

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

A. 510(k) Number:

K083606

B. Purpose for Submission:

To add Doxycycline on the Sensititre® 18-24 hour MIC or Breakpoint (BP) panel for testing appropriate gram negative and gram positive organisms.

C. Measurand:

Doxycycline 0.03 – 16µg/mL

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 Test Powder

2. Classification:

Class II

3. Product code:

JWY – Manual reading of AST of >16 hrs incubation
LRG – Automated readings of AST of >16 hrs incubation

4. Panel:

Microbiology

H. Intended Use:

1. Intended use(s):

The Sensititre® 18 – 24 hour MIC or Breakpoint Susceptibility System is an *in-vitro* diagnostic product for clinical susceptibility testing of non-fastidious Gram negative and Gram positive organisms.

2. Indication(s) for use:

This 510(k) is for addition of Doxycycline in the dilution range of 0.03 – 16µg/mL for testing Gram negative and Gram positive isolates on the Sensititre® 18 – 24 hour Susceptibility system. The approved primary “Indications for Use” and clinical significance of Doxycycline is for: Aerobic and facultative Gram negative and Gram positive microorganisms:

Escherichia coli,

Klebsiella species

Enterobacter aerogenes

Acinetobacter species,

Streptococcus pyogenes

Enterococcus species (*faecalis* and *faecium*)

*Staphylococcus aureus**

* Doxycycline is not the drug of choice in the treatment of any type of staphylococcal infection.

3. Special conditions for use statement(s):

For prescription use only

Use an alternative testing method with lysed horse blood to test *S. pyogenes* when no growth or poor growth is observed in the positive growth control well.

The ability of this Sensititre plate to detect resistance to doxycycline in *S. pyogenes* is unknown because resistant *S. pyogenes* organisms were not tested in comparative studies.

4. Special instrument requirements:

Use Sensititre AutoInoculator for inoculation

I. Device Description:

The Sensititre Susceptibility Systems is a micro-version of the classic broth dilutions method and can provide both qualitative and quantitative susceptibility results in a dried plate format. Each micro-dilution plate is dosed with antimicrobial agents at appropriate dilutions and then dried.

The isolates to be tested must be a pure culture and be preliminarily identified as gram positive or gram negative.

Colonies are then suspended in broth, and equated to a 0.5 McFarland with the recommendation to use Sensititre nephelometer. A further dilution is made into an AST broth, a cation-adjusted formulation of Mueller-Hinton broth containing Tween 80. The AST inoculum final concentration is 5×10^5 CFU/ml. A volume of 50µl of broth suspension is transferred to each well of the microtiter plate by **the Sensititre AutoInoculator**. After inoculation, plates are sealed with an adhesive seal, incubated at 34 -36°C for 18 – 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):

Dade MicroScan®

2. Predicate K number(s):

K010159

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
1. Intended Use	The Sensititre® 18 – 24 hour MIC or Breakpoint Susceptibility System is an in-vitro diagnostic product for clinical susceptibility testing of 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. Result Reported	Report results as minimum inhibitory concentration (MIC) and interpretation (SIR)	Same

Similarities		
Item	Device	Predicate
5. Type of Test	Automated or Manual	Same

Differences		
Item	Device	Predicate
1. Incubation Time	18-24 hours	16-20 hours
2. Antibiotic	Doxycycline 0.03 – 16ug/mL	Gatifloxacin 0.004 – 32ug/mL
3. Technology	Fluorescence detection of growth	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-S18) “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 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 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 substrate already added to the plate. Enzymatic action of the bacterial surface enzymes on the specific substrates cleaves this bond releasing the fluorophore which is now capable of fluorescing. 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 negative and 25 Gram positive isolates appropriate for testing with doxycycline. These were tested one 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, Stability, Expected values (controls, calibrators, or methods):

The FDA and CLSI recommended Quality Control (QC) isolates, *S. aureus* 29213, *E. faecalis* 29212, and *E. coli* 25922, were tested daily. QC was also performed at all sites using both manual and autoread methods. The mode of the manual read of the test device was similar to that of the reference but one dilution lower with the autoread. All results are within the expected range. 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.

This non-fastidious Sensititre plate does not utilize lysed horse blood in its test procedure. Therefore, *S. pneumoniae* ATCC 49619 can not be used as the QC organism for the *Streptococcus pyogenes*. The recommended QC organism for this non-fastidious Sensititre plate is *S. aureus* ATCC 29213.

Doxycycline QC Table

<i>ORGANISM</i>	Conc ug/mL	Sensititre® Autoread	Sensititre® manual	Reference
<i>E. coli</i> ATCC 25922 Expected Range : 0.5 – 2 µg/mL	0.5	48	39	21
	1	12	20	39
	2	0	1	0
<i>S. aureus</i> ATCC 29213 Expected Range : 0.12 – 0.5 µg/mL	0.12	50	48	37
	0.25	7	13	22
	0.5	1	0	1
<i>E. faecalis</i> ATCC 29212 Expected Range : 2 – 8 µg/mL	2	38	5	4
	4	18	53	52
	8	1	0	1

The Sensititre Nephelometer was used at each site to standardize the inoculum and it was calibrated every time it was switched on.

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 935 Gram negative and Gram positive isolates at three sites which included 800 fresh clinical and 135 stock challenge isolates. The growth rate for the manual and automated read methods was greater than 90%. The performance evaluations are reflected below.

Summary table for Gram Negatives (Manual Read)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#R	min	maj	vmj
Clinical	458	456	99.6	321	321	100	439	96.1	166	19	0	0
Challenge	66	66	100	41	41	100	66	100	26	0	0	0
Total Isolates	524	522	99.8	362	362	100	505	98.1	192	19	0	0

Summary table for Gram Negatives (Automated Read)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#R	min	maj	vmj
Clinical	458	454	99.1	322	320	99.4	442	96.6	168	16	0	0
Challenge	66	66	100	41	41	100	66	100	27	0	0	0
Total Isolates	524	520	99.5	363	361	99.7	508	98.3	195	16	0	0

Summary table for Gram Positives (Manual Read)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#R	min	maj	vmj
Clinical	448	448	100	436	436	100	438	97.5	28	10	0	0
Challenge	81	81	100	75	75	100	77	95.1	9	4	0	0
Total Isolates	529	529	100	511	511	100	515	97.4	37	14	0	0

Summary table for Gram Positives (Automated Read)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA%	#R	min	maj	vmj
Clinical	447	444	99.2	437	434	99.2	436	97.0	25	11	0	0
Challenge	81	79	97.5	73	73	100	76	93.8	8	5	0	0
Total Isolates	528	510	98.1	510	507	99.4	512	96.7	33	16	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. 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”.

Auto-read results were very similar to the manual readings. There were no vmj or maj errors. The combined (clinical + challenge) EA and CA were 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:

≤ 4 (S), 8 (I), ≥ 16 (R)

FDA interpretive criteria have been used to evaluate performance data.

N. Proposed Labeling:

The expected value range, interpretive criteria and QC are included in the package insert. 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.