

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

A. 510(k) Number:

K053504

B. Purpose for Submission:

For addition of Erythromycin on the MicroScan® Synergies plus™ Gram-Positive for testing appropriate *Staphylococcus* spp

C. Measurand:

Erythromycin 0.12 – 16 µg/mL; 0.5 – 4 µg/mL (4 Dilution Sequence BP); or 0.5-1, 4 µg/mL (3 Dilution Sequence BP)

D. Type of Test:

Quantitative and Qualitative growth based detection algorithm using optics light detection

E. Applicant:

Dade Behring Inc, MicroScan®

F. Proprietary and Established Names:

MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panels

G. Regulatory Information:

1. Regulation section:

866.1645 - Fully automated short-term incubation cycle antimicrobial susceptibility system

866.1640 - Antimicrobial Susceptibility Test Powder

2. Classification:

Class II

3. Product code:

LON – Automated AST system short incubation

LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems

JWY - Manual Antimicrobial Susceptibility Test Systems

LTT – Panels, Test, Susceptibility, Antimicrobial

4. Panel:

83 Microbiology

H. Intended Use:

1. Intended use(s):

Erythromycin at concentrations of 0.12 to 16 µg/mL (Long Dilution); 0.5 – 4 µg/mL (4 Dilution Sequence BP); or 0.5-1, 4 µg/mL (3 Dilution Sequence BP) on the MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panel is intended for use with MicroScan® Synergies plus™ Panels read on the WalkAway® -SI System (including upgraded WalkAway® -40 or WalkAway® -96 to meet WalkAway® SI equivalence).

MicroScan® panels are designed for use in determining identification to the species level of colonies, grown on solid media, of rapidly growing aerobic and facultative anaerobic gram-positive cocci and *Listeria*; the panels also provide quantitative and/or qualitative antimicrobial agent susceptibility for staphylococci and enterococci.

2. Indication(s) for use:

The addition of erythromycin at concentrations of 0.12 to 16 µg/mL (Long Dilution); 0.5 – 4 µg/mL (4 Dilution Sequence BP); or 0.5-1, 4 µg/mL (3 Dilution Sequence BP) to the gram-positive test panel for testing *Staphylococcus* spp. at 4.5-16 hours or 16-20 hours for an overnight reading.

3. Special conditions for use statement(s):

- Turbidity method of inoculum preparation only.
- For prescription use only.

4. Special instrument requirements:

Not Applicable

I. Device Description:

Each panel contains two control wells: a negative control well, and a growth control well (contains test medium without antibiotic). Antibiotics are diluted in water, buffer, or minute concentrations of broth to selected concentrations prior to dehydration of the panels. The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum prepared in 0.4% saline with PLURONIC®, then 0.1ml transferred to 25ml of inoculum Synergies plus Pos Broth with PLURONIC®) for a final inoculum concentration of $3-7 \times 10^5$ CFU/ml. Panels are incubated in a Walk-Away® System and read periodically starting at 4.5 hours until sufficient growth to determine the MIC. Alternately the panels may be incubated at 35° C in a non-CO₂ for 16-24 hours and read by visual observation of growth.

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
k020185
3. Comparison with predicate:

| Similarities | | |
|----------------------|---|---|
| Item | Device | Predicate |
| Intended use | MicroScan® panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility and/or identification to the species level of colonies, grown on solid media, of rapidly growing aerobic and facultative anaerobic organisms | Same |
| Specimen | Isolated colonies from culture used | Same |
| Inoculum | Inoculum density to 0.5 McFarland standard | Same |
| Incubation | <16 hours 16 – 20 hours | Same |
| Results | Quantitative with qualitative interpretations | Same |
| Technology | Growth based | Same |
| Differences | | |
| Item | Device | Predicate |
| Panels | Dried erythromycin in water | Dried clindamycin or gentamicin in broth |
| Reading | Uses both an early read and overnight methods in the same system | Overnight system uses only the overnight reading methods and <16 hour instruments use only the <16 hour read methods. |
| Inoculum preparation | Turbidity method of inoculation only. | Inoculum prepared from isolated colonies using either the Turbidity method or Prompt® system |
| Instrument | WalkAway® -SI System or equivalent | autoScan® -4 or WalkAway® |
| Antibiotic | Erythromycin 0.12 – 16 µg/mL | Different concentrations depending on the |

| | | |
|--|--|------------|
| | | 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) M7 (M100-S16) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard”.

L. Test Principle:

The WalkAway® SI uses a Colorimetric Optics System consisting of a color wheel/lamp assembly and a Photosensor. There is an initial read at 2.5 hours with a possible final read at 4.5, 5.5, 6.5, 8, 12, 16, or 18 hours (overnight instrument readings, manual readings) depending on the growth rate of the organism being tested. The time of final read is dependent on the growth rate of the organism and the sensitivity of the automatic reader since cell densities below 2×10^7 cells/ml are not detected.

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. The study included the testing on the WalkAway® SI read at <16 hours, WalkAway® 16-18 hour readings and manual readings at 16-20 hours incubation. The WalkAway® SI read at <16 hours had 4 results that did not grow in ≤16 hours for a no growth rate of 1.5%. All results were >95% reproducible.

