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

A. 510(k) Number:
K060447

B. Purpose for Submission:
Submission of the antibiotics Nitrofurantoin at concentrations of 8 - 512 µg/mL, Trimethoprim-Sulfamethoxazole at concentrations of 0.5/9.5 – 16/304 µg/mL, and Nalidixic Acid at concentrations of 2 - 32 µg/mL, for additional organism groups to the Gram Negative ID/AST or AST only Phoenix™ panel.

C. Measurands:
Nitrofurantoin at 8 - 512 µg/mL
Trimethoprim-Sulfamethoxazole at 0.5/9.5 – 16/304 µg/mL
Nalidixic Acid at 2 - 32 µg/mL

D. Type of Test:
Antimicrobial Susceptibility Test (Quantitative and Qualitative) colorimetric oxidation-reduction, growth-based

E. Applicant:
Becton, Dickinson & Company

F. Proprietary and Established Names:
BD Phoenix™ Automated Microbiology System – Nitrofurantoin at 8 - 512 µg/mL, Trimethoprim-Sulfamethoxazole at 0.5/9.5 – 16/304 µg/mL, Nalidixic Acid at 2 - 32 µg/mL, Gram Negative (GN) panel

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial
2. Classification:
   Class II
3. Product Code:
   LON
4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):
   Nitrofurantoin at concentrations of 8 - 512 µg/mL, Trimethoprim-Sulfamethoxazole at concentrations of 0.5/9.5 – 16/304 µg/mL and Nalidixic Acid at concentrations of 2 - 32 µg/mL on the Phoenix™ Gram Negative ID/AST or AST only panels are intended for use with the BD Phoenix™ Automated Microbiology System for the *in vitro* quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most gram-negative aerobic and facultative anaerobic bacteria belonging to the family *Enterobacteriaceae* and non – E*nterobacteriaceae* and gram-positive bacteria belonging to the genera *Staphylococcus, Streptococcus* and *Enterococcus*.

2. Indication(s) for use:
   Submission of the antibiotics Nitrofurantoin at 8 - 512 µg/mL, Trimethoprim-Sulfamethoxazole at 0.5/9.5 – 16/304 µg/mL and Nalidixic Acid at 2 - 32 µg/mL for additional organism groups to the Gram Negative ID/AST or AST only Phoenix™ panel.

3. Special condition for use statement
   Serratia marcescens will be suppressed from reporting SXT in the Phoenix™ system.
   An alternate method should be used when this combination has been identified.
   Prescription Use Only
4. Special instrument Requirements:
   Not Applicable

I. Device Description:

This submission is for the AST Panel only. The ID System was not reviewed.
The BD Phoenix™ Automated Microbiology System includes instrumentation and software, sealed and self-inoculating molded polystyrene trays with 136 micro-wells containing dried reagents, and specific inoculum broth formulations for AST Indicator. The organism to be tested must be a pure culture and be preliminarily identified as gram positive or gram negative. Colonies are then suspended in broth, and equated to a 0.5 McFarland with the recommendation to use the BD CrystalSpec™ Nephelometer. A further dilution is made into an AST broth, which contains an AST indicator, prior to inoculating the panel. The AST broth is a cation-adjusted broth containing Tween 80. After adding the indicator solution to the AST inoculum, the color is blue, and after inoculation and incubation, it changes to pink then colorless as reduction in the panel well proceeds. Inoculated panels are barcode scanned and loaded into the BD Phoenix™ Automated Microbiology System instrument where the panels are continuously incubated at 35°C. The resulting AST has a final inoculum of 5×10^5 CFU/ml. The instrument incubates, reads and records the results of the biochemical substrates and antimicrobial

agents and interprets the reactions to give a MIC value and category interpretation of the antimicrobial agents. Organisms growing in the presence of a given antimicrobic agent reduce the indicator, signaling organism growth and resistance to the antimicrobic agent. Organisms killed or inhibited by a given antimicrobic do not cause reduction of the indicator and therefore do not produce a color change. Additional interpretation is done using software driven "EXPERT" System using rules derived from the Clinical and Laboratory Standards Institute (CLSI). Readings are taken every 20 minutes with an AST result available between 4-16 hours. This is only an autoread result; there are no manual readings possible.

J. Substantial Equivalence Information:

1. Predicate device name(s):
   VITEK® System

2. Predicate K number(s):
   N50510

3. Comparison with predicate:

Similarities		
Item	**Device**	**Predicate**
Intended use	Intended for the *in vitro* rapid quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria.	same
Isolates	Isolated colonies from culture used	Isolated colonies from culture used
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)
Incubation conditions	<16 hours	<16 hours
Type of Test	Automated	Automated

Differences		
Item	**Device**	**Predicate**
Reading algorithm	Results are determined from serial twofold dilutions of antimicrobial agents	Results are determined from extrapolation of doubling dilutions
Technology	Automated growth based enhanced by use of a redox indicator (colorimetric oxidation-reduction) to	Automated growth based with detection using an attenuation of light measured by an optical

	detect organism growth.	scanner.

