510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K221826

B Applicant

BD Diagnostic Systems
Becton Dickinson, and Company

C Proprietary and Established Names

BD BBL Sensi-Disc Cefiderocol 30ug (FDC-30)

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
JTN	Class II	21 CFR 866.1620 - Antimicrobial Susceptibility Test Disc	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain substantial equivalence determination for Cefiderocol Antimicrobial Susceptibility Test Disc.

B Measurand:

Cefiderocol 30 µg (FDC30)

C Type of Test:

Antimicrobial Susceptibility Test Disc

III Intended Use/Indications for Use:

A Intended Use(s):
See Indications for Use below.

B Indication(s) for Use:
BD BBL Sensi-Disc Antimicrobial Susceptibility Test (AST) Discs are used in the semi-quantitative agar diffusion test method for in vitro susceptibility testing.

BD BBL Sensi-Disc Cefiderocol Disc 30 µg (FDC30) can be used to determine susceptibility to Cefiderocol against the following bacteria, as described in the FDA-approved package insert for this antimicrobial agent.

Active *in vitro* and in Clinical Infections Against:

Complicated Urinary Tract Infections, Including Pyelonephritis
Gram-negative Bacteria
Escherichia coli
Enterobacter cloacae complex
Klebsiella pneumoniae
Proteus mirabilis
Pseudomonas aeruginosa

Hospital-acquired Bacterial Pneumonia and Ventilator-associated Bacterial Pneumonia (HABP/VABP)
Gram-negative Bacteria
Acinetobacter baumannii complex
Escherichia coli
Enterobacter cloacae complex
Klebsiella pneumoniae
Pseudomonas aeruginosa
Serratia marcescens

Active *in vitro* Against:

Citrobacter freundii complex
Citrobacter koseri
Klebsiella aerogenes
Klebsiella oxytoca
Morganella morganii
Proteus vulgaris
Providencia rettgeri

C Special Conditions for Use Statement(s):
Rx - For Prescription Use Only

Limitations:

- The ability of the BD BBL Sensi Disc to detect resistance with the following combination(s) is unknown because an insufficient number of resistant strains were encountered at the time of comparative testing: Cefiderocol (30µg) and Enterobacterales group, *P. aeruginosa* and *Acinetobacter baumannii*. If such a

strain is encountered, it should be submitted to a reference laboratory for further testing.

- While the categorical agreement for BD BBL Sensi-Disc Cefiderocol compared to FDA cleared Disk analysis was > 95% for *Pseudomonas aeruginosa* and *Acinetobacter baumannii* complex, categorical agreement for BD BBL Sensi-Disc Cefiderocol compared to historical BMD MIC values was below 90%, caused by the occurrence of false susceptible results and minor errors. Test results for Cefiderocol/*P. aeruginosa* which provide a disc zone of inhibition ≥ 22 mm, and test results for Cefiderocol/*A. baumannii* which provide a disc zone of inhibition ≥ 19 mm, should be interpreted in conjunction with other clinical and laboratory information.

- While the categorical agreement for BD BBL Sensi-Disc Cefiderocol compared to FDA cleared Disk analysis was > 95% for Enterobacterales group organisms, categorical agreement for BD BBL Sensi-Disc Cefiderocol compared to historical BMD MIC values resulted in false susceptible results. *Citrobacter freundii* complex, *Citrobacter koseri*, *Klebsiella pneumoniae*, *Morganella morganii*, and *Proteus mirabilis* isolates that provide a disc zone of inhibition ≥ 16 mm should be interpreted in conjunction with other clinical and laboratory information.

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

The BD BBL Sensi-Disc Cefiderocol 30 µg (FDC30) device is comprised of 6 mm discs prepared by impregnating high quality absorbent paper with accurately determined amounts of Cefiderocol. Discs are clearly marked on both sides with the code FDC30. The code designates the agent Cefiderocol (FDC) and the drug content (30 µg).

