

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

A. 510(k) Number:

k081013

B. Purpose for Submission:

Addition of Cefoxitin screen to the MicroScan® Dried Gram-Positive MIC/Combo Panels

C. Measurand:

Cefoxitin 4 µg/mL

D. Type of Test:

Qualitative growth based detection algorithm

E. Applicant:

Siemens Healthcare Diagnostics, Inc.

F. Proprietary and Established Names:

MicroScan® Dried Gram-Positive MIC/Combo Panels

G. Regulatory Information:

1. Regulation section:
866.1640 Antimicrobial Susceptibility Test (AST) Powder
2. Classification:
Class II
3. Product code:
LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems
JWY - Manual Antimicrobial Susceptibility Test Systems
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 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 Limitation of Procedure Section for use with fastidious streptococci.

The MicroScan® Dried Gram-Positive MIC/Combo Panel is used to determine qualitative antimicrobial agent susceptibility of colonies grown on solid media of rapidly growing aerobic and facultative gram-positive cocci.

2. Indication(s) for use:

This submission is indicated for the addition of Cefoxitin Screen at a cefoxitin concentration of 4 µg/mL to the gram positive susceptibility panel for testing *Staphylococcus aureus*, and *Staphylococcus lugdunensis* only.

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 method. The stationary and log inoculum methods should not be used with this antibiotic.

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 and Gram-Negative MIC/Combo Panels
2. Predicate 510(k) number(s):
K862140
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	See above	Same
Inoculum preparation	Inoculum prepared from isolated colonies using either the Turbidity method or Prompt® system	Same
Technology	Growth based after 16 hours incubation	Same
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
Instrument	autoScan® -4 or WalkAway®	Same
Differences		
Item	Device	Predicate
Components	Dried Cefoxitin Screen Well (CfxS) 4 ug/mL	Different concentrations depending on the antibiotic
Test organism	Gram-Positive organisms	Varies according to the antibiotic
Limitations	The performance for Cefoxitin Screen Well has not been established with Stationary and Log Inoculum methods. Inoculum should be prepared with turbidity or Prompt® method.	None

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

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) 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 Cefoxitin Screen uses the 18 hour result from a well containing cefoxitin at 4 µg/mL and growth media, labeled CfxS, and the oxacillin MIC at 18 hours. Isolates that are CfxS positive (MIC>4) are considered to be resistant to oxacillin. If the result is negative (MIC≤4), the oxacillin MIC is used to make a final assessment of the susceptibility to penicillinase stable beta-lactams.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was demonstrated using 10 isolates tested at 3 sites on 3 separate days in triplicate. Acceptable reproducibility was demonstrated with only category agreement (Negative, Positive) since that is all that is detected. The study included the testing of the following inoculum and reading variables; turbidity inoculum method and Prompt® method of inoculation with reading performed manually using a touchScan® SR, autoScan 4® or the WalkAway® instrument.

b. *Linearity/assay reportable range:*

Not Applicable

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

Quality Control was performed daily with the turbidity method, and Prompt® method with the following results and expected ranges as stated. The values repeat the number of times a result was obtained at each concentration.

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> ATCC 29213 Exp. Range: <=4 µg/mL	4	112	109	69	71	122	117	124
	6					1	1	1
	8					1	1	1
	16							
	>16						1	1
<i>S. aureus</i> ATCC 43300 Exp. Range: >4 µg/mL	8			1	1	1	1	1
	16	96	105	67	69	76	94	102
	>16	15	5	1		45	23	21

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Quality control results demonstrated the ability of all variables of the procedure (reading and inoculation) to produce acceptable results most of the time. Although the modes are the same, the Prompt® inoculation method appears to have more results at MIC of >4 with the *S. aureus* ATCC 29213. The Prompt® inoculation method with *S. aureus* ATCC 43300 also had more results at the >16 when compared to the Turbidity method.

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® method of inoculation had an average of 1.05×10^6 CFU/mL for *S. aureus* ATCC 43300 with a range of 1.9×10^5 to 2.38×10^6 CFU/mL and an average of 1.82×10^6 CFU/mL for *S. aureus* ATCC 29213 with a range of 2.7×10^5 to 7.9×10^6 CFU/mL. The CFU study demonstrated that the *S. aureus* has a higher concentration of organism that reproduces a more resistant result which would explain the more resistant results with the QC study. The inoculum of the Prompt® method 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-A7 with the following deviations from that recommendation: Pluronic-F is used as the inoculum in the frozen reference panels. This is composed of water which contains a very small amount of Pluronic to provide 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 N	%CA	# Resistant	# Susceptible	maj	vmj
Efficacy	306	305	99.6	150	156	1	0
Challenge	75	75	100	34	41	0	0
Combined	381	380	99.7	184	197	1	0

CA-Category Agreement

maj-major discrepancies

vmj-very major discrepancies

CA is when the interpretation of the reference method agrees exactly with the interpretation of the MicroScan® results.

The challenge set of organisms was also tested using the Prompt® method and turbidity method of inoculation with all reading methods. This included 75 challenge isolates that were tested at two sites. 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 results.

Inoculation method	Read method	No. Tested	CA N	% CA	maj	vmj
Turbidity	Manual	75	75	100	0	0
Turbidity	WalkAway®	75	75	100	0	0
Turbidity	autoScan® 4	75	75	100	0	0
Prompt®	Manual	75	75	100	0	0
Prompt®	WalkAway®	75	75	100	0	0
Prompt®	autoScan® 4	75	75	100	0	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:

S. aureus and *S. lugdunensis* ≤ 2 (S), ≥ 4 R

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.

