August 8, 2025

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

Re: K251713
Trade/Device Name: BD Phoenix Automated Microbiology System - GN Eravacycline (0.125-2 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: June 3, 2025
Received: June 3, 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.

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)
Branch 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)*
K251713

Device Name
BD Phoenix Automated Microbiology System – GN Eravacycline (0.125-2 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 Eravacycline at a concentration of 0.125-2 µg/mL. Testing is indicated for Enterobacterales as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC).

The BD Phoenix Automated Microbiology System - GN Eravacycline (0.125-2 µg/mL) has demonstrated acceptable performance with the following organisms:

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

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:

August 4, 2025

I Background Information:

A 510(k) Number
K251713

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 – GN Eravacycline (0.125-2 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 Eravacycline to the BD Phoenix™ Gram negative ID/AST and AST only Phoenix panels

B Measurand:

Eravacycline (0.125-2µg/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 order 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 Eravacycline at a concentration of 0.125-2 µg/mL. Testing is indicated for Enterobacterales as recognized by the FDA Susceptibility Test Interpretive Criteria (STIC).

The BD Phoenix Automated Microbiology System - GN Eravacycline (0.125-2 µg/mL) has demonstrated acceptable performance with the following organisms:

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

C Special Conditions for Use Statements(s):

Rx- For Prescription Use Only

The ability of the BD Phoenix AST system to detect non-susceptibility to eravacycline in the following species is unknown because non-susceptible strains were not available or insufficient at the time of comparative testing: *C. freundii, C. koseri, C. amalonaticus*, *C. braakii*, *C. farmeri*, *C. youngae* and *K. oxytoca.*

For *Enterobacter cloacae*, two of the five potential very major errors were within essential agreement when compared to the reference method. Due to the susceptible-only category, the potential very major error rate was adjusted to 15.8% (3/19). If deemed necessary for patient care, confirmatory testing with an alternate method could be performed for this organism before reporting Phoenix MIC results of 0.25 µg/mL.

For *Klebsiella pneumoniae*, eight of the eleven potential very major errors were within essential agreement when compared to the reference method. Due to the susceptible-only category, the potential very major error rate was adjusted to 8.1% (3/37). If deemed necessary for patient care, confirmatory testing with an alternate method could be performed

for this organism before reporting Phoenix MIC results of 0.25 µg/mL.

For *Klebsiella aerogenes*, neither of the two potential very major errors were within essential agreement when compared to the reference method. Due to the susceptible-only category, the potential very major error rate was adjusted to 20% (2/10). If deemed necessary for patient care, confirmatory testing with an alternate method could be performed for this organism before reporting Phoenix MIC results of 0.25 µg/mL.

For *Escherichia coli*, none of the three potential very major errors were within essential agreement when compared to the reference method. Due to the susceptible-only category, the potential very major error rate was not adjusted and remained at 100% (3/3). These errors occurred with a very low percentage of the total isolates evaluated (3/376, 0.8%). If deemed necessary for patient care, confirmatory testing with an alternate method could be performed for this organism before reporting Phoenix MIC results of ≤0.125 µg/mL or 0.25 µg/mL.

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 Eravacycline (0.125-2 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 Tigecycline (0.25-16 µg/mL)

B Predicate 510(k) Numbers(s):

K132909

C Comparison with Predicate(s):

Table 2. Comparison with the Predicate

Device & Predicate Device(s):	Device: (K251713) Eravacycline (0.125-2 µg/mL)	Predicate: K132909 Tigecycline (0.25-16 µg/mL)
Device Trade Name	BD Phoenix™ Automated Microbiology System - GN Eravacycline (0.125-2 µg/mL)	BD Phoenix™ Automated Microbiology System - GN Tigecycline (0.25-16 µg/mL)
Antimicrobial Agent	Eravacycline	Tigecycline
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 order 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
Incubation Time	< 16 hours	Same
General Device Characteristic Differences		
Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (S, NS)	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (S, I, R)
Breakpoints	Enterobacterales: (S) ≤ 0.5	Enterobacterales: (S/I/R) ≤2/ 4 / ≥8
Reporting Range	0.125-2 µg/mL	0.25-16 µg/mL

Device & Predicate Device(s):	Device: (K251713) Eravacycline (0.125-2 µg/mL)	Predicate: K132909 Tigecycline (0.25-16 µg/mL)
Tested Organisms	Enterobacterales *(Citrobacter amalonaticus, Citrobacter braakii, Citrobacter farmeri, Citrobacter freundii, Citrobacter koseri, Citrobacter youngae, Enterobacter cloacae, Escherichia coli, Klebsiella aerogenes, Klebsiella oxytoca,* and *Klebsiella pneumoniae).*	Active *In Vitro* and in Clinical Infections Against: *Citrobacter freundii* *Enterobacter cloacae* *Escherichia coli* *Klebsiella oxytoca* *Klebsiella pneumoniae* Active In Vitro but clinical significance is unknown *Citrobacter koseri* *Klebsiella aerogenes* (previously known as *Enterobacter aerogenes*) *Serratia marcescens*
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*. 35th ed. CLSI supplement M100. Clinical and Laboratory Standards Institute; 2025.