BD BBL Sensi-Disc Antimicrobial Susceptibility Test Discs are supplied in cartridges containing 50 discs each. The last disc in each cartridge is marked "X" and contains the drug as coded. BD BBL Sensi-Disc Antimicrobial Susceptibility Test Discs can be dispensed using a BD BBL Sensi-Disc Dispenser.

B Principle of Operation:

Filter paper discs impregnated with specified concentrations of antimicrobial agents are used to perform disk diffusion susceptibility testing. The test is performed by inoculating pure cultures of clinical isolates onto the suitable medium and placing the AST disc on the surface of the medium. The antibiotic within the disc diffuses into the agar. After incubation, the zones of

inhibition around the discs are measured and compared against recognized zone diameter ranges for the specific antimicrobial agent/organism combinations being tested.

V Substantial Equivalence Information:

A Predicate Device Name(s):

HardyDisk AST Cefiderocol 30ug (FDC30)

B Predicate 510(k) Number(s):

K193504

C Comparison with Predicate:

Device & Predicate Device:	Device: K221826	Predicate: K193504
Device Trade Name	BD BBL Sensi-Disc Cefiderocol 30 µg (FDC30)	HardyDisk AST Cefiderocol 30 µg (FDC30)
General Device Characteristic Similarities		
Regulation	866.1620	Same
Product Code	JTN	Same
Intended Use/ Indications for Use	semi-quantitative agar diffusion test method for in vitro susceptibility testing.	Same
Antimicrobial Agent	Cefiderocol	Same
Antimicrobial Agent Concentration	30 µg	Same
Interpretation	The user will interpret the zone diameter according to the established interpretive criteria for the drug.	Same
Methodology	Kirby-Bauer Disk Diffusion Susceptibility Test Protocol requires the user to determine categorical interpretations (S/I/R) using the measured zone diameters.	Same
Result Interpretation Method	Measurement of zone size.	Same
General Device Characteristic Differences		
Manufacturing Specifications	BD's specifications	Hardy Diagnostics' specifications

VI Standards/Guidance Documents Referenced:

- CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 31st ed. CLSI supplement M100. Clinical and Laboratory Institute; 2021.
- CLSI. *Performance Standards for Antimicrobial Susceptibility Testing*. 32nd ed. CLSI supplement M100. Clinical and Laboratory Institute; 2022.
- CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Reproducibility was conducted at one external site using 15 isolates, tested in triplicate with two disc lots on three separate days using one lot of BD Mueller Hinton agar (MHA) media. Each test was visually read by three independent readers with results blinded to avoid any bias results, resulting in 270 data points for evaluation (15 isolates x 2 disc lots x 3 days = 90 test results read by 3 independent readers = 270 data points).

The reproducibility study included the following species, indicated on the FDA-approved drug label: 11 Enterobacterales (1 *Citrobacter koseri*, 1 *Enterobacter cloacae*, 2 *Escherichia coli*, 1 *Klebsiella aerogenes*, 3 *Klebsiella pneumoniae*, 1 *Morganella morganii*, 1 *Proteus mirabilis*, 1 *Proteus vulgaris*, 1 *Serratia marcescens*), 2 *Pseudomonas aeruginosa*, and 1 *Acinetobacter baumannii*.

Reproducibility was calculated as the percent of results which were within ±3 mm difference in zone diameter comparing test results with the modal zone diameter value. Summary results between disc lots and across readers are shown in **Table 1**.

Table 1: Reproducibility Summary

Between Disc Lots			Across Readers			
Lot #1	**Lot #2**	**All Lots**	**Reader #1**	**Reader #2**	**Reader #3**	**All Readers**
100% (135/135)	99.26% (134/135)	99.63% (269/270)[a]	100% (90/90)	100% (90/90)	99% (89/90)	99.63% (269/270)

The reproducibility performance between disc lots and across readers is >95% and meets the acceptance criteria.

