

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

A. 510(k) Number:

K063101

B. Purpose for Submission:

To add the option for automated reading of Cefotaxime at 0.015 – 8 µg/mL to the MICroSTREP *plus*® Panel on the MicroScan® WalkAway System

C. Measurand:

Cefotaxime at 0.015 – 8 µg/mL

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® MICroSTREP *plus*® Panel – Cefotaxime at 0.015 – 8 µg/mL

G. Regulatory Information:

1. Regulation section:
21 CFR 866.1640 – Antimicrobial Susceptibility Test Powder
2. Classification:
Class II
3. Product Code:
LRG – Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility System
LTT – Panels, Test, Susceptibility, Antimicrobial
4. Panel:
83 Microbiology

H. Intended Use:

1. Intended use(s):
Cefotaxime at 0.015 – 8 µg/mL is for use with MICroSTREP *plus*® Panels.

MICroSTREP *plus*® Panels are designed for use in determining quantitative

and/or qualitative antimicrobial agent susceptibility of colonies grown on solid media of aerobic streptococci, including *Streptococcus pneumoniae*.

2. Indication(s) for use:

This submission is for adding the option for automated reading of the antibiotic Cefotaxime at concentrations of 0.015 – 8 µg/mL to MICroSTREP *plus*® Panels on the MicroScan® WalkAway System for testing *Streptococcus pneumoniae*, *Streptococcus pyogenes*, and *Streptococcus* species.

3. Special condition for use statement(s):

Prescription Use Only

Turbidity method of inoculum preparation only

The absence of resistant strains of beta hemolytic streptococci precludes defining any results categories other than “susceptible”. For isolates yielding results suggestive of a “nonsusceptible” category, organism identification and antimicrobial susceptibility results should be confirmed.

4. Special instrument Requirements:

Not Applicable

I. Device Description:

The MicroScan® MICroSTREP *plus*® Panel is a 96-well plastic dish which contains microdilutions of each antimicrobial in various concentrations dried in aqueous solutions. The panel is rehydrated and inoculated at the same time with a Mueller-Hinton broth supplemented with lysed horse blood (2 – 5%). The target inoculum concentration for each well should be approximately 5×10^5 colony forming units (CFU)/mL. Panels are incubated in a 35° C non-CO₂ incubator for 20-24 hours. After incubation, the panels are read manually for growth. Additionally, panels may be incubated in and read by a MicroScan® WalkAway instrument. Each panel contains a “growth” but it does not contain a “no growth” control well.

J. Substantial Equivalence Information:

1. Predicate device name(s):

MICroSTREP *plus*®

2. Predicate K number(s):

K021111

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	Determination of susceptibility to antimicrobics with aerobic streptococci including <i>Streptococcus pneumoniae</i>	Same

Isolates	For use with aerobic streptococci including <i>Streptococcus pneumoniae</i> isolated colonies from culture	Same
Results	Quantitative with qualitative interpretations	Same
Incubation	20 – 24 hours	Same
Panels	Cefotaxime dried in aqueous solution	Same
Differences		
Item	Device	Predicate
Technology	Growth based using algorithm with optics light detection	Growth based
Reading	Overnight method Manual or automated	Overnight method Manual read only
Instrument	MicroScan® WalkAway System or Microdilution viewer	Microdilution viewer

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

L. Test Principle:

The antimicrobial susceptibility tests are miniaturizations of the broth dilution susceptibility test that have been diluted in water and dehydrated. Various antimicrobial agents are diluted in water, buffer or minute concentrations of broth to concentrations bridging the range of clinical interest. Panels are rehydrated with 115 µL Mueller-Hinton broth supplemented with 2-5% lysed horse blood (LHB), after inoculation of the broth with a standardized suspension of the organism. The target inoculum concentration for each well should be approximately 5×10^5 colony forming units (CFU)/mL. After incubation in a non-CO₂ incubator for 20-24 hours, the minimum inhibitory concentration (MIC) for the test organisms is determined by observing the lowest antimicrobial concentration showing inhibition of growth. Panels can be read manually using indirect light or the panels can be read on the MicroScan® WalkAway instrument using optics light detection.

M. Performance Characteristics (if/when applicable):

This submission is for the AST Panel only. The ID System was not reviewed.

The Reproducibility studies, QC performance data, and Challenge isolates evaluated by the manual and automated reading methods are required to demonstrate that there is no difference between manual reading and automated reading in the MicroScan®

WalkAway System. The clinical efficacy performance was previously established using the manual read method and was therefore not required for this submission.