There are two breakpoint (BP) dilutions included in this submission using different reading algorithms namely 3 Dilution sequence and 4 Dilution sequence. Both BP dilutions were done on the same 10 isolates with reproducibility reading based only on category agreement. Less than 16 hour readings resulted in a no growth rate of 1.5%. The other 2 methods did not have any isolates that did not grow. All three read methods had an acceptable reproducibility of >95%.

b. *Linearity/assay reportable range:*

Not Applicable

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

The recommended QC isolate, *S. aureus* ATCC 29213 was tested a sufficient

number of times with acceptable results on all testing days with the reference method. All results grew in the 4.5-16 hour window on the Synergies Plus. Quality control results demonstrated the ability of the different reading parameters (manual and instrument) to produce acceptable results.

The following table provides the frequency of the results in each concentration with the expected range stated.

| Organism | Conc in $\mu\text{g/mL}$ | # reference | Results | | |
|--|--------------------------|-------------|------------------|----------------------|----------------|
| | | | MicroScan® | | |
| | | | Manual overnight | Instrument overnight | Synergies Plus |
| | | | | | |
| <i>S. aureus</i> ATCC 29213 Expected Range: 0.25 – 1 $\mu\text{g/mL}$ | ≤ 0.12 | | | | |
| | 0.25 | 3 | 3 | 1 | 35 |
| | 0.5 | 81 | 81 | 83 | 49 |
| | | | | | |
| | | | | | |

The 3 Dilution sequence and 4 Dilution sequence breakpoint panels using separate reading algorithms also demonstrated acceptable quality control results with all results at $\leq 0.5 \mu\text{g/mL}$.

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

- 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 conducted at 3 sites using fresh isolates supplemented with stock isolates. A total of 301 *Staphylococci* spp isolates were tested of which 263 were fresh isolates and 38 were stock isolates. There were 75 challenge isolates 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. The Synergies plus™ readings were obtained between 4.5 and 16 hours of incubation for > 95% of the results. An additional comparison was done with readings on the instrument after overnight incubation and also read manually when incubated

16- 18 hours. Performance by these alternate reading methods was also acceptable with no apparent differences or trends. The recommended CLSI reference method was followed with the exception of the use of a small amount (0.1%) PLURONIC® in the final inoculum. A validation of the use of PLURONIC® in the frozen reference panels was conducted. Similar calculations for the different reading methods were performed with very little difference. The test device had a no growth rate of <10%.

The charts below demonstrated the performance of all three reading methods (Synergies plus™ readings at <16 hours, overnight on the WalkAway® and manually read at 18 hours using the touchScan®-SR) with the long dilution sequence when compared to the reference method.

Summary Table for the Rapid Instrument Read (Long Dilution)

| | Total | EA | %EA | Total evaluab le | EA of evaluab le | %EA | CA | %CA | #R | min | maj | vmj |
|------------------|-------|-----|------|---------------------|---------------------|------|-----|------|-----|-----|-----|-----|
| Efficacy | 301 | 290 | 96.3 | 107 | 103 | 96.3 | 292 | 97.0 | 192 | 7 | 1 | 1 |
| Challenge | 75 | 74 | 98.7 | 28 | 28 | 100 | 75 | 100 | 44 | 0 | 0 | 0 |
| Combined | 376 | 364 | 96.8 | 135 | 131 | 97.0 | 367 | 97.6 | 236 | 7 | 1 | 1 |

Summary Table for the Overnight Instrument Read (Long Dilution)

| | Total | EA | %EA | Total evaluab le | EA of evaluab le | %EA | CA | %CA | #R | min | maj | vmj |
|------------------|-------|-----|------|---------------------|---------------------|------|-----|------|-----|-----|-----|-----|
| Efficacy | 301 | 300 | 99.7 | 109 | 108 | 99.1 | 299 | 99.3 | 192 | 1 | 1 | 0 |
| Challenge | 75 | 75 | 100 | 28 | 28 | 100 | 75 | 100 | 44 | 0 | 0 | 0 |
| Combined | 376 | 375 | 99.7 | 137 | 136 | 99.3 | 374 | 99.5 | 236 | 1 | 1 | 0 |

Summary Table for the Overnight Manual Read (Long Dilution)

| | Total | EA | %EA | Total evaluab le | EA of evaluab le | %EA | CA | %CA | #R | min | maj | vmj |
|------------------|-------|-----|-----|---------------------|---------------------|-----|-----|-----|-----|-----|-----|-----|
| Efficacy | 301 | 301 | 100 | 108 | 108 | 100 | 301 | 100 | 192 | 0 | 0 | 0 |
| Challenge | 75 | 75 | 100 | 28 | 28 | 100 | 75 | 100 | 44 | 0 | 0 | 0 |
| Combined | 376 | 376 | 100 | 136 | 136 | 100 | 376 | 100 | 236 | 0 | 0 | 0 |

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

maj-major discrepancies

vmj-very major discrepancies

min- minor discrepancies

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one dilution variability. EA is when there is agreement between the reference method and the MicroScan® within plus or minus one serial two-fold dilution of antibiotic. CA is when the interpretation of the reference method agrees exactly with the interpretation of the MicroScan® result.

Similar results were obtained when the algorithm for reading the 3

Dilution sequence with 0.5, 1 and 4 µg/mL wells and algorithm for reading the 4 Dilution sequence with 0.5, 1, 2 and 4 wells were applied with no difference in CA. EA was not calculated for these readings since insufficient numbers of concentrations were available for the evaluation.

- 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:
Staphylococcus spp. ≤0.5 (S), 1 – 4 (I), ≥8 (R)

N. Proposed Labeling:

The interpretative criteria are the same as recommended by the FDA and CLSI. All values are included in the package insert.

O. Conclusion:

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