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

## I Background Information:

### A 510(k) Number

K250447

### B Applicant

Becton, Dickinson and Company

### C Proprietary and Established Names

BD Phoenix Automated Microbiology System - GN Imipenem-relebactam (0.0625/4-16/4 µg/mL)

### D Regulatory Information

| Product Code(s) | Classification | Regulation Section | Panel |
|---|---|---|---|
| LON | Class II | 21 CFR 866.1645 - Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System | MI - Microbiology |

## II Submission/Device Overview:

### A Purpose for Submission:

The addition of imipenem-relebactam (0.0625/4-16/4 µg/mL) to the BD Phoenix Gram negative ID/AST and AST only Phoenix panels

### B Measurand:

Imipenem-relebactam (0.0625/4-16/4 µg/mL)

### C Type of Test:

Antimicrobial susceptibility test (quantitative) colorimetric, oxidation-reduction, growth based.

## III Intended Use/Indications for Use:

### A Intended Use(s):

The BD Phoenix Automated Microbiology System is intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of Gram Negative aerobic and facultative anaerobic bacteria belonging to the family Enterobacterales and non-Enterobacterales.

### B Indication(s) for Use:

The BD Phoenix Automated Microbiology System is intended for *in vitro* quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of most Gram-negative aerobic and facultative anaerobic bacteria isolates from pure culture for Enterobacterales and Non-Enterobacterales and most Gram-positive bacteria isolates from pure culture belonging to the genera *Staphylococcus, Enterococcus,* and *Streptococcus*.

This premarket notification is for the BD Phoenix Automated Microbiology System with imipenem-relebactam at concentrations of 0.0625/4-16/4 µg/mL. Testing is indicated for *Acinetobacter calcoaceticus-baumannii* complex, Enterobacterales, and *Pseudomonas aeruginosa*, as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC).

The BD Phoenix Automated Microbiology System - GN Imipenem-relebactam (0.0625/4 - 16/4 µg/mL) has demonstrated acceptable performance with the following organisms:

*Acinetobacter calcoaceticus-baumannii* complex

Enterobacterales (*Citrobacter amalonaticus, Citrobacter braakii, Citrobacter farmeri, Citrobacter freundii, Citrobacter koseri, Citrobacter youngae, Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae,* and *Serratia marcescens*)

*Pseudomonas aeruginosa*

### C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

### D Special Instrument Requirements:

BD Phoenix Automated Microbiology System and software (V2.20.0.0 or higher)

PhoenixSpec Nephelometer

BD Phoenix AP Instrument

## IV Device/System Characteristics:

### A Device Description:

This submission is for addition of imipenem-relebactam (0.0625/4-16/4 µg/mL) to the BD Phoenix ID/AST or AST only panels. The ID portion of the ID/AST combination panel was not subject to review in this submission.

The Phoenix AST method is a broth-based microdilution test. The Phoenix panel is a sealed and self-inoculating molded polystyrene tray with 136 micro-wells containing dried reagents. The ID/AST combination panel includes an ID side (51 wells) with dried substrates for bacterial identification and an AST side (85 wells). The AST panel contains a wide range of two-fold doubling dilution concentrations of antimicrobial agents and growth and fluorescent controls at appropriate well locations. The AST panel does not include wells for isolate identification. The Phoenix System utilizes a redox indicator for the detection of organism growth in the presence of an antimicrobial agent. 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 ID broth and equated to a 0.5 McFarland suspension using a nephelometer device. A further dilution is made into AST broth (a cation-adjusted formulation of Mueller-Hinton broth containing 0.010% Tween 80), to which the redox-buffered oxidation-reduction AST indicator solution is added producing a blue color in the wells. The concentration of organisms in the final AST broth suspension is approximately $5 \times 10^5$ CFU/mL.

The Phoenix AST Broth is poured into the inoculation port of the AST panel and the inoculum flows into the panel, filling panel wells. Polyethylene caps are applied to seal the inoculation ports. An air admittance port is located in the panel lid to ensure adequate oxygen tension in the panel for the duration of the test. Inoculated panels are barcode scanned and loaded into the BD Phoenix Automated Microbiology System instrument where panels are continuously incubated at 35°C ± 1 °C.