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

VII Performance Characteristics (if/when applicable):

A Analytical Performance

1. Precision/Reproducibility:

Reproducibility was conducted at three clinical sites using 12 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 324 data points (12 strains x 3 replicates x 3 sites x 3 days = 324). The isolates tested in the reproducibility study included, *Citrobacter freundii* (1), *Enterobacter cloacae* (5), *Klebsiella oxytoca* (1), and *Klebsiella pneumoniae* (5). 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 3.

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

Table 3. Summary of Reproducibility Studies- BD Phoenix Eravacycline

Inoculation Method	Best Case	Worst Case
Manual PhoenixSpec™ Nephelometer	100% (324/324)	100% (324/324)
Phoenix™ AP Instrument	100% (324/324)	100% (324/324)

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, and *P. aeruginosa* ATCC 27853) 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. Although the majority of QC results were off-scale, the expected range for *P. aeruginosa* ATCC 27853 was partially on-scale and the expected ranges of the two QC strains included values that span the reporting range. The results are summarized in Table 4. Results were acceptable for greater than 95% of tests performed using both inoculation methods.

Table 4. Quality Control Results- Eravacycline

Organism	Concentration (µg/mL)	Reference	BD Phoenix	
			Manual Inoculation (PhoenixSpec)	Phoenix AP Inoculation
Escherichia coli ATCC® 25922† Expected Range: 0.016-0.125 µg/mL	≤ 0.125	133	89	82
	0.25			
	0.5			
	1			
	2			
	>2			
Pseudomonas aeruginosa ATCC® 27853†† Expected Range: 2-16 µg/mL	≤ 0.125	3		
	0.25	1		
	0.5	1		
	1	4		
	2	12	33	20
	>2	111	55	62

†The lowest dilution of the BD Phoenix Automated Microbiology System – GN Eravacycline MIC range is ≤0.125µg/mL. Obtaining this value was considered an indicator that the quality control test results were acceptable.

††The highest dilution of the BD Phoenix Automated Microbiology System – GN Eravacycline MIC range is >2 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 Eravacycline (0.125/4–2 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 Eravacycline panel. The BD PhoenixSpec™ 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 PhoenixSpec™ 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 626 fresh and 159 stock isolates for a total of 785 clinical isolates. These consisted of *Citrobacter freundii* (23 isolates), *Citrobacter koseri* (26 isolates), *Citrobacter* species (9 isolates), *Enterobacter cloacae* (60 isolates), *Escherichia coli* (359 isolates), *Klebsiella aerogenes* (57 isolates), *Klebsiella oxytoca* (51 isolates), and *Klebsiella pneumoniae* (200 isolates).

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 84 isolates including *Citrobacter freundii* (3 isolates), *Citrobacter koseri* (2 isolates), *Enterobacter cloacae* (21 isolates), *Escherichia coli* (17 isolates), *Klebsiella aerogenes* (4 isolates), *Klebsiella oxytoca* (3 isolates), and *Klebsiella pneumoniae* (34 isolates).A total of 71 non-susceptible strains of Enterobacterales were evaluated. No non-susceptible strains of the following species were evaluated: *C. freundii, C. amalonaticus*, *C. braakii*, *C. farmeri*, and *C. youngae*. Only one isolate each of *C. koseri* and *K. oxytoca* was non-susceptible. As a result, the sponsor included the following limitation in the device labeling:

The ability of the BD Phoenix AST system to detect non-susceptibility to eravacycline in the following species is unknown because non-susceptible strains were not available or insufficient at the time of comparative testing: C. freundii, C. koseri, C. amalonaticus, *C. braakii*, *C. farmeri*, *C. youngae and K. oxytoca.*

Results for clinical and challenge isolates were evaluated separately and combined. Table 5 below illustrates the performance of testing Eravacycline using the manual inoculation method only.