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 (QC) Testing:
   The CLSI-recommended quality control (QC) isolates, *Escherichia coli* (ATCC 25922), and *Pseudomonas aeruginosa* (ATCC 27853) were tested a sufficient number of times (i.e., a minimum of 20 replicates per lot per reader). One FDA cleared comparator disc lot and two BD disc lots were used. Each test was visually read by three independent readers, resulting in 148 data point (74 data points per lot) and 74 comparator disc data points. The performance is shown in **Table 2**.

Table 2: Quality Control Performance of Cefiderocol (30 µg)

QC Organism	Zone Diameter (mm) Range	BD Lot 1[1] (*N*)	BD Lot 2[1] (*N*)	Comparator Disc[2] (*N*)
Escherichia coli ATCC25922 Expected Range: 25-31 mm	22			
	23			
	24		2	2
	25	7	11	11
	26	18	12	16
	27	15	13	14
	28	21	21	20
	29	11	14	10
	30	1		
	31			
	32			
	33			
	34			
Pseudomonas aeruginosa ATCC 27853 Expected Range: 22-31 mm	19			
	20			
	21			
	22			1
	23	2	3	4
	24	10	7	14
	25	23	17	28
	26	32	38	23
	27	6	8	4
	28	1	1	
	29			
	30			
	31			
	32			

QC Organism	Zone Diameter (mm) Range	BD Lot 1[1] (*N*)	BD Lot 2[1] (*N*)	Comparator Disc[2] (*N*)
	33			
	34			

ATCC = American Type Culture Collection
[1]Two BD disc lots were tested (Lot a and Lot 2).
[2]One FDA cleared comparator disc lot was tested.

The BD disc QC performance is > 95% and is acceptable.

Inoculum Density Check:
Colony counts were conducted for all QC, reproducibility isolates and clinical isolates. All were within the expected range.

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   The BD BBL Sensi-Disc Cefiderocol 30 µg (FDC30) was compared with an FDA cleared disc (of the same antimicrobial, mass/concentration, and content). The study was conducted at one external testing site. Three independent operators participated in reading of test results with isolates evenly distributed to mimic testing at multiple sites. Testing was performed with one lot of disc of each test manufacturer (BD and comparator FDA-cleared disc) utilizing MHA media following the method outlined in CLSI M02 13th edition method.

   Clinical:
   Clinical testing was performed at one U.S. site with both the BD BBL Sensi-Disc Cefiderocol and the comparator FDA cleared disc using a total of 296 clinical isolates including 207 Enterobacterales (10 *Citrobacter freundii,* 2 *Citrobacter koseri*, 10 isolates of *Enterobacter cloacae*, 30 isolates of *Escherichia coli*, 3 isolates of *Klebsiella aerogenes*, 18 isolates of *Klebsiella oxytoca*, 62 isolates of *Klebsiella pneumoniae*, 17 isolates of *Morganella morganii*, 30 isolates of *Proteus mirabilis*, 2 isolates of *Proteus vulgaris*, 8 isolates of *Providencia rettgeri*, 15 isolates of *Serratia marcescens*), 52 *Pseudomonas aeruginosa,* 37 *Acinetobacter baumannii* complex.

   Challenge:
   Challenge testing was performed at one U.S site. A total of 61 challenge isolates were tested which included 49 Enterobacterales (1 *Citrobacter braakii,* 3 *Citrobacter freundii,* 2 *Citrobacter koseri*, 1 *Enterobacter asburiae ,* 3 *Enterobacter cloacae*, 6 *Escherichia*, 3 *Klebsiella aerogenes*, 2 *Klebsiella oxytoca*, 9 *Klebsiella pneumoniae*, 3 *Morganella*

morganii, 2 *Proteus mirabilis*, 5 *Proteus vulgaris*, 4 *Providencia rettgeri*, 1 *Providencia stuartii,* 4 *Serratia marcescens*), 5 *Pseudomonas aeruginosa,* 7 *Acinetobacter baumannii* complex.