Continuous measurements of changes to the indicator as well as bacterial turbidity are used in the determination of bacterial growth. The instrument takes readings every 20 minutes. Organisms growing in the presence of a given antimicrobial agent reduce the indicator (changing it to a pink color). This signals organism growth and resistance to that antimicrobial agent. Organisms killed or inhibited by the antimicrobial agent do not cause reduction of the indicator and therefore do not produce a color change. The Phoenix instrument reads and records the results of the antimicrobial tests contained in the panel and interprets the reactions (based on the organism identification) to give a minimal inhibitory concentration (MIC) value and category interpretations (susceptible, intermediate, resistant, or not susceptible). AST results are available within 16 hours. This is an auto read result; no manual readings are possible with this system.

Additional comments concerning specific organism/antimicrobial combinations are provided from the software-driven expert system (BDXpert), using rules derived from CLSI documentation and/or the FDA-approved drug labeling.

## B Principle of Operation:

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” that contain no antibiotic.

## V Substantial Equivalence Information:

### A Predicate Device Name(s):
BD Phoenix Automated Microbiology System- Imipenem (0.0625-32 µg/mL)

### B Predicate 510(k) Number(s):
K123404

### C Comparison with Predicate(s):

| **Device & Predicate Device(s):** | Device<br>K250447 | Predicate<br>K123404 |
|---|---|---|
| Device Trade Name | BD Phoenix Automated Microbiology System - GN Imipenem-relebactam (0.0625/4-16/4 µg/mL) | BD Phoenix Automated Microbiology System - GN Imipenem (0.0625-32 µg/mL) |
| **General Device Characteristic Similarities** | | |
| Intended Use | The BD Phoenix Automated Microbiology System is intended for the *in vitro* rapid identification (ID) and quantitative determination of antimicrobial susceptibility by minimal inhibitory concentration (MIC) of Gram Negative aerobic and facultative anaerobic bacteria belonging to the family Enterobacterales and non-Enterobacterales. | Same |
| Source of Microorganisms for Testing | Bacterial colonies isolated from culture | Same |
| Technology | Automated growth-based detection | Same |
| Methodology | Determination of MIC using serial two-fold | Same |

| | | |
|---|---|---|
| | dilution format | |
| Read Method | Automated | Same |
| Inoculation Methods | Manual: BD PhoenixSpec nephelometer<br>Automated: BD Phoenix AP Instrument | Same |
| Result Reported | Report results as minimum inhibitory concentration (MIC) and categorical interpretation (S, I, R) | Same |
| Incubation Time | < 16 hours | Same |
| **General Device Characteristic Differences** | | |
| Antimicrobial Agent | Imipenem-relebactam | Imipenem |
| Reporting Range | 0.0625/4-16/4 µg/mL | 0.0625-32 µg/mL |
| Tested Organisms | *Acinetobacter calcoaceticus-baumannii* complex<br><br>Enterobacterales *(Citrobacter amalonaticus, Citrobacter braakii, Citrobacter farmeri, Citrobacter freundii, Citrobacter koseri, Citrobacter youngae, Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca, Klebsiella pneumoniae,* and *Serratia marcescens)*<br><br>*Pseudomonas aeruginosa* | *Acinetobacter spp.*<br>*Citrobacter spp.*<br>*Enterobacter cloacae*<br>*Escherichia coli*<br>*Klebsiella pneumoniae*<br>*Pseudomonas aeruginosa*<br>*Serratia marcescens* |

## VI Standards/Guidance Documents Referenced:

Guidance for Industry and FDA, Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems, August 28, 2009.

CLSI. Performance Standards for Antimicrobial Susceptibility Testing. 34th ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2024.

CLSI. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically. 12th ed. CLSI supplement M07. Clinical Laboratory Standards Institute; 2024.

