

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

A. 510(k) Number:

K081182

B. Purpose for Submission:

Addition of a new antimicrobial test- Inducible Clindamycin test for the MicroScan[®]
Dried Gram-Positive MIC/Combo panels

C. Measurand:

Inducible Clindamycin: 4 mcg/ml erythromycin and 0.5 mcg/ml clindamycin

D. Type of Test:

Quantitative and Qualitative growth based detection algorithm

E. Applicant:

Siemens Healthcare Diagnostics Inc.

F. Proprietary and Established Names:

MicroScan[®] Dried Gram-Positive MIC/Combo Panels with the Inducible
Clindamycin test

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 Auto Reader & Interpretation of Overnight Antimicrobial
Susceptibility Systems

LTT – Panels, Test, Susceptibility, Antimicrobial
LTW – Susceptibility Test Cards, Antimicrobial

4. Panel:

83 Microbiology

H. Intended Use:

1. Intended use(s):

The MicroScan Inducible Clindamycin test (ICd) is intended for use with the MicroScan[®] Dried Gram Positive MIC/Combo Dried Gram Positive Breakpoint Combo and Dried Gram Positive ID Type 2 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 anaerobic gram-positive cocci, some fastidious aerobic gram positive cocci and *Listeria monocytogenes*. Refer to Limitation 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 cocci. After inoculation, panels are incubated for 16 – 24 hours at 35⁰ Celsius plus or minus 1⁰ Celsius in a non- CO₂ incubator and reads either visually or with MicroScan[®] instrumentation, according to the package insert.

The MicroScan Inducible Clindamycin test (ICd) is intended to detect inducible clindamycin resistance in staphylococci in a broth microdilution system. The ICd test applies to isolates that are erythromycin resistant or intermediate and clindamycin susceptible or intermediate.

This submission is for the addition of the Inducible Clindamycin test, consisting of 4 mcg/ml of erythromycin and 0.5 mcg/ml of clindamycin, to the test panel. The Gram positive organisms which may be used for the Inducible Clindamycin test in this panel are: *Staphylococcus* species.

3. Special conditions for use statement(s):

For prescription use only

The Prompt method of inoculation is an alternate method of inoculation preparation that is supported in the methodology along with the turbidity. The log and stationary inoculum methods should not be used with the Inducible Clindamycin test.

4. Special instrument requirements:

These panels can be read at ≥ 16 hours of incubation either manually, automatically on the autoScan® 4, or with the WalkAway® instrument systems.

I. Device Description:

The MicroScan® Dried Gram-Positive MIC/Combo Panel contains microdilutions of each antimicrobial agent in various concentrations with Mueller Hinton Broth and various nutrients which are dehydrated and dried in panels. Each panel contains two control wells: a no-growth control well (contains water only/no nutrients or broth), and a growth control well (contains test medium without antibiotic). The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum prepared in water, then 0.1ml transferred to 25ml of inoculum water containing pluronic-D/F-a wetting solution) for a final inoculum concentration of $3-7 \times 10^5$. The Prompt® method of inoculation is also recommended as an alternate means of preparing the inoculum. The panels are incubated at 35° C in a non-CO₂ for 16-20 hours and read by visual observation of growth. Panels may also be read automatically with the WalkAway® or the AutoScan®4.

J. Substantial Equivalence Information:

1. Predicate device name(s):

MicroScan Dried Gram Positive MIC/Combo Panels

2. Predicate K number(s):

K862140

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Detection of inducible clindamycin resistance in <i>staphylococci</i>	Determination of susceptibility to antimicrobials with gram-positive bacteria
Technology	Overnight microdilution MIC susceptibility tests	Same
Inoculum Preparation	Inoculum prepared from isolated colonies using either the Turbidity method or Prompt system.	Same

Similarities		
Item	Device	Predicate
Instrument	autoSCAN [®] 4, or with the WalkAway [®]	Same
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same

Differences		
Item	Device	Predicate
Antibiotic	4 ug/ml erythromycin 0.5 ug/ml clindamycin	Varies according to antibiotic
Limitations	The performance of the Inducible Clindamycin test has not been established with Stationary and Log Inoculum methods. Inoculum should be prepared with turbidity or Prompt [®] method.	None
Test organism	<i>Staphylococcus spp.</i>	Varies according to antibiotic

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

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”; Clinical and Laboratory Standards Institute (CLSI), Document M100-S18: “Performance Standards for Antimicrobial Susceptibility Testing; Approved Standard”.

L. Test Principle:

After incubation in a non-CO₂ incubator for 16-20 hours, the minimum inhibitory concentration (MIC) for the test organisms are read by determining the lowest antimicrobial concentration showing inhibition of growth. The panels are read either manually using the MicroScan[®] Microdilution Viewer or with the autoSCAN[®] 4 or the WalkAway[®] instruments, which uses an optics systems with growth algorithms to directly measure organism growth.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was verified using 10 isolates at three clinical trial sites. Each strain was tested at each site in replicates of three over three days (total of 27 replicates per strain). The two inoculum methods tested were the turbidity and prompt with readings performed using the MicroScan[®] Microdilution Viewer or with the autoSCAN[®] 4 or the WalkAway[®] instruments. Acceptable reproducibility was demonstrated with >99% Agreement for all sites combined.

b. *Linearity/assay reportable range:*

Not applicable

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

Quality control was performed daily using three *staphylococci* strains, *S. aureus* ATCC 29213, *S. aureus* ATCC BAA-976 and *S. aureus* ATCC BAA-977 as recommended by CLSI. Testing was performed using both the turbidity and prompt inoculation methods and all read methods (manually or with the autoSCAN[®] 4 or the WalkAway[®] instruments) with the following results and expected ranges as stated. The values repeat the number of times a result was obtained at each concentration.

