

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

A. 510(k) Number:

K131275

B. Purpose for Submission:

To obtain a substantial equivalence determination for the addition of Tigecycline to the MicroScan Dried Gram-Positive MIC/Combo Panel

C. Measurand:

Tigecycline concentrations of 0.12 - 8 mcg/mL

D. Type of Test:

Antimicrobial Susceptibility Test growth-based detection method

E. Applicant:

Siemens Healthcare Diagnostics

F. Proprietary and Established Names:

MicroScan Dried Gram-Positive MIC/Combo Panels with Tigecycline (0.12 - 8 mcg/mL)

G. Regulatory Information:

1. Regulation section:

866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

II

3. Product code:

JWY – Manual Antimicrobial Susceptibility Test Systems

LRG – Instrument for Auto Reader and Interpretation of Overnight Susceptibility

LTT – Panels, Test, Susceptibility, Antimicrobial

LTW – Susceptibility Test Cards, Antimicrobial

4. Panel:

83, Microbiology

H. Intended Use:

1. Intended use(s):

For use with MicroScan Dried Gram Positive MIC/Combo, Dried Gram Positive Breakpoint Combo and Dried Gram Positive ID Type 2 or 3 Panels. MicroScan Positive panels are designed for use in determining antimicrobial agent susceptibility and/or identification to the species level of rapidly growing aerobic and facultative gram-positive cocci, some fastidious aerobic gram-positive cocci and *Listeria monocytogenes*. Refer to Limitations of Procedure Section for use with fastidious streptococci.

2. Indication(s) for use:

The MicroScan Dried Gram-Positive MIC/Combo Panel is used to determine quantitative and/or qualitative antimicrobial agent susceptibility of colonies grown on solid media of rapidly growing aerobic and facultative anaerobic gram-positive bacteria. After inoculation, panels are incubated for 16-20 hours at 35° C ± 1° C in a non-CO₂ incubator and read either visually or with MicroScan instrumentation, according to the Package Insert.

This particular submission is for the addition of the antimicrobial Tigecycline at concentrations of 0.12 - 8 mcg/mL to the test panel. MicroScan Dried Gram-Positive Tigecycline is a qualitative test.

Tigecycline has been shown to be active against the organisms listed below according to the FDA label for the antimicrobial.

Active *in vitro* and in clinical infections:

Enterococcus faecalis (vancomycin-susceptible isolates)

Staphylococcus aureus (methicillin-susceptible and -resistant isolates)

Active *in vitro* but clinical significance unknown:

Staphylococcus epidermidis (methicillin-susceptible and -resistant isolates)

3. Special conditions for use statement(s):

For prescription use only.

4. Special instrument requirements:

MicroScan panels can be read either manually, or automatically on the autoScan-4 or the WalkAway instrument systems.

I. Device Description:

MicroScan Dried Gram-Positive MIC/Combo Panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility of colonies grown on solid media of rapidly growing aerobic and facultative anaerobic gram-positive bacteria.

The antimicrobial susceptibility tests are miniaturizations of the broth dilution susceptibility test that have been diluted in broth and dehydrated. Antimicrobial agents are diluted in broth to concentrations bridging the range of clinical interest. The MicroScan Dried Gram-Positive Panel evaluated in this submission contained ten doubling dilutions of Tigecycline from 0.015 to 8 mcg/mL.

Panels are rehydrated with water after inoculation with a standardized suspension of the organism. After incubation in a non-CO₂ incubator for 16-20 hours, the minimum inhibitory concentration (MIC) for the test organism is read by determining the lowest antimicrobial concentration showing inhibition of growth. The panels can be read manually using the MicroSCAN Microdilution Viewer or on automated MicroSCAN instrumentation (autoSCAN-4 or WalkAway systems).

Tigecycline is a glycycline antibiotic and a derivative of Tetracycline. Tigecycline inhibits protein synthesis by preventing t-RNA from binding to the ribosome. This prevents incorporation of amino acid residues into elongating peptide chains. Tigecycline is indicated for treatment of complicated bacterial skin and skin structure infections, complicated intra-abdominal infections and community-acquired pneumonia, when caused by designated susceptible bacteria.

