May 19, 2025

Becton, Dickinson and Company
Kamisha Gray
Senior Regulatory Affairs Specialist
7 Loveton Circle
Sparks, Maryland 21152

Re: K250447
Trade/Device Name: BD Phoenix™ Automated Microbiology System - GN Imipenem-relebactam (0.0625/4 - 16/4 µg/mL)
Regulation Number: 21 CFR 866.1645
Regulation Name: Fully Automated Short-Term Incubation Cycle Antimicrobial Susceptibility System
Regulatory Class: Class II
Product Code: LON
Dated: February 14, 2025
Received: February 18, 2025

Dear Kamisha Gray:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

Please note that if you modify your IVD in the future to exceed any of the limitations to the exemption found in 21 CFR 866.9(c), your device will require a new 510(k) prior to marketing this device in the United States and will not be exempt from the premarket notification requirements so long as it exceeds the limitations to the exemption found in 21 CFR 866.9.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

FDA's substantial equivalence determination also included the review and clearance of your Predetermined Change Control Plan (PCCP). Under section 515C(b)(1) of the Act, a new premarket notification is not required for a change to a device cleared under section 510(k) of the Act, if such change is consistent with an established PCCP granted pursuant to section 515C(b)(2) of the Act. Under 21 CFR 807.81(a)(3), a new premarket notification is required if there is a major change or modification in the intended use of a device, or if there is a change or modification in a device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process. Accordingly, if deviations from the established PCCP result in a major change or modification in the intended use of the device, or result in a change or modification in the device that could significantly affect the safety or effectiveness of the device, then a new premarket notification would be required consistent with section 515C(b)(1) of the Act and 21 CFR 807.81(a)(3). Failure to submit such a premarket submission would constitute adulteration and misbranding under sections 501(f)(1)(B) and 502(o) of the Act, respectively.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (https://www.fda.gov/media/99812/download) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (https://www.fda.gov/media/99785/download).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label

and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ribhi Shawar -S

Ribhi Shawar, Ph.D. (ABMM)
Chief
General Bacteriology and Antimicrobial Susceptibility Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 07/31/2026
See PRA Statement below.

510(k) Number *(if known)*
K250447

Device Name
BD Phoenix™ Automated Microbiology System – GN Imipenem-relebactam (0.0625/4-16/4 µg/mL).

Indications for Use *(Describe)*
Indications 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 a concentration 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

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

510(k) Summary

Summary Preparation Date:

February 14, 2025

I Background Information:

A 510(k) Number
K250447

B Applicant
BD Diagnostic Systems
Becton, Dickinson and Company
7 Loveton Circle
Sparks, Maryland 21152
Establishment Registration Number: 1119779
Contact: Kamisha Gray
Telephone: 410-316-4000

C Proprietary and Established Names

BD Phoenix™ Automated Microbiology System – 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 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 a concentration 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 Statements(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 X 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 Names(s):

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

B Predicate 510(k) Numbers(s):

K123404

C Comparison with Predicate(s):

Table 1. Comparison with the Predicate

Device & Predicate Device(s):	Device: K250447 Imipenem-relebactam (0.0625/4-16/4 µg/mL)	Predicate: K123404 Imipenem (0.0625-32 µg/mL)
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)
Antimicrobial Agent	Imipenem-relebactam	Imipenem
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 dilution format	Same
Read Method	Automated	Same
Inoculation Methods	Manual: BD PhoenixSpec nephelometer 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		
Breakpoints	Enterobacterales: (S/I/R) ≤1/4 / 2/4 / ≥4/4 *Pseudomonas aeruginosa*: (S/I/R) ≤2/4 / 4/4 / ≥8/4 *Acinetobacter calcoaceticus-baumaannii* complex: (S/I/R) ≤2/4 / 4/4 / ≥8/4	Enterobacterales: (S/I/R) ≤1/ 2 / ≥4 *Pseudomonas aeruginosa*: (S/I/R) ≤2/ 4 / ≥8 *Acinetobacter* species: (S/I/R) ≤2/ 4 / ≥8
Reporting Range	0.0625/4-16/4 µg/mL	0.0625-32 µg/mL

Device & Predicate Device(s):	Device: K250447 Imipenem-relebactam (0.0625/4-16/4 µg/mL)	Predicate: K123404 Imipenem (0.0625-32 µg/mL)
Organisms Tested	*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*	Active *In Vitro* and in Clinical Infections Against: *Acinetobacter spp.* *Citrobacter spp.* *Enterobacter cloacae* *Escherichia coli* *Klebsiella pneumoniae* *Pseudomonas aeruginosa* *Serratia marscescens*
Breakpoint Change Evaluation Procedure	Procedure added	None

VI Standards/Guidance Documents Referenced

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

2. CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 33rd ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2023.

3. CLSI. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically*. 11th ed. CLSI supplement M07. Clinical Laboratory Standards Institute; 2018.

