510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K241060

B Applicant

Hardy Diagnostics

C Proprietary and Established Names

HardyDisk AST Cefiderocol 30µg (FDC30)

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:

1. To obtain a substantial equivalence determination for cefiderocol antimicrobial susceptibility test disk.
2. Establish a Pre-Determined Change Control Plan (PCCP) to address future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage.

B Measurand:

Cefiderocol 30µg

C Type of Test:

Antimicrobial Susceptibility Test Disks

III Intended Use/Indications for Use:

A Intended Use(s):

HardyDisk AST Disks are used for semi-quantitative *in vitro* susceptibility testing by the agar diffusion test procedure (Kirby-Bauer) of rapidly growing and certain fastidious bacterial pathogens. Standardized methods for agar diffusion testing have been described for Enterobacterales, *Staphylococcus* spp., *Pseudomonas* spp., *Acinetobacter* spp., *Listeria monocytogenes*, *Enterococcus* spp., and by modified procedures, *Candida* spp., *Haemophilus* spp., *Neisseria gonorrhoeae*, *Neisseria meningitidis* and *Streptococcus* spp., including *Streptococcus pneumoniae*.

B Indication(s) for Use:

HardyDisk AST Disks are used for semi-quantitative *in vitro* susceptibility testing by the agar diffusion test procedure (Kirby-Bauer) of rapidly growing and certain fastidious bacterial pathogens. Standardized methods for agar diffusion testing have been described for Enterobacterales, *Staphylococcus* spp., *Pseudomonas* spp., *Acinetobacter* spp., *Listeria monocytogenes*, *Enterococcus* spp., and by modified procedures, *Candida* spp., *Haemophilus* spp., *Neisseria gonorrhoeae*, *Neisseria meningitidis* and *Streptococcus* spp., including *Streptococcus pneumoniae*.

Use of HardyDisk AST Cefiderocol 30µg (FDC30) for *in vitro* agar diffusion susceptibility testing is indicated when there is the need to determine the susceptibility of microorganisms to Cefiderocol.

HardyDisk AST Cefiderocol at concentration 30µg can be used to determine the zone diameter (mm) of Cefiderocol against the following microorganisms.

Active both *in vitro* and clinical infections against:

<u>Gram-negative bacteria</u>

Escherichia coli

Enterobacter cloacae complex

Klebsiella pneumoniae

Proteus mirabilis

Pseudomonas aeruginosa

Acinetobacter baumannii complex

Serratia marcescens

Active *in vitro* against:

Gram-negative bacteria

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

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

HardyDisk AST Cefiderocol 30µg (FDC30) is a high quality 6 mm diameter white filter paper disk that is impregnated with 30µg Cefiderocol. The disks are clearly marked on both sides with FDC30, designating the agent and the drug content. The disks are supplied in plastic cartridges containing 50 disks each. HardyDisk AST Cefiderocol 30µg (FDC30) is intended to be used for *in vitro* agar diffusion susceptibility testing.

B Principle of Operation:

The HardyDisk AST Disk is based on the agar diffusion (Kirby-Bauer) methodology. It utilizes dried filter paper disks impregnated with a known concentration of an antimicrobial agent that are placed onto the test medium surface. Three to five similar colonies are transferred to 4-5 mL of a suitable broth medium. The broth is incubated at 35°C for 2-6 hours to develop a turbidity that exceeds or is equivalent to a 0.5 McFarland standard. Alternatively, a direct broth or saline suspension of colonies may be prepared from an overnight culture. The final inoculum density should be equivalent to a 0.5 McFarland turbidity standard. The inoculum density may also be standardized photometrically.

Within 15 minutes of inoculum preparation, the Mueller Hinton agar plate is streaked with an inoculated swab to obtain an even inoculation of organism. Disks are aseptically placed onto the agar surface with a disk dispenser and the disks are pressed down with a sterile needle or forceps to contact the agar surface. Agar plates are incubated in an ambient air incubator at 35±2°C for 16-18 hours.

After incubation, the agar medium is examined for a zone of inhibition around the disks. The zones of inhibition are measured to the nearest millimeter and compared to recognized zone size ranges for the antimicrobial agent being tested.