Table 1: Interpretive Criteria for Tigecycline

Organism	Susceptibility Interpretive Criteria (MIC in µg/mL)		
	S	I ^a	R ^a
<i>Staphylococcus aureus</i> (methicillin-susceptible and - resistant isolates)	≤ 0.5	N/A	N/A
<i>Enterococcus faecalis</i> (vancomycin-susceptible isolates)	≤ 0.25	N/A	N/A

^a There are no intermediate or resistant interpretive criteria for Tigecycline. The current absence of resistant isolates precludes defining any results other than “Susceptible.” Isolates yielding MIC results suggestive of the “Nonsusceptible” category should be submitted to a reference laboratory for further testing.

S = Susceptible; I = Intermediate; R = Resistant; N/A = Not Applicable

J. Substantial Equivalence Information:

1. Predicate device name(s):

MicroScan Dried Gram-Positive MIC/Combo Panels - Linezolid

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

K003619

3. Comparison with predicate:

Table 2: Comparison with the Predicate Device

Similarities		
Item	<u>Device</u> MicroScan Dried Gram-Positive MIC/Combo Panels - Tigecycline	<u>Predicate</u> MicroScan Dried Gram-Positive MIC/Combo Panels - Linezolid
Intended Use	Determination of susceptibility to Tigecycline with gram-positive bacteria	Determination of susceptibility to Linezolid with gram-positive bacteria
Technology	Overnight microdilution MIC susceptibility tests	Same
Specimen	Isolated colonies from cultures	Same
Inoculum	Prepared using turbidity and Prompt methods	Same
Incubation Temperature	35 °C ± 1°C	Same
Incubation Atmosphere	Aerobic	Same
Incubation Time	16 – 20 hours	Same
Reading Method	Automated or Manual	Same

Differences		
Item	Device	Predicate
Antibiotic	Dried Tigecycline 0.12 - 8 µg/mL	Dried Linezolid 0.06 – 64 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 Bacteria That Grow Aerobically; Approved Standard – Ninth Edition. CLSI document M07-A9. 2012.

L. Test Principle:

The antimicrobial susceptibility tests are miniaturizations of the broth dilution susceptibility test which have been dehydrated. Various antimicrobial agents are diluted in Mueller-Hinton broth with calcium and magnesium to concentrations bridging the range of clinical interest. After inoculation and rehydration with a standardized suspension of organism and incubation at 35° C for 16-20 hours, the minimum inhibitory concentration (MIC) or a qualitative susceptibility (Susceptible, Intermediate or Resistant) for the test organism is determined by observing the lowest antimicrobial concentration showing inhibition of growth.

M. Performance Characteristics:

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility data for nine *S. aureus* isolates (eight challenge isolates and one QC strain) including six methicillin-susceptible and three methicillin-resistant isolates, and three *E. faecalis* isolates (two challenge isolates and one QC strain) were generated at 3 clinical trial sites. Organism selection was based on the intended use of the antimicrobial. Each strain was tested at each site in triplicate over three days using 2 inoculation methods (Turbidity and Prompt) and 3 reading methods (manual, WalkAway Instrument and autoSCAN-4 Instrument).

The mode of the test panel MIC results was determined for each isolate. MIC results at each site were compared to the mode value for each strain. Results were considered in agreement if the test panel MIC was equal to or within ± 1 dilution of the mode for that isolate. Agreement was calculated assuming any off-scale results were within one well from the mode (best case) and by assuming any off-scale results were greater than one well from the mode (worst case). Data were analyzed for all 10 dilutions of Tigecycline (0.015 - 8 mcg/mL). The agreement was calculated for each site and for the three sites combined.

All MIC results were on-scale for both inoculation methods and all reading methods; therefore, best case and worst case scenarios were identical.

For each site and for all sites combined, agreement within 1 \pm dilution from the mode for all inoculation and reading methods was 100.0%. The reproducibility study results are acceptable.

Table 3: Reproducibility of Tigecycline MIC Testing with *S. aureus* (Methicillin-Susceptible and Methicillin-Resistant and *E. faecalis* (Vancomycin Susceptible)

(All Sites Combined)

Reading Method	Inoculation Method	
	Turbidity ^a	Prompt ^a
Manual	324/324 (100%)	324/324 (100%)
WalkAway	324/324 (100%)	324/324 (100%)
autoSCAN-4	324/324 (100%)	324/324 (100%)

^a Number of results within ± 1 dilution of the mode/total number of result (%)

b. Linearity/assay reportable range:

Not applicable

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

Quality Control: The recommended quality control isolates, *S. aureus* ATCC 29213 and *E. faecalis* ATCC 29212 were tested a sufficient number of times at all testing sites using both the Turbidity and Prompt inoculation methods and all three reading methods (Manual, WalkAway, autoScan4). Acceptable results were obtained for all inoculation and reading methods (≥ 98.5 % of results within the acceptable range). The Tigecycline quality control test results demonstrate that the system can produce QC results within the expected range.