4. U.S. FDA Antibacterial Susceptibility Test Interpretive Criteria Website: https://www.fda.gov/drugs/development-resources/antibacterial-susceptibility-test-interpretive-criteria

VII Performance Characteristics (if/when applicable):

A Analytical Performance

1. Precision/Reproducibility:

Reproducibility was conducted at three clinical sites using 15 on-scale isolates of non-fastidious Gram-negative organisms. The isolates were tested at each site in triplicate over three different days using both inoculation methods (i.e., manual and

BD Phoenix AP) resulting in 405 data points (15 strains x 3 replicates x 3 sites x 3 days = 405). 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 manually prepared inocula or inocula prepared using the BD Phoenix AP. The best- and worst-case reproducibility was calculated as described in the AST Special Controls Guidance document. The results of the study demonstrate that for this antimicrobial agent and the Gram-negative organisms tested, there was an overall reproducibility across test sites of greater than 95% (± 1 dilution) agreement when compared to the test mode. The reproducibility results for each inoculation method are shown in Table 2.

Note: The testing for the Phoenix™ AP Instrument was performed at three internal BD sites.

Table 2. Summary of Reproducibility Studies- BD Phoenix Imipenem-relebactam

Inoculation Method	Best Case	Worst Case
Manual PhoenixSpec Nephelometer	100% (405/405)	100% (405/405)
Phoenix AP Instrument	100% (405/405)	100% (405/405)

2. Linearity:

   Not applicable

3. Analytical Specificity/Interference:

   Not applicable

4. Assay Reportable Range:

   Not applicable

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 sufficient number of times (i.e., at least 20/site) at each of three testing sites. It was tested using both manual and Phoenix AP inoculation methods and read by the BD Phoenix instrument. The results are summarized in Table 3. Results were acceptable for greater than 95% of tests performed using both inoculation methods.

Table 3. Quality Control Results- Imipenem-relebactam

Organism	Concentration (µg/mL)	Reference	BD Phoenix	
			Manual Inoculation (PhoenixSpec)	Phoenix AP Inoculation
Escherichia coli ATCC® 25922 Expected Range: 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			
Pseudomonas aeruginosa ATCC® 27853 Expected Range: 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			
Escherichia coli ATCC® 35218 Expected Range: 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			
Klebsiella pneumoniae ATCC® 700603 Expected Range: 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			

Organism	Concentration (µg/mL)	Reference	BD Phoenix	
			Manual Inoculation (PhoenixSpec)	Phoenix AP Inoculation
Klebsiella pneumoniae ATCC® BAA-1705† Expected Range: 0.03125/4-0.25/4 µg/mL	≤ 0.0625	4	80	47
	0.125	84	11	34
	0.25	39		
	0.5	4		
	1	1		
	2			
	4			
	8			
	16			
	>16	1		
Klebsiella pneumoniae ATCC® BAA-2814 Expected Range: 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			

†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.

6. Detection Limit:

   Not applicable

7. Assay Cut-Off:

   Not applicable

B Comparison Studies:

1. Method Comparison with Predicate Device:

   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. 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. The BD Phoenix AP instrument, the secondary inoculation method, was used to test challenge, QC, and reproducibility isolates. It is designed to standardize the ID broth inoculum equivalent to the BD Phoenix Spec Nephelometer, add the preset amount of AST indicator broth to the AST broth tube, and transfer the required aliquot of ID broth inoculum to AST broth tubes.

   Clinical:

   Clinical testing was conducted at three U.S. sites using 862 fresh and 249 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:

   Additional stock challenge isolates were tested at each study site. These isolates consisted of organisms with known resistance mechanisms to challenge the ability of AST system to correctly identify the susceptibility category. Challenge testing was conducted using 85 isolates including *Acinetobacter baumannii* (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. Table 4 below illustrates the performance of testing Imipenem-relebactam using the manual inoculation method only.

Table 4. Combined (Clinical and Challenge) Performance Summary of BD Phoenix with Clinical and Challenge Isolates – Manual Inoculation Method

Imipenem-relebactam	EA Total	EA N	%EA Total	Eval EA Tot	Eval EA N	%EA Eval	CA Total	CA N	%CA	#R	Min	Maj	Vmj
***Acientobacter baumanii/ calcoaceticus* complex ≤2 (Susceptible), 4 (Intermediate), ≥8 (Resistant)**													
Clinical	83	80	96.4	72	69	95.8	83	81	97.6	10	2	0	0
Challenge	7	7	100.0	3	3	100.0	7	7	100.0	5	0	0	0
Combined	90	87	96.7	75	72	96.0	90	88	97.8	15	2	0	0
Enterobacterales ≤1 (Susceptible), 2 (Intermediate), ≥4 (Resistant)													
Clinical	852	791	92.8	781	720	92.2	852	841	98.7	5	11	0	0
Challenge	63	60	95.2	47	44	93.6	63	61	96.8	19	2	0	0
Combined	915	851	93.0	828	764	92.3	915	902	98.6	24	13	0	0
***Pseudomonas aerugionosa* ≤2 (Susceptible), 4 (Intermediate), ≥8 (Resistant)**													
Clinical	176	174	98.9	176	174	98.9	176	174	98.9	1	2	0	0
Challenge	15	15	100.0	11	11	100.0	15	13	86.7	6	2	0	0
Combined	191	189	99.0	187	185	98.9	191	187	97.9	7	4	0	0

