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

A. 510(k) Number:

k073424

B. Purpose for Submission:

To add Doripenem on the Sensititre® 18 – 24 hour MIC or Breakpoint (BP) panel for testing appropriate gram negative organisms

C. Measurand:

Doripenem 0.008 – 64 µg/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 MIC or BP Susceptibility plates

G. Regulatory Information:

1. Regulation section:

   866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

   Class 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:

   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 isolates comprising of *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and other non- *Enterobacteriaceae*.

2. Indication(s) for use:

   This 510k will include Doripenem in the dilution range of 0.008 – 64 μg/mL for testing *Acinetobacter baumannii, Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, Citrobacter freundii, Enterobacter cloacae, Enterobacter aerogenes, Klebsiella oxytoca, Morganella morganii, and Serratia marcescens* on the Sensititre® 18 – 24 hour MIC or BP panel.

3. Special conditions for use statement(s):

   Prescription use

4. Special instrument requirements:

   Not applicable

I. Device Description:

The Sensititre® MIC or BP Susceptibility system is a microversion of the classic broth dilution methods and can provide both qualitative and quantitative susceptibility results. Each microdilution plate is dosed with antimicrobial agents at appropriate dilutions then dried. 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):

   Pasco MIC and MIC/ID Panels

2. Predicate K number(s):

   K033119

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	an *in vitro* diagnostic product for clinical susceptibility testing of gram negative and gram positive organisms.	same
Inoculum	Prepared from colonies using the direct inoculation method	Prepared from colonies using the direct inoculation method
Inoculation method	Direct equated to a 0.5 McFarland	Direct equated to a 0.5 McFarland

Differences		
Item	Device	Predicate
Type panel	Dried antibiotics	100 µl/well frozen
Incubation	18-24 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-S17) "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 form 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 cleave 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 isolates appropriate for testing with doripenem. 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 recommended Quality Control (QC) isolates, *E. coli* ATCC 25922, and *P. aeruginosa* ATCC 27853, were tested daily. Quality Control was also performed at all sites using both manual and autoread methods. Although the modes for these two QC organisms are different for the test device and reference method, results are still 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.

   Quality Control Table for Gram Negative Isolates

ORGANISM	**Conc ug/mL**	**Sensititre® Autoread**	**Sensititre® manual**	**Reference**
E. coli ATCC 25922 Expected Range : 0.015 – 0.06 µg/mL	0.015	56	48	18
	0.03	6	13	35
	0.06	0	1	9
P. aeruginosa ATCC 27853 Expected Range : 0.12 – 0.5 µg/mL	0.12	0	0	25
	0.25	32	32	14
	0.5	28	28	21

Nephelometer was used at each site to standardize the inoculum and it was calibrated each 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 484 gram negative isolates at three sites which included fresh and stock clinical isolates and a set of challenge organisms. The comparison resulted in the following performance evaluations as reflected below. Results of each organism group cannot be combined as they have different interpretive criteria.

Summary Table for **Gram Negative Panel** (**Manual Read Method**)

	EA Tot	**EA N**	**EA %**	**Eval EA Tot**	**Eval EA N**	**Eval EA %**	**CA N**	**CA %**	**#NS**
Enterobacteriaceae	**328**	**326**	**99.7**	**327**	**325**	**99.7**	**328**	**100**	**0**
A. baumanii	**60**	**60**	**100**	**59**	**59**	**100**	**60**	**100**	**31**
***Acinetobacter* spp.**	**28**	**28**	**100**	**28**	**28**	**100**	**-**	**-**	**0**
P. aeruginosa	**68**	**68**	**100**	**68**	**68**	**100**	**68**	**100**	**8**

Summary Table for **Gram Negative Panel** (**Auto Read Method**)

	EA Tot	**EA N**	**EA %**	**Eval EA Tot**	**Eval EA N**	**Eval EA %**	**CA N**	**CA %**	**#NS**
Enterobacteriaceae	**328**	**325**	**99.5**	**327**	**324**	**99.5**	**328**	**100**	**0**
A. baumanii	**60**	**60**	**100**	**59**	**59**	**100**	**60**	**100**	**30**
***Acinetobacter* spp.**	**28**	**28**	**100**	**28**	**28**	**100**	**-**	**-**	**0**
P. aeruginosa	**68**	**68**	**100**	**68**	**68**	**100**	**68**	**100**	**9**

EA - Essential Agreement
CA - Category Agreement
NS – Not Susceptible

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".

There are no intermediate or resistant breakpoints for *Enterobacteriaceae, Acinetobacter baumannii,* and *Pseudomonas aeruginosa* therefore categorical errors are not possible. A limitation statement has been added to the package insert to address the absence of intermediate or resistant isolates.

There is no category agreement for *Acinetobacter* spp. because it does not have FDA-approved interpretative criteria or indications.

The growth rate for the automated and manual read method is greater than 90%.

Autoread results were very similar to the manual readings. There appears to be a slight trend observed with the *Enterobacteriaceae* group, and the *P. aeruginosa* group in the clinical studies. This observation was also noted in the QC results. The test device appears to be more susceptible with the *Enterobacteriaceae* group but appears to be more resistant than the reference method in the *P. aeruginosa* group.

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:

Enterobacteriaceae	≤0.5
P. aeruginosa	≤2
Acinetobacter baumannii	≤1

*** Limitation statement:** The current absence of resistant isolates precludes defining any category other than "Susceptible". Isolates yielding MIC results suggestive of "Nonsusceptible" category should be subjected to additional testing.

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