Data was analyzed for all 10 dilutions of Tigecycline contained in the test panels (0.015 - 8 mcg/mL).

Dilutions of 0.12 - 8 $\mu\text{g/mL}$ will be included in the marketed panels; this dilution range will not cover the entire acceptable MIC range of the QC organisms as noted by the CLSI and the FDA. The sponsor included the following footnote to the Dried Gram Pos Antimicrobial Quality Control Table: “The MicroScan Gram Positive panel does not include the full CLSI/FDA-recommended dilution ranges for QC testing of Tigecycline.”

Table 4: QC Results Obtained for All Inoculation and Read Methods at Three Testing Sites^a

	MIC Range ($\mu\text{g/mL}$)	MIC Value ($\mu\text{g/mL}$)	Turbidity Inoculation Method			Prompt Inoculation Method		
			Manual Read	WAW Read	AS-4 Read	Manual Read	WAW Read	AS-4 Read
<i>S. aureus</i> ATCC 29213	0.03 - 0.25	≤ 0.015	0	0	0	0	0	0
		0.03	0	0	0	0	0	0
		0.06	1	0	0	3	1	2
		0.12	67	63	67	18	15	39
		0.25	39	8	4	83	54	29
		0.5	0	0	0	3	0	0
		1	0	0	0	0	0	0
2	0	0	0	0	0	0		

		4	0	0	0	0	0	0
		8	0	0	0	0	0	0
		>8	0	0	0	0	0	0

<i>E. faecalis</i> ATCC 29212	0.03– 0.12	≤ 0.015	0	0	0	0	0	0
		0.03	1	0	0	0	0	0
		0.06	98	71	70	72	68	67
		0.12	10	0	1	33	1	2
		0.25	0	0	0	2	1	1
		0.5	0	0	0	0	0	0
		1	0	0	0	0	0	0
		2	0	0	0	0	0	0
		4	0	0	0	0	0	0
		8	0	0	0	0	0	0
		>8	0	0	0	0	0	0

^a WAW = WalkAway read method; AS-4 = autoSCAN-4 read method

Table 5: QC Result Summary for All Inoculation and Read Methods^{a, b}

	Turbidity Inoculation Method			Prompt Inoculation Method		
	Manual Read	WAW Read	AS-4 Read	Manual Read	WAW Read	AS-4 Read
<i>S. aureus</i> ATCC 29213	107/107 (100)	71/71 (100)	71/71 (100)	104/107 (97.2)	70/70 (100)	70/70 (100)
<i>E. faecalis</i> ATCC 29212	109/109 (100)	71/71 (100)	71/71 (100)	105/107 (98.1)	69/70 (98.6)	69/70 (98.6)

^a Number of test panel results in range/total number of results (%)

^b WAW = WalkAway read method; AS-4 = autoSCAN-4 read method

Growth Failure Rate: All isolates tested during the clinical (efficacy) trials grew in both the frozen reference panel and the dried MicroScan panels.

Inoculum Density Check: The MicroScan Turbidity Meter (K864542) was used to spectrophotometrically standardize the inocula for clinical isolates. The acceptable turbidity range was 0.08 ± 0.02 (equivalent to a 0.5 McFarland barium sulfate turbidity standard); the digital reading was recorded for each organism tested ensuring that the reading was in the acceptable range.

Data was also collected during the Reproducibility phase for inocula prepared using the Prompt inoculum preparation method. Colony counts were performed for each

reproducibility strain and once per week for the *S. aureus* QC strain. The colony counts provided for the Prompt method are comparable to counts observed in previous clinical trials.

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 MicroScan Dried Gram-Positive MIC/Combo Panel with Tigecycline results were compared to results obtained using a frozen broth microdilution reference panel at three testing sites in the U.S. The reference panel was prepared according to CLSI M07-A9 guidelines except for the use of Pluronic-F in the inoculum water for the reference panel. Both the MicroScan and reference panels contained ten dilutions of Tigecycline that were appropriate for the interpretive breakpoints of the drug. For each organism tested, MIC panels were inoculated using the same standardized suspension, further diluted into 25 mL of water with either Pluronic-D (for the MicroScan dried panels) or Pluronic-F (for the frozen reference panels). Performance was analyzed using FDA breakpoints for Tigecycline (except for *S. epidermidis*, for which no FDA breakpoints exist), and results were compared based on the guidelines provided in the Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems.