QC Table

Organism	Conc. In ug/mL	Reference result Turbidity inoc.	Turbidity inoculation with Read methods			Prompt [®] inoculation with Read		
			Manual	Walk-Away [®]	Auto-Scan [®]	Manual	Walk-Away [®]	Auto-Scan [®]
<i>S. aureus</i> BAA 976 Exp. Range: ≤4 ug/mL	≤4/0.5	109	110	69	71	119	116	118
	>4/0.5			1		3	2	6
<i>S. aureus</i> BAA 977 Exp. Range: >4 ug/mL	≤4/0.5					2	1	1
	>4/0.5	110	110	70	71	123	119	126
<i>S. aureus</i> ATCC 29213 Exp. Range: ≤4 ug/mL	≤4/0.5	112	110	69	71	124	120	125
	>4/0.5							2

Quality control results demonstrated the ability of all variables of the procedure (reading and inoculation) to produce acceptable results.

Inoculum density control: A turbidity meter was used for the turbidity inoculation

method. The Prompt® method of inoculation had colony counts (CC) performed periodically throughout the study to determine the average inoculum density since there is no visual check of the inoculum using this device. The Prompt® inoculation method had an average colony count of 4.69×10^5 CFU/mL for *E. faecalis* ATCC 29212 with a range of 6.0×10^4 to 8.9×10^5 CFU/mL, *S. aureus* BAA 976 had an average colony count of 1.83×10^6 CFU/mL with a range of $2.9 \times 10^5 - 4.5 \times 10^6$ CFU/mL, *S. aureus* BAA 977 had an average colony count of 1.53×10^6 CFU/mL with a range of $4.1 \times 10^5 - 5.6 \times 10^6$ CFU/mL, *S. aureus* ATCC 29213 had an average colony count of 1.82×10^6 CFU/mL with a range of $2.7 \times 10^5 - 7.9 \times 10^6$ CFU/mL. The CFU study demonstrated that the *S. aureus* has a higher concentration of organism that reproduces a more resistant result. The inoculum of the Prompt® method of inoculation generally provides a higher number of CFU with more variability than a method using a turbidity meter.

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:

Clinical testing was performed at three sites using fresh isolates supplemented with stock isolates of gram positive cocci. A comparison of the MicroScan® Dried Gram-Positive test panel results was made to the reference method as recommended in the CLSI standard M7-A6 with the following deviations from that recommendation: Pluronic-F is used as the inoculum in the frozen reference panels. Pluronic is a wetting agent which provides a smoother draw of liquid into the inoculator. Testing of the reference method and the MicroScan panels was performed at the same time. A challenge set was also tested at one site and compared to the reference broth dilution result mode that was determined by previous testing of each isolate multiple times in the recommended reference panel. All isolates tested grew in the MicroScan panels.

Summary Table

	Total	CA	CA%	# Neg	# Pos	maj	vmj
<i>S. aureus</i>	268	263	98.1	60	208	0	3
<i>S. epidermidis</i>	54	54	100	26	28	0	0
Coagulase-negative <i>Staphylococcus</i>	58	58	100	25	33	0	0

CA-Category Agreement
maj – major errors

vmj – very major errors

CA is when the interpretation (S –I-R) of the reference method agrees exactly with the interpretation of the MicroScan® result.

Essential Agreement and minor errors are not applicable since the Inducible Clindamycin test is a one dilution test.

The challenge set of organisms was also tested using the Prompt® method and turbidity method of inoculation with all reading methods. This included seventy five challenge isolates that were tested at one site. Organism selection was based on isolates that were erythromycin resistant or intermediate and clindamycin susceptible or intermediate, and included 38 D-zone positive and 37 D-zone negative strains. The inoculum was prepared by the turbidity or Prompt® method and incubated in the WalkAway® instrument. All panels had additional readings performed after the WalkAway® reading was completed using the autoScan®-4 and then manually on the touchSCAN®-SR. The table below demonstrates the numbers that were in exact agreement with the reference method result and those that differed by one or more wells.

Read Method	Inoculation Method	Total	CA	CA%	# Pos	# Neg	maj	vmj
Manual	Turbidity	75	75	100	38	37	0	0
Walkaway	Turbidity	75	75	100	38	37	0	0
autoSCAN4	Turbidity	75	75	100	38	37	0	0
Manual	Prompt	75	75	100	38	37	0	0
Walkaway	Prompt	75	75	100	38	37	0	0
autoSCAN4	Prompt	75	75	100	38	37	0	0

CA-Category Agreement
maj – major errors

vmj – very major errors

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):

See comparison studies.

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The MicroScan Inducible Clindamycin test uses the result from a single well containing 4 mcg/ml of erythromycin and 0.5 mcg/ml of clindamycin. Isolates that are ICd positive (MIC > 4/0.5) are considered to be clindamycin resistant. If ICd is negative (MIC ≤ 4/0.5), the result indicates no inducible clindamycin resistance and isolates are reported as tested (i.e. clindamycin susceptible or intermediate). The gram-positive organisms which may be reported for the Inducible Clindamycin test in this panel are: *Staphylococcus spp.*

Test	Negative	Positive
Inducible Clindamycin Test-Staphylococci	≤4/0.5 mcg/ml	>4/0.5 mcg/ml

N. Proposed Labeling:

The labeling is sufficient and it 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.