## VII Performance Characteristics (if/when applicable):

### A Analytical Performance:

1. Precision/Reproducibility:
   Reproducibility of the BD Phoenix Automated Microbiology System - GN Imipenem – relebactam (0.0625/4-16/4 µg/mL) was conducted at three clinical sites using a panel of 15 on-scale isolates. The isolates were tested at each site in triplicate over three different days using both inoculation methods (manual and BD Phoenix AP) resulting in 405 data points (15 strains × 3 replicates × 3 sites × 3 days = 405) for each inoculum method. The isolates tested in the reproducibility study included, *Enterobacter cloacae* (2), *Escherichia coli* (5), *Klebsiella aerogenes* (1), *Klebsiella pneumoniae* (3) *and Pseudomonas aeruginosa* (4). The reproducibility was calculated based on MIC values falling within ±1 dilution of the predetermined mode of the reference MIC values. There were no "off-scale" MIC results for both inoculum method. The results of the study demonstrate that there was an overall reproducibility across test sites of 100% (± 1 dilution) when compared to the test mode for both inoculation methods (manual and BD Phoenix AP). The reproducibility results met the acceptance criteria of >95% and were determined to be acceptable.

2. Linearity:

   Not applicable

3. Analytical Specificity/Interference:

   Not applicable

4. Assay Reportable Range:

   This submission is for addition of imipenem-relebactam with reporting range of 0.0625/4-16/4 µg/mL.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

   Quality Control Testing:
   The CLSI recommended QC organisms (*E. coli* ATCC 25922, *P. aeruginosa* ATCC 27853, *E. coli* ATCC 35218, *K. pneumoniae* ATCC 700603, *K. pneumoniae* ATCC BAA-1705, and *K. pneumoniae* ATCC BAA-2814) were tested a minimum of 20 times per site using both manual and Phoenix AP inoculation methods and read by the BD Phoenix instrument. The QC strains were also tested with the reference method.

The results demonstrate that BD Phoenix Automated Microbiology System - GN Imipenem – relebactam produced quality control results in the recommended range >95% of the time (Table 1). Results were acceptable.

**Table 1. Quality Control for Imipenem – relebactam**

| QC Organism* | Expected Range | Concentration (µg/mL) | Reference | BD Phoenix | |
|---|---|---|---|---|---|
| | | | | Manual | Phoenix AP |
| *E. coli* ATCC 25922 | 0.0625/4-0.5/4 µg/mL | ≤ 0.0625 | 12 | | |
| | | 0.125 | 108 | 26 | 4 |
| | | 0.25 | 13 | 45 | 42 |
| | | 0.5 | | 18 | 35 |
| | | 1 | | | 1 |
| | | 2 | | | |
| | | 4 | | | |
| | | 8 | | | |
| | | 16 | | | |
| | | >16 | | | |
| *P. aeruginosa* ATCC 27853 | 0.25/4-1/4 µg/mL | ≤ 0.0625 | | | |
| | | 0.125 | | | |
| | | 0.25 | 81 | 76 | 60 |
| | | 0.5 | 50 | 12 | 22 |
| | | 1 | 2 | | |
| | | 2 | | | |
| | | 4 | | | |
| | | 8 | | | |
| | | 16 | | | |
| | | >16 | | | |
| *E. coli* ATCC 35218 | 0.0625/4-0.25/4 µg/mL | ≤ 0.0625 | | | |
| | | 0.125 | 124 | 40 | 7 |
| | | 0.25 | 6 | 50 | 75 |
| | | 0.5 | | | |
| | | 1 | | | |
| | | 2 | | | |
| | | 4 | | | |
| | | 8 | | | |
| | | 16 | | | |
| | | >16 | | | |
| *K. pneumoniae* ATCC 700603 | 0.0625/4-0.5/4 µg/mL | ≤ 0.0625 | | | |
| | | 0.125 | 94 | 79 | 31 |
| | | 0.25 | 30 | 11 | 52 |
| | | 0.5 | 4 | | |
| | | 1 | 1 | | |
| | | 2 | | | |
| | | 4 | | | |
| | | 8 | | | |
| | | 16 | | | |
| | | >16 | | | |
| *K. pneumoniae* ATCC BAA-1705† | 0.03125/4-0.25/4 µg/mL | ≤ 0.0625 | 4 | 80 | 47 |
| | | 0.125 | 84 | 11 | 34 |
| | | 0.25 | 39 | | |
| | | 0.5 | 4 | | |