A validation study was performed to demonstrate equivalence between reference panels inoculated with organisms suspended in water supplemented with Pluronic-F and reference panels inoculated with autoclaved distilled water without Pluronic-F. Eight isolates of *S. aureus* and two isolates of *E. faecalis* were tested. The essential agreement of MICs obtained using Pluronic-F as the diluent as compared to MICs obtained using autoclaved distilled water as the diluent was 100%.

A total of 399 clinical isolates were tested at three clinical sites. The organisms tested consisted of *E. faecalis*, vancomycin-susceptible (47 fresh isolates), *S. aureus* (305 isolates including 288 fresh and 17 stock isolates) and *S. epidermidis* (47 fresh isolates). Clinical isolates were evaluated using the turbidity inoculation method and read manually.

A total of 75 challenge strains were tested at one clinical site. Challenge strains included 59 isolates of *S. aureus* (41 MSSA, 15 MRSA, 3 SA) and 16 isolates of vancomycin-susceptible *E. faecalis*. Challenge strains were selected from a variety of sources and had on-scale MICs as determined by the reference method. Results obtained with tigecycline in the MicroScan panels were compared to expected results. Expected results were determined from the mode result obtained from 18 replicates of each isolate tested using a frozen reference panel prepared using CLSI M07-A9 guidelines. Challenge isolates were tested using inocula prepared using both the turbidity method and the Prompt Inoculation System. MIC results were read using three methods: manual read, WalkAway Instrument and autoSCAN-4 Instrument.

In the FDA pharmaceutical labeling Tigecycline is listed as being active *in vitro* against *S. epidermidis* but the clinical significance unknown. In addition, there are no FDA or CLSI interpretive breakpoints for Tigecycline and *S. epidermidis*. The MicroScan product labeling was modified to indicate the absence of breakpoints for *S. epidermidis* and to list the performance of Tigecycline with *S. epidermidis* (using breakpoints for *S. aureus*) and without *S. epidermidis*. For ease of reporting, in this document, performance of Tigecycline with *S. epidermidis* was determined using *S. aureus* breakpoints unless otherwise noted.

The sponsor originally submitted data in a “mapped” format which truncated the range of evaluated Tigecycline concentrations to 0.12 - 8 µg/mL. With the mapped format, the overall EA was 96.2%. However, mapping reduced the number of evaluable results, limiting FDA’s ability to assess EA based on evaluable results. FDA requested that results be re-evaluated using the long dilution format.

Using the long dilution format (spanning the entire dilution range of 0.015 - 8 µg/mL), the overall essential agreement of MIC values obtained for MicroScan Dried Gram Positive Tigecycline using turbidity inoculation preparation and manual read did not meet acceptable performance for a quantitative claim.

Of a total of 474 clinical and challenge isolates tested (including *S. aureus*, vancomycin-susceptible *E. faecalis* and *S. epidermidis*), 369 (77.8%) were in essential agreement with the CLSI broth microdilution reference method. A total of 469 isolates yielded on-scale MICs; 366 (78.0%) of the isolates with on-scale MICs were in essential agreement with the reference method. The on-scale MIC results were evaluated for MIC trends and the following results were obtained when MicroScan results were compared to the reference method: 78.0% (366/469) were within ± one doubling dilution; 21.3% (100/469) of the MicroScan MICs were higher by more than one doubling dilution; 0.6% (3/469) of the MicroScan MICs were lower by more than one doubling dilution. The MicroScan product labeling was modified to include this information.

Using the long dilution format, combined results from clinical and challenge studies demonstrated an overall categorical agreement (CA) of 99.4% (471/474) for the turbidity inoculation preparation method with manual read. The overall percent CA

meets the acceptance criteria of greater than or equal to 90% and supports the claim for qualitative testing of Tigecycline.

Excluding *S. epidermidis*, the overall essential agreement (including clinical and challenge isolates) for MicroScan Dried Gram Positive Tigecycline using turbidity inoculation preparation and manual read was 78.0% (333/427) and categorical agreement was 99.3% (424/427).