V Substantial Equivalence Information:

A Predicate Device Name(s):

HardyDisk AST Sulbactam/Durlobactam 10/10µg (SUD20)

B Predicate 510(k) Number(s):

K231568

C Comparison with Predicate(s):

Device & Predicate Device(s):	Device K241060	Predicate K231568
Device Trade Name	HardyDisk AST Cefiderocol 30µg (FDC30)	HardyDisk AST Sulbactam/Durlobactam 10/10µg (SUD20)
General Device Characteristic Similarities		
Intended Use	Semi-quantitative *in vitro* susceptibility testing by the agar diffusion test procedure (Kirby-Bauer) of rapidly growing and certain fastidious bacterial pathogens.	Same
Test Method	Antimicrobial susceptibility testing using paper disks impregnated with an antimicrobial agent	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
Inoculum	Prepared from pure isolated	Same

Device & Predicate Device(s):	Device K241060	Predicate K231568
	colonies to match the turbidity equivalent of a 0.5 McFarland in Tryptic Soy Broth.	
Inoculum Method	Dip a sterile swab into the prepared inoculum and streak an appropriate agar plate's surface three times. Add the disks impregnated with the antimicrobial agent to the surface of the plate. The temperature, atmospheric conditions and duration of incubation is dependent on the organism tested.	Same
Reading Method	The user will interpret the zone diameters according to the established interpretive criteria for the drug.	Same
General Device Characteristic Differences		
Antimicrobial Agent	Cefiderocol	Sulbactam/Durlobactam
Concentration	30µg	10/10µg

VI Standards/Guidance Documents Referenced:

- CLSI M02-13th ed. *Performance Standards for Antimicrobial Disk Susceptibility Tests* (January 2018).
- CLSI M100-34th ed. *Performance Standards for Antimicrobial Susceptibility Testing* (February 2024).

VII Performance Characteristics (if/when applicable):

The premarket submission for HardyDisk Cefiderocol included a letter dated December 14, 2023, indicating the right of reference to NDA 209445. Descriptive characteristics were sufficient for the HardyDisk Cefiderocol 30µg (FDC30) disk based on data from microbiology disk studies evaluated by CDER which were used to generate the breakpoints identified by FDA on the susceptibility test interpretive criteria webpage. In addition, CDER concurred with the disk QC ranges that were established by CLSI. The disk data used to support this submission included data from testing organisms shown to be active *in vitro* and/or in clinical infections within the spectrum of activity of Cefiderocol and as noted in the device's intended use.

Data obtained from stability, quality control, disk to MIC correlation, reproducibility (from disk content optimization) studies were generated in accordance with the CDER

Clinical/Antimicrobial guidance, *Microbiology Data for Systemic Antibacterial Drugs-Development, Analysis, and Presentation* to ensure precise, accurate, and reproducible results.

For this review, the interpretive criteria are applied to Enterobacterales, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii* complex according to the FDA STIC website. As required under 511A(2)(2)(B) of the Federal Food, Drug and Cosmetic Act, the following statement is included in the Precautions section of the HardyDisk AST Cefiderocol 30µg package insert:

> *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.*

A Analytical Performance:

1. Precision/Reproducibility:

   Not applicable.

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):

   Not applicable.

6. Detection Limit:

   Not applicable.

7. Assay Cut-Off:

   Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

   Not applicable.

2. Matrix Comparison:

   Not applicable.

C Clinical Studies:

1. Clinical Sensitivity:

   Not applicable.

2. Clinical Specificity:

   Not applicable.

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

   Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

The FDA-identified susceptibility interpretive criteria for Cefiderocol are listed below.

FDA-Identified Disk Diffusion Interpretive Criteria (zone diameter in mm) for Cefiderocol

Organisms	Interpretive Criteria		
	Susceptible (S)	Intermediate (I)	Resistant I
Enterobacterales[a,b]	≥ 16	9 – 15	≤ 8
Pseudomonas aeruginosa	≥ 22	13 – 21	≤ 12
Acinetobacter baumannii complex	≥ 19	12 – 18	≤ 11

[a]Clinical efficacy was shown for *Escherichia coli*, *Klebsiella pneumoniae*, *Proteus mirabilis*, and *Enterobacter cloacae* complex in patients with complicated urinary tract infections (cUTI).
[b]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).

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 predetermined change control plan (PCCP) that was reviewed and accepted by FDA. This PCCP addresses future revisions to device labeling in response to breakpoint changes that are recognized on the FDA STIC webpage (https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/ucm410971.htm). The PCCP outlined the specific procedures and acceptance criteria that Hardy Diagnostics intends to use to evaluate the HardyDisk AST Cefiderocol 30µg (FDC30) when revised breakpoints for cefiderocol are published on the FDA STIC webpage. The PCCP included with the submission indicated that if specific criteria are met, Hardy Diagnostics will update the HardyDisk AST Cefiderocol 30µg (FDC30) device label to include the new breakpoints.