	0	0	0	0
S. agalactiae	86	82	96.5%	82	79	96.3%	86	100.0%	0	0	0	0
S. pneumoniae	151	151	100.0%	99	99	100.0%	151	100.0%	2	0	0	0
Total	455	452	99.3%	340	337	99.1%	454	99.8%	4	0	1	0
Challenge												
S. aureus	27	27	100.0%	27	27	100.0%	27	100.0%	0	0	0	0
S. pyogenes	13	0	100.0%	0	0	N/A	13	100.0%	0	0	0	0
S. agalactiae	12	12	100.0%	12	12	100.0%	12	100.0%	0	0	0	0
S. pneumoniae	25	25	100.0%	25	25	100.0%	25	100.0%	0	0	0	0
Total	77	64	100.0%	64	64	100.0%	77	100.0%	0	0	0	0
Clinical and Challenge Combined												
Total	532	529	99.4%	404	401	100.0%	531	99.6%	4	0	1	0

VIZION

Clinical data

Organism group	Total Tested	#EA	%EA Total	Total Evaluable	#EA of Evaluable	%EA Evaluable	#CA	%CA	#NS	#vmj	#maj	#min
S. aureus	142	142	100.0%	141	141	100.0%	141	99.3%	2	0	1	0
S. pyogenes	76	76	100.0%	18	18	100.0%	75	98.7%	0	0	1	0
S. agalactiae	86	86	100.0%	82	79	96.3%	86	100.0%	0	0	0	0
S. pneumoniae	152	152	100.0%	100	100	100.0%	152	100.0%	1	0	0	0
Total	456	456	100.0%	341	338	100.0%	454	99.6%	3	0	2	0
Challenge												
S. aureus	27	27	100.0%	27	27	100.0%	27	100.0%	0	0	0	0
S. pyogenes	13	13	100.0%	0	0	N/A	13	100.0%	0	0	0	0
S. agalactiae	12	12	100.0%	12	12	100.0%	12	100.0%	0	0	0	0
S. pneumoniae	25	25	100.0%	25	25	100.0%	25	100.0%	0	0	0	0
Total	77	77	100.0%	64	64	100.0%	77	100.0%	0	0	0	0
Clinical and Challenge Combined												
Total	533	533	100.0%	405	402	99.3%	531	99.6%	3	0	2	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:

Organism	Susceptibility Interpretive Criteria (MIC* in µg/mL):		
	S	I	R
Staphylococcus aureus (includes methicillin-resistant isolates)	≤ 1	_	_
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Streptococcus pyogenes	≤ 0.015	_	_
Streptococcus pneumoniae	≤ 0.25	_	_

*Currently there are no intermediate or resistant interpretive criteria for Ceftaroline. The current absence of data on resistant isolates precludes defining any categories other than "Susceptible." Isolates yielding MIC results suggestive of a "Non-Susceptible" category should be retested, and if the result is confirmed, the isolate should be submitted to a reference laboratory for further testing.

N. Proposed Labeling:

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.