Table 5. Combined (Clinical and Challenge) Performance Summary of BD Phoenix with Clinical and Challenge Isolates – Manual Inoculation Method

Eravacycline	EA Total	EA N	%EA Total	Eval EA Tot	Eval EA N	%EA Eval	CA Total	CA N	%CA	#NS	Min	Original Maj	Adjusted Maj	Original Vmj	Adjusted Vmj
Enterobacterales ≤0.5 (Susceptible)															
Clinical	785	769	98.0	348	332	95.4	785	768	97.8	41	N/A	2	0	15	10
Challenge	84	81	96.4	55	52	94.5	84	76	90.5	30	N/A	2	0	6	1
Combined	869	850	97.8	403	384	95.3	869	844	97.1	71	N/A	4	0	21	11

EA - Essential Agreement Maj – major discrepancies
CA - Category Agreement Vmj - very major discrepancies
NS – Non-susceptible isolates Min – minor discrepancies

N/A- Not applicable due to only a susceptible interpretive criterion for Eravacycline.

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.

Eravacycline only has a susceptible breakpoint; therefore, isolates are categorized as susceptible or non-susceptible. When categorical errors occur, these are considered potential errors. The BD Phoenix Eravacycline met the combined acceptance criteria of EA and CA for all indicated organisms, with overall EA and CA rates greater than 90%. Note that the CA for the *Klebsiella pneumoniae* challenge isolates was 79.4%.

Due to the absence of an intermediate interpretive criteria category, further analysis of potential errors was performed. Adjustments were made by considering the MIC values where the errors occurred. If potential errors were in EA, they were removed from the adjusted calculation. As summarized in Table 5, there were 4 potential major errors, resulting in a rate of 0.5% (4/798). All potential major errors had MIC values one doubling dilution from the reference, placing them within essential agreement. Therefore, the adjusted potential major error rate is 0%, which is below the FDA's acceptable limit of ≤ 3%.

As summarized in Table 5, a total of 21 potential very major errors (VMEs) were observed across all organisms tested, resulting in an initial VME rate of 29.6% (21/71). Upon further analysis, 10 of these errors had MIC values within one doubling dilution of the reference method and were thus considered to be in essential agreement (EA).
Excluding these, the adjusted potential VME rate is 15.5% (11/71), which remains above the FDA's acceptable threshold.

A comprehensive review of the 11 unresolved adjusted potential very major errors (VMEs), which were not in essential agreement, showed the following distribution by MIC:

- 9 adjusted potential VMEs occurred at an MIC of 0.25 µg/mL for:
  - *Enterobacter cloacae* (3 VMEs)
  - *Klebsiella pneumoniae* (3 VMEs)
  - *Klebsiella aerogenes* (2 VMEs)
  - *Escherichia coli* (1 VME)
- 2 adjusted potential VMEs occurred at an MIC of ≤0.125 µg/mL for:
  - *Escherichia coli* (2 VME)

Despite the elevated adjusted potential VME rate, the overall number of potential VMEs is low relative to the total number of isolates tested, reflecting the low resistance rate to Eravacycline. To support clinical laboratories in interpreting Phoenix MIC results, organisms- and MIC- specific limitation statements have been included in the product insert. These statements recommend confirmatory testing with an alternate method, when necessary, particularly for MIC values associated with higher adjusted potential VME rates:

- *Enterobacter cloacae*
  For *Enterobacter cloacae*, two of the five potential very major errors were within essential agreement when compared to the reference method. Due to the susceptible-only category, the potential very major error rate was

adjusted to 15.8% (3/19). If deemed necessary for patient care, confirmatory testing with an alternate method could be performed for this organism before reporting Phoenix MIC results of 0.25 µg/mL.

- *Klebsiella pneumoniae*
  For *Klebsiella pneumoniae*, eight of the eleven potential very major errors were within essential agreement when compared to the reference method. Due to the susceptible-only category, the potential very major error rate was adjusted to 8.1% (3/37). If deemed necessary for patient care, confirmatory testing with an alternate method could be performed for this organism before reporting Phoenix MIC results of 0.25 µg/mL.

- *Klebsiella aerogenes*
  For Klebsiella aerogenes, neither of the two potential very major errors were within essential agreement when compared to the reference method. Due to the susceptible-only category, the potential very major error rate was adjusted to 20% (2/10). If deemed necessary for patient care, confirmatory testing with an alternate method could be performed for this organism before reporting Phoenix MIC results of 0.25 µg/mL.

- *Escherichia coli*
  For *Escherichia coli*, none of the three potential very major errors were within essential agreement when compared to the reference method. Due to the susceptible-only category, the potential very major error rate was not adjusted and remained at 100% (3/3). These errors occurred with a very low percentage of the total isolates evaluated (3/376, 0.8%). If deemed necessary for patient care, confirmatory testing with an alternate method could be performed for this organism before reporting Phoenix MIC results of ≤0.125 µg/mL or 0.25 µg/mL.