Table 3: Performance of the BD BBL Sensi-Disc Cefiderocol Dis vs. Comparator FDA Cleared Disc

	Total	CA#	CA%	S(#)	I(#)	R(#)	VMJ	MAJ	MIN
Enterobacterales Combined [Breakpoints (in mm): ≥16(S), 9-15(I), ≤8(R)]									
Clinical	207	207	100.0%	207	0	0	0	0	0
Challenge	49	45	91.8%	37	10	2	0	0	4
Combined	256	252	98.4%	244	10	2	0	0	4
***Pseudomonas aeruginosa* [Breakpoints (in mm), ≥22(S), 13-21(I), ≤12(R)]**									
Clinical	52	51	98.1	51	1	0	0	0	1
Challenge	5	5	100.0	2	2	1	0	0	0
Combined	57	56	98.2	53	3	1	0	0	1
***Acinetobacter baumannii* complex [Breakpoints (in mm), ≥19(S), 12-18(I), ≤11(R)]**									
Clinical	37	35	94.6	28	5	4	0	0	2
Challenge	7	7	100.0	2	2	3	0	0	0
Combined	44	42	95.5	30	7	7	0	0	2

CA – Category Agreement
S – Susceptible isolates
I – Intermediate isolates
R – Resistant isolates
MIN – minor errors
MAJ – major errors
VMJ – very major errors
Category Agreement (CA) is when the BD result interpretation agrees exactly with the comparator result interpretation.

Performance when testing the total 357 clinical and challenge isolates are shown in **Table 3** and summarized below.

- The overall performance of the BD BBL Sensi-Disc Cefiderocol disc as compared to the FDA cleared comparator disc for Enterobacterales group (**Table 3**) is acceptable with 98.4% CA. There were 4 minor errors and no major or very major errors.

- The overall performance of the BD BBL Sensi-Disc Cefiderocol disc as compared to the FDA cleared comparator disc for *P. aeruginosa* group (**Table 3**) is acceptable with 98.2% CA. There was 1 minor error and no major or very major errors.

- The overall performance of the BD BBL Sensi-Disc Cefiderocol disc as compared to the FDA cleared comparator disc for *Acinetobacter baumannii* group (**Table 3**) is acceptable with 95.5% CA. There were 2 minor errors and no major or very major errors.

As required under 511A(b)(2)(C)(ii)(I) of the Federal Food, Drug and Cosmetic Act, the following statement is included in the 'Warnings and Precautions' section in the device labeling to address testing of non-indicated species:

> *"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 labeling for specific antimicrobial drugs provides the uses for which the antimicrobial drug is approved."*

Resistance Isolates:

A total of 357 clinical and challenge isolates were tested when the BD BBL Sensi-Disc was compared to the FDA cleared comparator disc. However, an insufficient number of resistant isolates were available for testing. To address the lack of resistant strains encountered during the clinical evaluation, the following limitation was added in the device labeling:

"The ability of the BD BBL Sensi Disc to detect resistance with the following combination(s) is unknown because an insufficient number of resistant strains were encountered at the time of comparative testing: Cefiderocol (30µg) and Enterobacterales group, P. aeruginosa and Acinetobacter baumannii. If such a strain is encountered, it should be submitted to a reference laboratory for further testing".

Secondary Analysis:

A secondary analysis of the results obtained with the 357 clinical and challenge isolates was also performed. The analysis was conducted to assess the qualitative categorical agreement (CA) of the BD BBL Sensi-Disc diffusion results compared to the reference broth microdilution (BMD) results (based on historical MIC data from BMD testing performed at the initial recovery of isolates during the drug clinical trial). Analysis of the BD BBL Sensi-Disc when tested against the historical MIC value for each isolate showed a high number of categorical errors. The results of the BD BBL Sensi-Disc Cefiderocol versus historical MIC values are summarized below.

- The analysis of the BD BBL Sensi-Disc Cefiderocol compared to historical BMD MIC values for *P. aeruginosa* had a low CA of 75.4% due to the high number of minor errors (6) and 8 very major errors (8/10 80.0%). There were no major errors. Refer to limitation below.