| QC Organism* | Expected Range | Concentration (µg/mL) | Reference | BD Phoenix | |
|---|---|---|---|---|---|
| | | | | Manual | Phoenix AP |
| | | 1 | 1 | | |
| | | 2 | | | |
| | | 4 | | | |
| | | 8 | | | |
| | | 16 | | | |
| | | >16 | 1 | | |
| *K. pneumoniae* ATCC BAA-2814 | 0.0625/4-0.5/4 µg/mL | ≤ 0.0625 | | | |
| | | 0.125 | 29 | 89 | 75 |
| | | 0.25 | 76 | 2 | 6 |
| | | 0.5 | 22 | | 1 |
| | | 1 | 3 | | |
| | | 2 | | | |
| | | 4 | | | |
| | | 8 | | | |
| | | 16 | | | |
| | | >16 | | | |

Grey shaded rows indicate expected range for the BD Phoenix Automated Microbiology System - GN Imipenem-relebactam.

* CLSI M100 ED34 recommends use of *Klebsiella pneumoniae* ATCC BAA-1705 and/or *Klebsiella pneumoniae* ATCC BAA-2814 for routine QC for Imipenem-relebactam.

†The lowest dilution of the BD Phoenix Automated Microbiology System – GN Imipenem – relebactam MIC range is ≤0.0625/4 µg/mL. Obtaining this value was considered an indicator that the quality control test results were acceptable.

**Inoculum Density Check:**
The BD PhoenixSpec Nephelometer was used to prepare the inocula for testing of the clinical, challenge, reproducibility, and QC isolates. The same inoculum suspension was used for both the Phoenix System and the reference method testing. The BD Phoenix AP instrument was used to standardize the inocula for challenge, QC, and reproducibility isolates. Validation data for both the PhoenixSpec and the Phoenix AP instrument was provided and found to be acceptable.

**Growth Failure Rate:**
The growth failure rate for both inoculation methods was 0%.

**Purity Check:**
Purity check plates were performed on all isolates from each inoculum preparation. Results were only included for pure cultures.

6. Detection Limit:

Not applicable

7. Assay Cut-Off:

Not applicable

## B Comparison Studies:

1. Method Comparison with Predicate Device:

**Imipenem-relebactam (0.0625/4-16/4 µg/mL):** Results obtained with the BD Phoenix Automated Microbiology System - GN Imipenem-relebactam (0.0625/4-16/4 µg/mL) panel were compared to results obtained with the CLSI frozen broth microdilution reference panel. Reference panels were prepared according to CLSI M07 guidelines. The range of dilutions evaluated with the reference panels was the same as that used for the BD Imipenem-relebactam panel.

**Medium:** BD Phoenix AST Broth – a cation-adjusted formulation of Mueller Hinton broth used in conjunction with the AST Indicator Solution, a redox indicator.

**Inoculum:** The BD Phoenix Spec Nephelometer, the primary inoculation method, was used to obtain a 0.50 – 0.60 McFarland for all challenge, clinical, QC and reproducibility isolates.

**Incubation:** 35°C ± 1°C

**Clinical:** Clinical testing was conducted at three U.S. sites using 862 (77.6%) fresh and 249 (22.4%) stock isolates for a total of 1,111 clinical isolates. These consisted of *Acinetobacter baumannii/calcoaceticus* complex (83 isolates), *Citrobacter freundii* (21 isolates), *Citrobacter species* (9 isolates), *Citrobacter koseri* (26 isolates), *Enterobacter cloacae* (60 isolates), *Escherichia coli* (359 isolates), *Klebsiella aerogenes* (58 isolates), *Klebsiella oxytoca* (47 isolates), *Klebsiella pneumoniae* (198 isolates), *Pseudomonas aeruginosa* (176 isolates), and *Serratia marcescens* (74).