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was demonstrated using 10 isolates tested at 4 sites on 3 separate days in triplicate, for a total of 360 results. The study included testing on the MicroScan® WalkAway System with automated reading at 20-24 hours, and manual readings at 20-24 hours incubation.

Both reading methods demonstrated >95% reproducibility, and no differences were observed.

b. Linearity/assay reportable range:

Not applicable

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

The recommended QC isolate *S. pneumoniae* ATCC 49619 was tested a sufficient number of times with acceptable results on all testing days with the reference method. 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 results in each concentration with the expected range stated. Both reading methods produced the same mode as the reference method.

Organism	Concentration µg/mL	Reference results	MicroScan® WalkAway results	
			Manual Overnight	Instrument Overnight
<i>S. pneumoniae</i> ATCC 49619 Expected range 0.03 – 0.12 µg/mL	0.03			1
	0.06	52	45	49
	0.12	31	44	39
	0.25			
	0.5			
	1			
	2			

Inoculum density control: A turbidity meter, which was verified each day of testing, was used for the turbidity inoculation method. Colony counts were performed weekly, on the ATCC *S. pneumoniae* with all results in the expected range of approximately 5×10^5 .

No trending was observed.

- 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 efficacy testing with manual result reading was conducted in the previous submission (K021111). In this submission, Challenge isolates were evaluated by the manual and automated reading methods to demonstrate that there is no difference between manual reading and instrument reading on the MicroScan® WalkAway System. There were 70 streptococcal challenge isolates, including 53 *Streptococcus pneumoniae* strains from the CDC Challenge Set tested internally and compared to the reference broth dilution result, which was obtained prior to beginning the design validation. A comparison was done with readings on the instrument after 20 hours incubation, and also read manually when incubated for 20-24 hours. Performance by the automated reading method was acceptable with no differences or trends. The read method comparison results are displayed in the tables below.

The recommended CLSI reference method was followed with the exception of the use of a small amount (0.1%) of Pluronic (a wetting agent) in the final inoculum. A validation of the use of Pluronic in the frozen reference panel was conducted. QC was also performed with no difference apparent in the results.

Read method comparison of *Streptococcus* species and Cefotaxime

Non-meningitis breakpoints	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	#R	min	maj	vmj
Challenge Manual	70	65	92.9	61	56	91.8	13	8	0	0
Challenge Automated	70	65	92.9	59	54	91.5	13	9	0	0

Meningitis breakpoints	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	#R	min	maj	vmj
Challenge Manual	70	65	92.9	61	56	91.8	23	6	0	1
Challenge Automated	70	65	92.9	59	54	91.5	23	9	0	1

EA-Essential Agreement
R-resistant isolates

maj-major discrepancies
vmj-very major discrepancies
min- minor discrepancies

Essential agreement (EA) is when the Microscan® MICroSTREP *plus*® panels agree with the reference test panel results exactly or within one doubling dilution of the reference method. Evaluable (Eval) are results that are within the test range and on scale.

Automated reading results were the same as the manual reading results with no trending.

There was one (1/22, 4.5%) vmj generated by one *Streptococcus pneumoniae* isolate with the automated reading method, evaluated with the Meningitis breakpoints. The same isolate produced a min error using the Nonmeningitis breakpoints with the automated reading method. The overall EA% of 92.9% and Eval EA% of 91.8% for the manual read and overall EA% of 92.5% and Eval EA% of 91.5% for the automated reading were both acceptable. No other differences or trending was observed between the manual and the automated reading method results. Therefore, the data are acceptable.

The test device had a growth rate of >95% for both the manual reading and the automated reading methods.

The comparison of the reading methods demonstrates that the manual reading method and the automated reading on the MicroScan® WalkAway System are no different. The efficacy data performed with the manual reading method would therefore be expected to have no differences.

The performance data currently documented in the package insert will not change.

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:

Cefotaxime	S	I	R
<i>Streptococcus pneumoniae</i>			
(nonmeningitis)	≤ 1	2	≥ 4
<i>Streptococcus pneumoniae</i>			
(meningitis)	≤ 0.5	1	≥ 2
<i>Streptococcus</i> spp. other than <i>Streptococcus pneumoniae</i>			
Beta hemolytic group*	≤ 0.5	---	---
Viridans group	≤ 1	2	≥ 4

The expected value range, interpretive criteria and QC as recommended by CLSI are included in the package insert.

*The absence of resistant strains of beta hemolytic streptococci precludes defining any results categories other than “susceptible”. For isolates yielding results suggestive of a “nonsusceptible” category, organism identification and antimicrobial susceptibility results should be confirmed.

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.