- The analysis of the BD BBL Sensi-Disc Cefiderocol compared to historical BMD MIC values for *Acinetobacter baumannii* complex had a low CA of 61.4% due to the high number of minor errors (7), very major errors (9/20, 45.0%) and one major error (1/24, 4.2%). This single major error was accepted as a random error and did not require a limitation.

To address the low CA due to categorical errors obtained with Cefiderocol when tested with *P. aeruginosa* and *A. baumannii* complex, the following limitation was added to the device labeling:

"While the categorical agreement for BD BBL Sensi-Disc Cefiderocol compared to FDA cleared Disk analysis was >95% for Pseudomonas aeruginosa and Acinetobacter baumannii complex, categorical agreement for BD BBL Sensi-Disc Cefiderocol compared to historical BMD MIC values was below 90%, caused by the occurrence of false susceptible results and minor errors. Test results for Cefiderocol/P. aeruginosa which provide a disc zone of inhibition ≥ 22 mm, and test results for Cefiderocol/A. baumannii complex which provide a disc zone of

inhibition ≥ 19 mm, should be interpreted in conjunction with other clinical and laboratory information".

- The analysis of the BD BBL Sensi-Disc Cefiderocol compared to historical BMD MIC values for Enterobacterales is acceptable with 93.0% CA. However, the very major error (VMJ) rate was 41.2% (7/17) which does not meet FDA's acceptance criteria of ≤ 2% VMJ error rate. There were 11 minor errors and no major errors. To address the categorical errors obtained with Cefiderocol when tested with Enterobacterales, the following limitation was added to the device labeling:

  "While the categorical agreement for BD BBL Sensi-Disc Cefiderocol compared to FDA cleared Disk analysis was > 95% for Enterobacterales group organisms, categorical agreement for BD BBL Sensi-Disc Cefiderocol compared to historical BMD MIC values resulted in false susceptible results. Citrobacter freundii complex, Citrobacter koseri, Klebsiella pneumoniae, Morganella morganii, and Proteus mirabilis isolates that provide a disc zone of inhibition ≥ 16 mm should be interpreted in conjunction with other clinical and laboratory information.

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):

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

The FDA-identified interpretive criteria for Cefiderocol are listed in **Table 4.**

Table 4: FDA Identified Interpretive Criteria for Cefiderocol[1]

	Minimum Inhibitory Concentrations (µg/mL)			Disk Diffusion (zone diameters in mm)		
Pathogen	**S**	**I**	**R**	**S**	**I**	**R**
Enterobacterales[2,3]	≤4	8	≥16	≥16	9-15	≤8
Pseudomonas aeruginosa	≤1	2	≥4	≥22	13-21	≤12
Acinetobacter baumannii complex	≤1	2	≥4	≥19	12-18	≤11

[1] According to the **FDA STIC Website**.
[2] Clinical efficacy was shown for *Escherichia coli, Klebsiella pneumoniae*, *Proteus mirabilis*, and *Enterobacter cloacae* complex in patients with complicated urinary tract infections (cUTI).
[3] Clinical efficacy was shown for *Escherichia coli, Klebsiella pneumoniae, Enterobacter cloacae* complex, and *Serratia marcescens* in patients with hospital-acquired bacterial pneumonia and ventilator-associated bacterial pneumonia (HABP/VABP).
S = Susceptible
I = Intermediate
R = Resistant

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 included a breakpoint change protocol that was reviewed and accepted by FDA. This protocol 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 protocol outlined the specific procedures and acceptance criteria that Becton Dickinson, and Company (BD Diagnostic Systems) intends to use to evaluate the BD BBL Sensi-Disc Cefiderocol 30µg (FDC-30) when revised breakpoints for Cefiderocol are published on the FDA STIC webpage. The breakpoint change protocol included with the submission indicated that if specific criteria are met, BD Diagnostic Systems will update the Cefiderocol 30µg 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.