EA - Essential Agreement Maj – major discrepancies
CA - Category Agreement Vmj - very major discrepancies
R - resistant isolates Min – minor 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 the BD Phoenix Imipenem-relebactam met the combined acceptance criteria for *all* tested organisms, with overall EA and CA rates greater than 90%. Note, the EA for the *Klebsiella pneumoniae* challenge isolates was 87.5%, and the CA for the *Pseudomonas aeruginosa* challenge isolates was 86.7%. There were 19 minor errors and no major errors or very major errors for the combined performance. Performance was calculated as described in the AST guidance, with the exception of evaluable EA. While the AST guidance indicates that all results with a reference value of "less than" or "greater than" a certain dilution are not considered evaluable, evaluable EA was calculated in line with the FDA's current thinking where evaluable results for EA can be defined as any result that either (i) has on-scale MIC values for both the reference and test, OR (ii) has an off-scale value for the reference and/or test that is at least two doubling dilutions from the other result.

Inoculum Preparation Methods:

The challenge organisms were also tested by one clinical site using suspensions prepared by the Phoenix AP instrument. The comparison between manual (PhoenixSpec) method and Phoenix AP is shown in Table 5. The overall % EA and % CA met the acceptance criteria of ≥90%, with the exception of the %CA for *Pseudomonas aeruginosa* using the manual method, which was 86.7%. As detailed in the clinical section above, the combined performance for *Pseudomonas aeruginosa* using the manual method was 97.9% (Table 4). Additionally, there was one very major error for the Phoenix AP method for Enterobacterales, specifically for *Klebsiella pneumoniae,* 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. In this case, only 64 Enterobacterales isolates were tested, with a low number of resistant strains (n=18), resulting in a very major error rate of 5.6%. There were zero very major errors for the manual method and zero major errors for both inoculation methods.

Table 5. Comparison of Inoculation Methods with Challenge Isolates Only

Imipenem-relebactam	Total	EA N	%EA Total	Eval EA Tot	Eval EA N	%EA Eval	CA Total	CA N	%CA	#R	Min	Maj	Vmj
***Acinetobacter baumannii/ calcoaceticus* complex ≤2 (Susceptible), 4 (Intermediate), ≥8 (Resistant)**													
Manual (PhoenixSpec)	7	7	100.0	3	3	100.0	7	7	100.0	5	0	0	0
Phoenix AP	6	6	100.0	4	4	100.0	6	6	100.0	4	0	0	0
***Enterobacterales* ≤1 (Susceptible), 2 (Intermediate), ≥4 (Resistant)**													
Manual (PhoenixSpec)	63	60	95.2	47	44	93.6	63	61	96.8	19	2	0	0
Phoenix AP	64	63	98.4	51	50	98.0	64	63	98.4	18	0	0	1
***Pseudomonas aeruginosa* ≤2 (Susceptible), 4 (Intermediate), ≥8 (Resistant)**													
Manual (PhoenixSpec)	15	15	100.0	11	11	100.0	15	13	86.7	6	2	0	0
Phoenix AP	15	15	100.0	12	12	100.0	15	14	93.3	6	1	0	0

EA - Essential Agreement
CA - Category Agreement
R - resistant isolates
Maj – major discrepancies
Vmj - very major discrepancies
Min – minor discrepancies

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:

The FDA-recognized susceptibility interpretive criteria for Imipenem-relebactam are as listed in Table 6.

Table 6. FDA-Recognized Interpretive Criteria for Imipenem-relebactam*

	Minimum Inhibitory Concentrations (µg/mL)		
Pathogen	**S**	**I**	**R**
Enterobacterales[a]	≤1/4	2/4	≥4/4
Pseudomonas aeruginosa	≤2/4	4/4	≥8/4
Acinetobacter calcoaceticus-baumannii complex	≤2/4	4/4	≥8/4

*According to the **FDA STIC Website**
S = Susceptible; I = Intermediate; R = Resistant
[a] Clinical efficacy was shown for *Klebsiella aerogenes, Enterobacter cloacae*, *Escherichia coli, Klebsiella pneumoniae*, *Citrobacter freundii*, *Klebsiella oxytoca.*

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device when evaluated with the current FDA-recognized Imipenem-relebactam breakpoints.

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 included a predetermined change control plan (PCCP) that was reviewed and accepted by FDA, as described in the Antimicrobial Susceptibility Test (AST) System Devices – Updating Breakpoints in Device Labeling guidance**.** 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/development-resources/antibacterial-susceptibility-test-interpretive-criteria). The PCCP outlined the specific procedures and acceptance criteria that BD intends to use to evaluate the cleared BD Phoenix antimicrobial Imipenem-relebactam when revised breakpoints are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, BD will update the 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.