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

**A. 510(k) Number:**
**K070809**

**B. Purpose for Submission:**
Submission of the antibiotic minocycline at concentrations of 1 - 32 µg/mL for Gram Positive ID/AST or AST only Phoenix™ panels.

**C. Measurand:**
Minocycline at 1 - 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 – Minocycline 1 – 32 µg/mL
Gram Positive panel (GP) ID/AST or AST only

**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):
   Minocycline at concentrations of 1 - 32 µg/mL on the Phoenix™ Gram Positive ID/AST or AST only panel is intended for use with the Phoenix™ system in clinical laboratories as an *in vitro* diagnostic test to determine the susceptibility from pure culture of *Staphylococcus aureus* to antimicrobial agents when used as instructed in the Phoenix™ system user's manual.

The BD Phoenix™ Automated Microbiology System is intended 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 most gram-positive bacteria belonging to the genera *Staphylococcus, Streptococcus* and *Enterococcus*.

2. Indication(s) for use:
   The antibiotic minocycline at concentrations of 1 – 32 µg/mL on the Phoenix™ GP ID/AST and AST only panels is indicated for testing against *Staphylococcus aureus.* Minocycline has been shown to be active against *S. aureus* in clinical infections and *in vitro* against *Enterococcus* species (vancomycin resistant).

3. Special condition for use statement(s):
   Prescription Use Only

   All Gram-positive organisms other than *Staphylococcus aureus* will be suppressed from reporting interpretive criteria against minocycline, by the BDXpert Rules software.

   Susceptibility testing should be performed with tetracycline since it predicts susceptibility testing to minocycline. However, certain organisms (e.g. *S. aureus*) may be more susceptible to minocycline and doxycycline than tetracycline.

   The Clinical Laboratory Standards Institute (CLSI) recommends that results for chloramphenicol, erythromycin, tetracycline (or doxycycline or minocycline), and rifampin should be reported for enterococcal isolates with an interpretation of intermediate or resistant to vancomycin (VRE). Consultation with an infectious disease practitioner is recommended.

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 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 x $10^5$ CFU/ml. The system 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 not growing 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 K number(s):
   N50510

3. Comparison with predicate:

| Similarities | | |
|---|---|---|
| **Item** | **Device** | **Predicate** |
| 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 |
| 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 detect organism growth. | Automated growth based with detection using an attenuation of light measured by an optical 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-S17) "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):**

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

1. Analytical performance:

*a.* ***Precision/Reproducibility***

The inter-site and intra-site reproducibility testing demonstrated greater than (>) 95% reproducibility. The ten isolate study design described in the guidance document was used with twelve organisms for a total of 324 results evaluated (12 organisms tested 3 times on 3 days at 3 sites). No trending was observed.

***b. Linearity/assay reportable range:***

Not applicable

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

The Phoenix™ results demonstrated that the system compared to the reference method can produce QC results for *Staphylococcus aureus* ATCC 29212 and *Enterococcus faecalis* ATCC 29213 in the recommended range >95% of the time. The following tables provide

the frequency of the results in each concentration tested with the expected range stated. The mode for the reference method results was the same as the mode for the Phoenix™ results.

No QC trending was observed.

| Organism | Concentration µg/mL | Reference results | Phoenix™ results |
|---|---|---|---|
| | | | |
| *E. faecalis* ATCC 29213 Expected range 1 - 4 µg/mL | <=1 | 64 | 39 |
| | 2 | 95 | 88 |
| | 4 | 3 | |
| | 8 | 2 | |
| | 16 | | |
| | >=32 | | |
| | Not compliant | 1 | 1 |

| Organism | Concentration µg/mL | Reference results | Phoenix™ results |
|---|---|---|---|
| | | | |
| *Staphylococcus aureus* ATCC 29212 Expected range 0.06 – 0.5 µg/mL | <=1 | 164 | 162 |
| | 2 | | |
| | 4 | | |
| | 8 | | |
| | 16 | | |
| | >=32 | | |
| | Not compliant | 1 | |

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

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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 four sites. The testing included 1619 isolates of which 103 were Challenge strains with known results and 1516 were Clinical strains. The 1516 Clinical strains were composed of 710 (46.8%) fresh clinical isolates, 640 (42.2%) recent isolates and 166 (10.9%) stock isolates.

The study included a variety of Gram-positive aerobic Clinical isolates, and the Challenge isolates consisted of a variety of *Enterococcus* species and *S. aureus* isolates, with the following performance (see table below). The FDA (CDRH) approved drug labeling provides breakpoints for minocycline only for *Staphylococcus aureus*. Therefore, the table below contains performance data for all Gram positive aerobic species for EA and Eval EA, and *S. aureus* only for CA.

**GP Clinical and Challenge data for Minocycline**

| | EA Tot | EA N | EA % | Eval EA Tot | Eval EA N | Eval EA % | CA Total* | CA N | CA % | #R | min | maj | vmj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Clinical** | **1516** | **1499** | **98.9** | **314** | **302** | **96.2** | **709** | **700** | **98.7** | **1** | **9** | **0** | **0** |
| **Challenge** | **103** | **101** | **98.1** | **26** | **26** | **100.0** | **36** | **34** | **100.0** | **0** | **2** | **0** | **0** |
| **Combined** | **1619** | **1600** | **98.8** | **340** | **328** | **96.5** | **745** | **734** | **98.5** | **1** | **11** | **0** | **0** |

***The CA Total applies to *Staphylococcus aureus* only**

**EA-**Essential Agreement
**CA-**Category Agreement
**R**-resistant isolates
**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 MIC results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the BD Phoenix™ panel result interpretation (susceptible-intermediate-resistant) agrees exactly with the reference panel result interpretation. Evaluable (Eval) are results that are within the test range and on scale.

The overall performance data demonstrates an EA of 98.8% and an Eval EA of 96.5%. There were no vmj or maj generated by *Staphylococcus aureus* and the CA is 98.5%, which meets the acceptance criteria.

The test device had a growth rate of >95% and the performance data are acceptable.

***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 aureus*
   Interpretive criteria = <=4 (S), 8 (I), >=16 (R)

## N. Labeling

The expected value range, interpretive criteria and QC for minocycline utilized in gram positive panels are included in the package insert. Minocycline is intended only for *Staphylococcus aureus*. All Gram-positive organisms other than *Staphylococcus aureus* will be suppressed from reporting interpretive criteria against minocycline, by the BDXpert Rules software.

Susceptibility testing should be performed with tetracycline since it predicts susceptibility testing to minocycline. However, certain organisms (e.g. *S. aureus*) may be more susceptible to minocycline and doxycycline than tetracycline.

The CLSI recommends that results for chloramphenicol, erythromycin, tetracycline (or doxycycline or minocycline), and rifampin should be reported for enterococcal isolates with an interpretation of intermediate or resistant to vancomycin (VRE). Consultation with an infectious disease practitioner is recommended.

The MIC only without an Interpretation will print on the final patient chart for *Enterococcus* species (VRE only).

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.