Inoculum Preparation Methods:

Challenge organisms were tested by one clinical site using suspensions prepared by the Phoenix™ AP instrument. Table 6 compares the manual (PhoenixSpec™) method and Phoenix™ AP. Eravacycline only has a susceptible breakpoint; therefore, isolates are categorized as susceptible or non-susceptible. When categorical errors occur, these are considered potential errors. The BD Phoenix Eravacycline met the combined acceptance criteria of EA and CA for all indicated organisms, with overall EA and CA rates greater than 90%.

Due to the lack of an intermediate interpretive criteria, further analysis of potential errors was performed. Adjustments were made by considering the MIC values where the potential errors occurred. If potential errors were in EA, they were removed from the adjusted calculation.
Table 6 shows 2 (2/54 = 3.7%) and 5 (5/58 = 8.6%) potential major errors for the manual and Phoenix AP methods, respectively. All potential major errors had MIC values one doubling dilution from the reference, thus in essential agreement.

Therefore, the adjusted potential major error rate is zero, which is below the acceptable limit of ≤ 3%.

Table 6 also shows 6 (6/30 = 20.0%) and 1(1/22= 4.5%) potential very major errors for the manual and Phoenix AP methods, respectively. Five of the 6 potential very major errors for the manual method and the one potential very major error for the Phoenix™ AP method had MIC values one doubling dilution from the reference, thus in essential agreement.
Therefore, the adjusted potential very major error rate is 3.3% for the manual method and zero for the Phoenix™ AP method. The adjusted potential very major error rate for the manual method is unacceptable but addressed with limitations in the product insert.

Table 6. Comparison of Inoculation Methods with Challenge Isolates Only

Eravacycline	Total	EA N	%EA Total	Eval EA Tot	Eval EA N	%EA Eval	CA Total	CA N	%CA	#NS	Min	Original Maj	Adjusted Maj	Original Vmj	Adjusted Vmj
Enterobacterales ≤0.5 (Susceptible)															
Manual (PhoenixSpec)	84	81	96.4	55	52	94.5	84	76	90.5	30	N/A	2	0	6	1
Phoenix AP	80	78	97.5	48	46	95.8	80	74	92.5	22	N/A	5	0	1	0

EA - Essential Agreement
CA - Category Agreement
NS - non-susceptible
Maj – major discrepancies
Vmj - very major discrepancies
Min – minor discrepancies

N/A- Not applicable due to only a susceptible interpretive criterion for Eravacycline.

MIC 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.

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.

Evaluation of results for species within Enterobacterales with eravacycline using the manual inoculation method are summarized in Table 5. A trend toward lower MIC values was observed for *Citrobacter freundii, Citrobacter koseri, and Escherichia coli* when compared to the CLSI broth microdilution reference method.

To address the MIC trending, the sponsor included the following footnote in the performance table in the device labeling:

"BD Phoenix Eravacycline MIC values tended to be in exact agreement or at least one doubling dilution lower when testing Citrobacter freundii, Citrobacter koseri, and Escherichia coli compared to the reference broth microdilution method."

Table 7. Trending of Eravacycline (0.125-2 µg/mL) Results with Manual Inoculation

Organism	Total Evaluable for Trending	≥ 1 Dilution Lower No. (%)	Exact No.	≥ 1 Dilution Higher No. (%)	Percent Difference (CI)	Trending Noted
Citrobacter freundii	22	11 (50.0)	10	1 (4.6)	-45% (-65%, -20)	Yes, Low
Citrobacter koseri	14	10 (71.4)	4	0 (0.0)	-71% (-88%, -38%)	Yes, Low
Enterobacter cloacae	78	24 (30.8)	49	5 (6.4)	-24% (-36%, -12%)	No
Escherichia coli	94	75 (79.8)	14	5 (5.3)	-74% (-82%, -63%)	Yes, Low
Klebsiella aerogenes	58	14 (24.1)	40	4 (6.9)	-17% (-30%, -4%)	No
Klebsiella oxytoca	34	9 (26.5)	12	13 (38.2)	12% (10%, 32%)	No
Klebsiella pneumoniae	227	40 (17.6)	162	25 (11.0)	-7% (-13%, 0%)	No

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 Eravacycline are as listed in Table 8.

Table 8. FDA-Recognized Interpretive Criteria for Eravacycline*

	Minimum Inhibitory Concentrations (µg/mL)		
Pathogen	**S**	**I**	**R**
Enterobacterales[a]	≤0.5	-	-

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

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device when evaluated with the current FDA-recognized Eravacycline 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 previously reviewed and accepted by FDA 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/development-resources/antibacterial-susceptibility-test- interpretive-criteria). The PCCP outlined the specific procedures and acceptance criteria that BD intends to use to evaluate the BD Phoenix Automated Microbiology System - GN Eravacycline when revised breakpoints for eravacycline are published on the FDA STIC webpage. The PCCP included with the submission indicated that if specific criteria are met, BD will update the eravacycline 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.