(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
k051272

B. Purpose for Submission:
Addition of clindamycin to the BD Phoenix™ SMIC/ID and
SMIC Panels

C. Measurand:
Clindamycin 0.0313 - 4 µg/mL

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

E. Applicant:
Becton, Dickinson & Company

F. Proprietary and Established Names:
BD Phoenix™ Automated Microbiology System – Clindamycin (Strep) 0.0313 - 4
µg/mL

G. Regulatory Information:

1. Regulation section:
   21 CFR 866.1645 Fully Automated Short-Term Incubation Cycle Antimicrobial
   Susceptibility System

2. Classification:
   II

3. Product code:
   LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation

4. Panel:
   83 Microbiology

H. Intended Use:

1. Intended use(s):
   The BD Phoenix™ Automated Microbiology System is intended for the *in vitro*
   quantitative determination of antimicrobial susceptibility by minimal inhibitory
   concentration (MIC) of gram-negative aerobic and facultative anaerobic bacteria

belonging to the family *Enterobacteriaceae* and non – *Enterobacteriaceae* and most gram-positive bacteria isolates from pure culture belonging to the genera *Staphylococcus, Enterococcus* and *Streptococcus*.

The BD Phoenix™ SMIC/ID and SMIC Panel is intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria isolates from pure culture belonging to the genera *Streptococcus*.

2. Indication(s) for use:
    This submission is for the addition of the antibiotic clindamycin at concentrations of 0.0313 - 4 µg/mL for testing *Streptococcus* spp., including *Pneumococcus* species only.

3. Special conditions for use statement(s):
    For prescription use only

4. Special instrument requirements:
    Not Applicable

I. Device Description:

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 ID and AST-S 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-S broth, which contains an AST- S indicator, prior to inoculating the panel. The AST-S broth is a non-blood, cation-adjusted broth containing purified water, Tween 80, pancreatic digest of casein, peptones and other additional supplements for optimization of streptococcal growth. After adding the indicator solution to the AST- S 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 an ID of the isolate and 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 ID result available between 2-12 hours and

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 510(k) number(s):
   N50510

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
1. Intended Use	Intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most bacteria.	Same
2. Isolates	Isolated colonies from culture used	Isolated colonies from culture used
3. Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)
4. Incubation Time	<16 hours	<16 hours
5. Type of Test	Automated	Automated

Differences		
Item	Device	Predicate
1. Results achieved	Results are determined from serial twofold dilutions of antimicrobial agents	Results are determined from extrapolation of doubling dilutions
2. Sample Preparation	Inoculum density equated to 0.5 McFarland standard	Inoculum density equated to 1.0 McFarland standard
3. Technology	Automated growth based enhanced by use of a redox indicator	Automated growth based with detection using an attenuation of light

Differences		
Item	Device	Predicate
	(colorimetric oxidation-reduction) to detect organism growth.	measured by an optical scanner.

K. Standard/Guidance Document Referenced (if applicable):
"Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA"; CLSI M7 (M100-S15) "Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard."

L. Test Principle:
The system employs conventional, colorimetric, fluorogenic and chromogenic substrates to identify the genus and species of the isolate. 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 contains no antibiotic.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*
   Thirteen isolates were evaluated for site to site and inter site reproducibility demonstrating >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 methods):*
   The CLSI recommended QC isolate, *S. pneumoniae* ATCC 49619 was tested on every test occasion with the reference method and the BD Phoenix™. The reference method QC results were in range for every day tested. The BD Phoenix™ was tested a sufficient number of times to demonstrate that the system can produce QC results in the CLSI recommended ranges. The BD Phoenix™ and reference method had the same mode.

Quality Control Table

ORGANISM	conc. (µg/mL)		Reference		BD Phoenix™	
S. pneumoniae	≤0.0313		2		30	
ATCC 49619	0.0625		103		91	
Expected Range:	0.125		20		1	
≤0.03 – 0.12 µg/mL						

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. Five *Streptococcal* strains were evaluated to demonstrate acceptable reproducibility performance.

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 CLSI recommended broth dilution reference panel was prepared according to the CLSI recommendation. Clinical testing was performed at four sites. The broth reference panel was set up on MH supplemented with 2% to 5% lysed horse blood as recommended by CLSI. The testing included both fresh clinical isolates and stock isolates along with a challenge set with known results. The test device had a growth rate of >95%. A comparison was provided to the reference method with the following agreement.

Summary Table for *Streptococcus spp.*

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	1823	1717	94.2	1173	1088	92.8	1772	97.2	158	16	34	1
Challenge	119	115	96.6	55	53	96.4	117	98.3	31	1	1	0
Combined	1942	1832	94.3	1228	1141	92.9	1889	97.3	189	17	35	1

EA-Essential Agreement **maj-**major discrepancies
CA-Category Agreement **vmj-**very major discrepancies
R-resistant isolates **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 result interpretation agrees exactly with the reference panel result interpretation. Evaluable EA is when the MIC result is on scale for both the BD Phoenix™ and the reference and have on-scale EA.

The 23 maj errors with the *S. agalactiae* group were further tested with an alternate method to determine if they have inducible resistance to clindamycin. All 23 strains gave a positive "D zone" indicating inducible clindamycin resistance. Therefore, these 23 strains are not true maj errors but should be reported as "clindamycin resistant" which would then make the maj error rate of 0.3% (1/333) for this group acceptable.

Summary Table for *Streptococcus spp.* (after Inducible Resistance to Clindamycin)

	EA Tot	EA N	EA %	Eval EA Tot	Eval EA N	Eval EA %	CA N	CA %	#R	min	maj	vmj
Clinical	1823	1717	94.2	1173	1088	92.8	1772	97.2	158	16	10	1
Challenge	119	115	96.6	55	53	96.4	117	98.3	31	1	1	0
Combined	1942	1832	94.3	1228	1141	92.9	1889	97.3	189	17	11	1

The table above reflects the number of maj errors after the 23 maj errors that are clindamycin resistant by induction have been removed.

   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:
   Streptococcus pneumoniae ≤0.25(S), 0.5(I), ≥1(R)
   Streptococcus spp. Other than *Streptococcus pneumoniae* ≤0.25(S), 0.5(I), ≥1(R)

N. Proposed Labeling:
   The Interpretative criteria, QC isolates and the expected ranges are the same as recommended by CLSI. All values will be included in the package insert.

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