**Challenge:** A total of 85 challenge isolates were evaluated at three U.S. sites using *Acinetobacter baumannii/calcoaceticus* complex (7 isolates), *Citrobacter freundii* (2 isolates), *Citrobacter koseri* (2 isolates), *Enterobacter cloacae* (12 isolates), *Escherichia coli* (19 isolates), *Klebsiella aerogenes* (4 isolates), *Klebsiella pneumoniae* (24 isolates), and *Pseudomonas aeruginosa* (15 isolates).

Results for clinical and challenge isolates were evaluated separately and combined.

The performance of testing imipenem-relebactam using the manual inoculation method is illustrated in the Table 2 below.

**Table 2. Imipenem-relebactam (0.0625/4-16/4 µg/mL) Results, Manual Inoculation**

| | Tot | No. EA | EA % | Eval EA Tot | No. Eval EA | Eval EA % | No. CA | CA % | No. R | No. S | min | major | vmj |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Acinetobacter baumannii/calcoaceticus* complex, [≤2/4 (S), I (4/4), ≥8/4 (R)]** | | | | | | | | | | | | | |
| Clinical | 83 | 80 | 96.4 | 72 | 69 | 96.0 | 81 | 97.6 | 10 | 73 | 2 | 0 | 0 |
| Challenge | 7 | 7 | 100 | 3 | 3 | 100 | 7 | 100 | 5 | 2 | 0 | 0 | 0 |
| Total | 90 | 87 | 96.7 | 75 | 72 | 96.1 | 88 | 97.8 | 15 | 75 | 2 | 0 | 0 |

| **Enterobacterales, [≤1/4 (S), I (2/4), ≥4/4 (R)]** | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Clinical | 852 | 791 | 92.8 | 781 | 720 | 92.2 | 841 | 98.7 | 5 | 837 | 11 | 0 | 0 |
| Challenge | 63 | 60 | 95.2 | 47 | 44 | 93.62 | 61 | 96.8 | 19 | 43 | 2 | 0 | 0 |
| Total | 915 | 851 | 93.0 | 828 | 764 | 92.3 | 902 | 98.6 | 24 | 880 | 13 | 0 | 0 |
| ***Pseudomonas aeruginosa*, [≤2/4 (S), I (4/4), ≥8/4 (R)]** | | | | | | | | | | | | | |
| Clinical | 176 | 174 | 98.9 | 176 | 174 | 98.9 | 174 | 98.9 | 1 | 173 | 2 | 0 | 0 |
| Challenge | 15 | 15 | 100 | 11 | 11 | 100 | 13 | 86.7 | 6 | 9 | 2 | 0 | 0 |
| Total | 191 | 189 | 99.0 | 187 | 185 | 98.9 | 187 | 97.9 | 7 | 182 | 4 | 0 | 0 |

EA – Essential Agreement
CA – Categorical Agreement
S – Susceptible
Maj – Major Discrepancies
EVAL – Evaluable MICs
R – Resistant
min – Minor Discrepancies
vmj – Very Major Discrepancies

Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of BD Phoenix within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on scale for both the BD Phoenix panel and the reference method or those in which an off-scale result is at least two doubling dilutions from the on-scale result. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the BD Phoenix result.

The BD Phoenix AP instrument, the secondary inoculation method, was evaluated using challenge, QC and reproducibility isolates. The BD Phoenix AP instrument is designed to standardize the ID broth inoculum equivalent to the BD Phoenix Spec Nephelometer. Following suspension standardization, the instrument adds the preset amount of AST indicator broth to the AST broth tube and transfers the required aliquot of ID broth inoculum to AST broth tubes.

The performance of testing imipenem-relebactam using the BD Phoenix AP inoculation method is illustrated in the Table 3 below.