According to the approved drug label for Tigecycline, only a susceptible interpretive category is defined. There are no intermediate or resistant breakpoints. In this study two MRSA clinical isolates were determined to be resistant to Tigecycline by the reference method. MicroScan results were susceptible for one of these isolates. Even though the approved drug label does not define “non-susceptible” breakpoints, FDA considered this to be a potential very major error. The sponsor included a limitation referencing the potential very major error when testing *S. aureus* with Tigecycline.

A total of 75 challenge isolates were tested using the Prompt inoculation method and read using three methods: manual, WalkAway and autoSCAN-4. Results were compared to results obtained with the reference method. Overall categorical agreement was 97.3% for all methods. The EA obtained for challenge isolates inoculated using the Prompt inoculation method and analyzed using the long dilution format was unacceptably low for *S. aureus* and results showed potential major errors. The labeling indicates that the turbidity standard method provides the most accurate inoculum for staphylococcal isolates and is the preferred method of inoculation. The labeling indicates that the Prompt System demonstrated potential major errors with Tigecycline and staphylococci.

The performance evaluation summary of categorical agreement results for challenge and clinical isolates with inocula prepared using the turbidity method and read manually is shown in the tables below.

Performance of Clinical and Challenge Isolates with Tigecycline Turbidity Inoculation Method with Manual Read

Table 6: Clinical Isolates, Turbidity Inoculum, Manual Read

Organism Group	Total Tested	# EA	% EA Total	Total Evaluable	# EA of Evaluable	% EA Evaluable	# CA	% CA	# NS	# vmj ^a	# maj ^a	# min ^a
<i>S. aureus</i>	305	N/A ^b	N/A	N/A	N/A	N/A	302	99.0	2	N/A ^c	N/A ^c	N/A
<i>E. faecalis</i> (vancomycin susceptible)	47	N/A	N/A	N/A	N/A	N/A	47	100	0	N/A	N/A	N/A
<i>S. epidermidis</i> ^d	47	N/A	N/A	N/A	N/A	N/A	47	100	0	N/A	N/A	N/A
Total	399	N/A	N/A	N/A	N/A	N/A	396	99.2	2	N/A ^c	N/A ^c	N/A

^a There are no intermediate or resistant interpretive criteria for Tigecycline. The current absence of resistant isolates precludes defining any results other than “Susceptible”.

^b N/A not applicable due to the qualitative only claim.

^c One *S. aureus* isolate that was resistant by the reference method tested susceptible with the test panel, a potential very major error; 2 *S. aureus* isolates that were susceptible by the reference method tested resistant with the test panel, a potential major error

^d *S. epidermidis* isolates were evaluated using *S. aureus* breakpoints

Table 7: Challenge Isolates, Turbidity Inoculum, Manual Read

Organism Group	Total Tested	# EA	% EA Total	Total Evaluable	# EA of Evaluable	% EA Evaluable	# CA	% CA	# NS	# vmj ^a	# maj ^a	# min ^a
<i>S. aureus</i>	59	N/A ^b	N/A	N/A	N/A	N/A	59	100	0	N/A	N/A	N/A
<i>E. faecalis</i> (vancomycin susceptible)	16	N/A	N/A	N/A	N/A	N/A	16	100	0	N/A	N/A	N/A
Total	75	N/A	N/A	N/A	N/A	N/A	75	100	0	N/A	N/A	N/A

^a There are no intermediate or resistant interpretive criteria for Tigecycline. The current absence of resistant isolates precludes defining any results other than “Susceptible”.

^b N/A not applicable due to the qualitative only claim.

Table 8: Combined Clinical and Challenge Isolates, Turbidity Inoculum, Manual Read

Organism Group	Total Tested	# EA	% EA Total	Total Evaluable	# EA of Evaluable	% EA Evaluable	# CA	% CA	# NS	# vmj ^a	# maj ^a	# min ^a
Clinical Total ^b	399	N/A ^c	N/A	N/A	N/A	N/A	396	99.2	2	N/A ^d	N/A ^d	N/A
Challenge Total	75	N/A	N/A	N/A	N/A	N/A	75	100	0	N/A	N/A	N/A
Total Clinical and Challenge	474	N/A	N/A	N/A	N/A	N/A	471	99.4	2	N/A ^d	N/A ^d	N/A

^a There are no intermediate or resistant interpretive criteria for Tigecycline. The current absence of resistant isolates precludes defining any results other than “Susceptible”.