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 AST portion of the BD Phoenix™ Automated Microbiology System is a broth based microdilution method that utilizes a redox indicator (colorimetric oxidation-reduction) to enhance detection of organism growth. The MIC is determined by comparing growth in wells containing serial two-fold dilutions of an antibiotic to the growth in "growth control wells" which contain no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. ***Precision/Reproducibility***

Intersite and Intrasite testing demonstrated >95% reproducibility. The ten isolate study described in the guidance document was used (10 organisms tested 3 times on 3 days at 3 sites).

b. Linearity/assay reportable range:

Not applicable

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

Quality Control was performed during the testing of all isolates on each day of testing with the following results. The tables below include the concentrations tested around the expected range with the frequency of the reference and the Phoenix™ results at each concentration.

Nitrofurantoin

Organism	Concentration µg/ml	Reference Results	Phoenix™ Results
E. coli ATCC 25922 Expected Range 4 – 16 µg/mL	<=8	359	338
	16	12	42
	32		2
	64		
	128		
	256		
	512		
	>512	1	2

Nalidixic Acid

Organism	Concentration µg/ml	Reference Results	Phoenix™ Results
E. coli ATCC 25922 Expected Range 1 – 4 µg/mL	<=2	331	369
	4	40	14
	8	2	
	16		
	32		
	>32	1	1

Trimethoprim-Sulfamethoxazole

Organism	Concentration µg/ml	Reference Results	Phoenix™ Results		Organism	Concentration µg/ml	Reference Results	Phoenix™ Results
E. coli ATCC 25922 Expected Range <=0.5/9.5 µg/mL	<=0.5/9.5	384	386		P. aeruginosa ATCC 25853 Expected Range 8/152 – 32/608 µg/mL	<=0.5/9.5	1	2
	1/19					1/19		
	2/38					2/38		
	4/76					4/76		3
	8/152					8/152	41	114
	16/304		1			16/304	98	265
	>16/304	1				>16/304	244	

Phoenix produced acceptable QC results as compared to the reference method results >95% of the time.

Inoculum density control: The organism suspension density of the ID broth was equivalent to a 0.5 McFarland standard using the BBL™ CrystalSpec™ Nephelometer which was verified each day of testing. Internal data was used to demonstrate that the use of the BBL™ CrystalSpec™ Nephelometer would produce reproducible results. Five different instruments were used.

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 broth dilution reference panel was prepared according to the CLSI recommendation and used to compare with the Phoenix™ results. Clinical testing was performed at six sites. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. Performance charts below include all data, original and the additional organisms for fresh and challenge organisms.

Nitrofurantoin (FM)

Nitrofurantoin (FM) - GN Clinical and Challenge Data for *Enterobacteriaceae* with Additional Organism Groups

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Combined	**2130**	**2040**	**95.8**	**1850**	**1772**	**95.8**	**2130**	**1797**	**84.4**	**536**	**312**	**21**	**0**

Trimethoprim-Sulfamethoxazole (SXT)

SXT - GN Clinical and Challenge Data for *Enterobacteriaceae* with Additional Organism Groups, but with a limitation on all *Serratia marcescens*

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Combined	**2212**	**2123**	**96.0**	**120**	**70**	**58.3**	**2212**	**2162**	**97.7**	**549**	**NA**	**31**	**19**

Nalidixic Acid (NA)

NA - GN Clinical and Challenge Data for *Enterobacteriaceae* with Additional Organism Groups

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA Tot	CA N	CA %	#R	min	maj	vmj
Combined	**2103**	**2023**	**96.2**	**819**	**771**	**94.1**	**2103**	**2023**	**96.2**	**587**	**NA**	**12**	**18**

EA-Essential Agreement
CA-Category Agreement
R-resistant isolates
NA-not applicable (no Intermediate breakpoint)

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

Essential agreement (EA) is when the BD Phoenix™ panels agree with the reference test panel results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the BD Phoenix™ panel (SIR) result interpretation agrees exactly with the reference panel result (SIR) interpretation. Evaluable (Eval) are results that are within the test range and on scale.

*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:

Nitrofurantoin	<=32 (S), 64 (I), >=128 (R)
Trimethoprim-Sulfamethoxazole	<=2/38 (S), NA, >=4/76 (R)
Nalidixic Acid	<=16 (S), NA, >=32 (R)

N. Proposed Labeling

The expected value range interpretive criteria and QC for gram negative panels are included in the package insert. 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.