**Table 3. Imipenem-relebactam (0.0625/4-16/4 µg/mL) Results, Phoenix AP inoculation Method**

| | **Tot** | **No. EA** | **EA %** | **Eval EA Tot** | **No. Eval EA** | **Eval EA %** | **No. CA** | **CA %** | **No. R** | **No. S** | **min** | **major** | **vmj** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Acinetobacter baumannii calcoaceticus* complex, [≤2/4 (S), I (4/4), ≥8/4 (R)]** | | | | | | | | | | | | | |
| Challenge | 6 | 6 | 100 | 4 | 4 | 100 | 6 | 100 | 4 | 2 | 0 | 0 | 0 |
| **Enterobacterales, [≤1/4 (S), I (2/4), ≥4/4 (R)]** | | | | | | | | | | | | | |
| Challenge | 64 | 63 | 98.44 | 51 | 50 | 98.0 | 63 | 98.4 | 18 | 44 | 0 | 0 | 1† |
| ***Pseudomonas aeruginosa*, [≤2/4 (S), I (4/4), ≥8/4 (R)]** | | | | | | | | | | | | | |
| Challenge | 15 | 15 | 100 | 12 | 12 | 100 | 14 | 93.33 | 6 | 9 | 1 | 0 | 0 |

† For *Klebsiella pneumoniae*, there was one very major discrepancy observed with the Phoenix AP inoculation method, which was considered a random error due to the limited number of resistant isolates tested. In addition, no very major discrepancies were observed with the same isolate tested with the manual inoculation method.

EA – Essential Agreement
CA – Categorical Agreement
EVAL – Evaluable MICs
R – Resistant

S – Susceptible
Maj – Major Discrepancies
min – Minor Discrepancies
vmj – Very Major Discrepancies

Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of BD Phoenix within plus or minus one serial two-fold dilution of the antibiotic. Evaluable results are those that are on scale for both the BD Phoenix panel and the reference method or those in which an off-scale result is at least two doubling dilutions from the on-scale result. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the BD Phoenix result.

The performance of manual inoculation method was evaluated using combined clinical and challenge data for 1196 isolates tested that includes 90 *Acinetobacter baumannii/calcoaceticus* complex (83 clinical and 7 challenge isolates), 915 Enterobacterales (852 clinical and 63 challenge isolates) and 191 *Pseudomonas aeruginosa* (176 clinical and 15 challenge isolates). Included in the results are 9 species drug label non-listed (all clinical isolates) represents <10% of the total number of isolates tested (0.7%, 9/1196). The performance data included in the device labeling included combined performance for *Acinetobacter baumannii/calcoaceticus* complex*,* Enterobacterales, and *Pseudomonas aeruginosa*.

For *Acinetobacter baumannii/calcoaceticus* complex using manual inoculation method, the combined clinical and challenge results (90 isolates) were acceptable at 96.7% and 97.8% for EA and CA respectively. There were two minor discrepancies, no major discrepancy and no very major discrepancy (Table 2). All individual species of *Acinetobacter baumannii/calcoaceticus* complex when evaluated for manual inoculation method resulted into acceptable performance (>89.9%) for both EA and CA.

For Enterobacterales using manual inoculation method, the combined clinical and challenge results (915 isolates) were acceptable at 93.0% and 98.6% for EA and CA respectively. There were 13 minor discrepancies, no major discrepancy and no very major discrepancy (Table 2). All individual species of Enterobacterales when evaluated combined for clinical and challenge isolates using manual inoculation method resulted into acceptable performance (>89.9%) for both EA and CA.

For *P. aeruginosa* using manual inoculation method, the combined clinical and challenge results (191 isolates) were acceptable at 99.0% and 97.9% for EA and CA respectively. There were four minor discrepancies, no major discrepancy and no very major discrepancy (Table 2). All individual isolates of *P. aeruginosa* when evaluated combined for clinical and challenge isolates using manual inoculation method resulted into acceptable performance (> 90%) for both EA and CA.

The performance of BD Phoenix AP inoculation method was evaluated using challenge data for 85 isolates tested at one internal site that includes *Acinetobacter baumannii/calcoaceticus* complex (6 isolates), *Citrobacter freundii* (2 isolates), *Citrobacter koseri* (2 isolates), *Enterobacter cloacae* (12 isolates), *Escherichia coli* (19 isolates), *Klebsiella aerogenes* (4 isolates), *Klebsiella oxytoca* (1 isolate), *Klebsiella pneumoniae* (24 isolates), and *Pseudomonas aeruginosa* (15 isolates).