^b *S. epidermidis* isolates were evaluated using *S. aureus* breakpoints.

^c N/A not applicable due to the qualitative only claim.

^d One *S. aureus* isolate that was resistant by the reference method tested susceptible with the test panel, a potential very major error; 2 *S. aureus* isolates that were susceptible by the reference method tested resistant with the test panel, a potential major error.

Table 9: Combined Clinical and Challenge Isolates (Excluding *S. epidermidis* Clinical Isolates), Turbidity Inoculum, Manual Read

Organism Group	Total Tested	# EA	% EA Total	Total Evaluable	# EA of Evaluable	% EA Evaluable	# CA	% CA	# NS	# vmj ^a	# maj ^a	# min ^a
Clinical Total	352	N/A ^b	N/A	N/A	N/A	N/A	349	99.2	2	N/A ^c	N/A ^c	N/A
Challenge Total	75	N/A	N/A	N/A	N/A	N/A	75	100	0	N/A	N/A	N/A
Total Clinical and Challenge	427	N/A	N/A	N/A	N/A	N/A	424	99.3	2	N/A ^c	N/A ^c	N/A

^a There are no intermediate or resistant interpretive criteria for Tigecycline. The current absence of resistant isolates precludes defining any results other than “Susceptible”.

^b N/A not applicable due to the qualitative only claim.

^c One *S. aureus* isolate that was resistant by the reference method tested susceptible with the test panel, a potential very major error; 2 *S. aureus* isolates that were susceptible by the reference method tested resistant with the test panel, a potential major error.

EA = Essential Agreement

R = Resistant Isolates

maj = major discrepancies

CA = Category Agreement

min = minor discrepancies

vmj = very major discrepancy

Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of MicroScan within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on scale for both the MicroScan panel and the reference method. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the MicroScan result.

Categorical agreement for challenge isolates with inocula prepared using the turbidity method were also determined using the WalkAway instrument and the autoScan-4 instrument. In addition, challenge isolates were tested using inocula prepared using the Prompt System and read by all three methods (manual, WalkAway, and autoScan-4). Results are summarized in the following table:

Table 10: Overall Categorical Agreement for Challenge Isolates by Inoculation and Read Method

	Turbidity Inoculation Method						Prompt Inoculation Method					
	Manual Read		WAW Read		AS-4 Read		Manual Read		WAW Read		AS-4 Read	
	#CA	%CA	#CA	%CA	#CA	%CA	#CA	%CA	#CA	%CA	#CA	%CA
All challenge isolates ^a	75	100	74	98.7	75	100	73	97.3	73	97.3	73	97.3

^a 75 challenge isolates (59 *S. aureus* and 16 vancomycin-susceptible *E. faecalis*)

Prompt Hold Study: An internal study was performed to determine the agreement of results obtained with the Prompt inoculation method using hold times of 0 hours and 4 hours prior to inoculation of the panels. Results of 4-hour holds were compared to 0-hour hold using the same inoculum and with expected results as determined by the reference method. Testing was performed with all three read methods. While categorical agreement with all methods and hold times was acceptable, potential major or very major errors were noted for *S. aureus* with each method inoculated after extended hold times.

The MicroScan product labeling indicates that the turbidity inoculum preparation method provides the most accurate inoculum, and is the preferred method for preparation of inocula for *Staphylococcus* isolates and certain antimicrobial agents. Additional limitations were incorporated in the labeling specific to the use of the Prompt System with Tigecycline and other antimicrobials.

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:

Table 11: Susceptibility Interpretive Criteria

Organism	Susceptibility Interpretive Criteria (MIC in µg/mL)		
	S	I ^a	R ^a
<i>Staphylococcus aureus</i> (methicillin-susceptible and - resistant isolates)	≤ 0.5	-	-
<i>Enterococcus faecalis</i> (vancomycin-susceptible isolates)	≤ 0.25	-	-

^a There are no intermediate or resistant interpretive criteria for Tigecycline. The current absence of resistant isolates precludes defining any results other than “Susceptible.” Isolates yielding MIC results suggestive of the “Nonsusceptible” category should be submitted to a reference laboratory for further testing.

S = Susceptible; I = Intermediate; R = Resistant; N/A = Not Applicable

N. Proposed Labeling:

The labeling is sufficient and it 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