The performance evaluation for the organism groups *Acinetobacter baumannii/calcoaceticus* complex, Enterobacterales, and *Pseudomonas aeruginosa* using BD Phoenix AP inoculation

method are acceptable at >89.9% for EA and CA. For *Acinetobacter baumannii/calcoaceticus* complex, there were no minor discrepancies, no major discrepancies and no very major discrepancies (Table 3). The individual species of *Acinetobacter baumannii/calcoaceticus* complex when evaluated for BD Phoenix AP inoculation method resulted in acceptable performance (>89.9%) for both EA and CA.

For Enterobacterales when evaluated using Phoenix AP inoculation method, there were no minor discrepancies and no major discrepancies but one very major discrepancy was observed (Table 3). This single very major discrepancy observed with the Phoenix AP inoculation method was due to a challenge isolate of *Klebsiella pneumoniae.* This isolate was also tested by the manual inoculation method and no very major discrepancies were observed. To provide clarity on the performance provided in the device labeling, following statement was included as a footnote to the performance table:

*"For Klebsiella pneumoniae, there was one very major discrepancy observed with the Phoenix AP inoculation method, which was considered a random error due to the limited number of resistant isolates tested. In addition, no very major discrepancies were observed with the same isolate tested with the manual inoculation method."*

For *Pseudomonas aeruginosa* when evaluated using the Phoenix AP inoculation method, there was one minor discrepancy and no major or very major discrepancies (Table 3).

In summary, the overall performance results for the BD Phoenix Automated Microbiology System - GN Imipenem-relebactam (0.0625/4-16/4 µg/mL) using manual inoculation and BD Phoenix AP inoculation are acceptable.

**Trending**

A trending analysis was conducted using the combined data (clinical and challenge) obtained from the manual inoculation method. This trending calculation takes into account MIC values that are determined to be one or more doubling dilutions lower or higher than the reference method irrespective of whether the device MIC values are on-scale or not. Results that are not clearly at least one dilution lower, at least one dilution higher or in exact agreement with the CLSI reference method are not considered in the trending analysis.

Organism groups or species for which the difference between the percentage of isolates with higher vs. lower readings was > 30% and for which the confidence interval was determined to be statistically significant were considered to show evidence of trending. Trending that showed higher or lower MIC values compared to the reference is addressed in the labeling.

Trending analysis results of Imipenem-relebactam (0.0625/4-16/4 µg/mL) with manual inoculation method are summarized in Table 4. A trend toward lower MIC values as observed for *Enterobacter cloacae* and higher MIC values was observed for *Escherichia coli* and *Klebsiella aerogenes* when compared to the CLSI broth microdilution reference method.

To address the MIC trending, following footnote was provided to include in the performance table in the labeling:

*"BD Phoenix Imipenem-relebactam MIC values tended to be in exact agreement or at least one doubling dilution lower when testing Enterobacter cloacae or at least one doubling*

*dilution higher when testing Escherichia coli and Klebsiella aerogenes compared to the reference broth microdilution method."*

**Table 4. Trending of Imipenem-relebactam (0.0625/4 – 16/4 µg/mL) with Manual Inoculation**

| Organism | Total Evaluable for Trending | ≥ 1 Dilution Lower No. (%) | Exact No. (%) | ≥ 1 Dilution Higher No. (%) | Percent Difference (CI) | Trending Noted |
|---|---|---|---|---|---|---|
| *Acinetobacter baumannii / calcoaceticus complex* | 78 | 12, (15.4) | 47 | 19, (24.4) | 9.0% , (-4%, 21%) | No |
| *Citrobacter amalonaticus* | 3 | 0, (0) | 2 | 1, (33.3) | 33% , (-29%, 79%) | Yes* |
| *Citrobacter braakii* | 4 | 2, (50) | 1 | 1, (25) | -25% , (-66%, 32%) | No |
| *Citrobacter farmeri* | 1 | 0, (0) | 0 | 1, (100) | 100% , (-12%, 100%) | Yes* |
| *Citrobacter freundii* | 22 | 8, (36.4) | 11 | 3, (13.6) | -23% , (-45%, 3%) | No |
| *Citrobacter koseri* | 25 | 5, (20) | 19 | 1, (4) | -16% , (-35%, 3%) | No |
| *Citrobacter youngae* | 0 | 0,0 | 0 | 0,0 | 0 | NA |
| *Enterobacter cloacae* | 69 | 33, (47.8) | 28 | 8, (11.6) | -36% , (-49%, -21%) | Yes |
| *Escherichia coli* | 363 | 31, (8.5) | 187 | 145, (39.9) | 31% , (25%, 37%) | Yes |
| *Klebsiella aerogenes* | 62 | 6, (9.7) | 30 | 26, (41.9) | 32% , (17%, 46%) | Yes |
| *Klebsiella oxytoca* | 45 | 10, (22.2) | 28 | 7, (15.6) | -7% , (-23%, 10%) | No |
| *Klebsiella pneumoniae* | 213 | 59, (27.7) | 86 | 68, (31.9) | 4% , (-4%, 13%) | No |
| *Pseudomonas aeruginosa* | 189 | 57, (30.2) | 114 | 18, (9.5) | -21% , (-28%, -13%) | No |
| *Serratia marcescens* | 73 | 15, (20.6) | 28 | 30, (41.1) | 21% , (6%, 34%) | No |

* Not statistically significant.

As required under 511A(2)(2)(B) of the Federal Food, Drug and Cosmetic Act, the following statement is added to the Precautions section of the device labeling:

*Per the FDA-Recognized Susceptibility Test Interpretive Criteria website, the safety and efficacy of antimicrobial drugs for which antimicrobial susceptibility is tested by this AST device, may or may not have been established in adequate and well-controlled clinical trials for treating clinical infections due to microorganisms outside of those found in the indications and usage in the drug label. The clinical significance of susceptibility information in those instances is unknown. The approved labelling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved.*

2. Matrix Comparison:

Not applicable.

**C Clinical Studies:**

1. Clinical Sensitivity:

Not applicable

2. Clinical Specificity:

Not applicable

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

Not applicable

**D Clinical Cut-Off:**

Not applicable

**E Expected Values/Reference Range:**

**Table 5: FDA – Identified Interpretive Criteria for Imipenem-relebactam[a]**

| Pathogens | Minimum Inhibitory Concentrations (µg/mL) | | |
|---|---|---|---|
| | Susceptible | Intermediate | Resistant |
| Enterobacterales | ≤1/4 | 2/4 | ≥4/4 |
| *Pseudomonas aeruginosa* | ≤2/4 | 4/4 | ≥8/4 |
| *Acinetobacter calcoaceticus-baumannii* complex | ≤2/4 | 4/4 | ≥8/4 |

[a] According to FDA STIC Webpage https://www.fda.gov/drugs/development-resources/fda-recognized-antimicrobial-susceptibility-test-interpretive-criteria

## VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

## IX Conclusion:

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

To support the implementation of changes to FDA-recognized susceptibility test interpretive criteria (i.e., breakpoints), this submission is incorporated by reference a breakpoint change protocol that includes the Predetermined Change Control Plan (PCCP) titled 'BD Phoenix Breakpoint Change Evaluation Procedure, which was previously reviewed and approved in submission K233986 cleared on March 15, 2024. This PCCP addresses future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm). The PCCP outlined the specific procedures and acceptance criteria that Becton, Dickinson and Company intend to use to evaluate the BD Phoenix Automated Microbiology System – GN

Imipenem-relebactam when revised breakpoints for imipenem-relebactam are published on the FDA STIC webpage. The PCCP included with the submission indicated that if specific criteria are met, Becton, Dickinson and Company will update the BD Phoenix Automated Microbiology System - GN Imipenem-relebactam device label to include (1) the new breakpoints, (2) an updated performance section after re-evaluation of data in this premarket notification with the new breakpoints, and (3) any new limitations as determined by their evaluation.