Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002
www.fda.gov

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

## I Background Information:

### A 510(k) Number

K191931

### B Applicant

Hardy Diagnostics

### C Proprietary and Established Names

HardyDisk AST Imipenem/relebactam 10/25µg (IMR10/25)

### 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 a substantial equivalence determination for Imipenem/Relebactam Antimicrobial Susceptibility Test Disk

### B Measurand:

Imipenem/Relebactam 10/25 µg

### 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 *Enterobacteriaceae, Staphylococcus* spp., *Pseudomonas* spp., *Acinetobacter* spp., *Listeria monocytogenes*, *Enterococcus* spp., and by modified procedures, *Haemophilus* spp., *Neisseria gonorrhoeae, N. 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 *Enterobacteriaceae, Staphylococcus* spp., *Pseudomonas* spp., *Acinetobacter* spp., *Listeria monocytogenes*, *Enterococcus* spp., and by modified procedures, *Haemophilus* spp., *Neisseria gonorrhoeae, N. meningitidis* and *Streptococcus* spp., including *Streptococcus pneumoniae*.

Use of HardyDisk AST Imipenem/Relebactam 10/25µg (IMR10/25) for *in vitro* agar diffusion susceptibility testing is indicated when there is the need to determine the susceptibility of bacteria to Imipenem/Relebactam.

HardyDisk AST Imipenem/Relebactam at concentration 10/25µg can be used to determine the zone diameter (mm) of Imipenem/Relebactam against the following bacteria for which Imipenem/Relebactam has been shown to be active both clinically and *in vitro*: *Citrobacter freundii, Klebsiella aerogenes, Klebsiella oxytoca, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa*.

Imipenem/Relebactam has been shown to be active *in vitro* against most of the following bacteria, but their clinical significance is unknown: *Citrobacter koseri* and *Enterobacter asburiae*.

### 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 Disks utilize 6-mm diameter white filter paper disks. The disks are prepared by impregnating absorbent paper with a known concentration of 10µg Imipenem and 25µg Relebactam. The disks are marked with the code IMR 10/25, on both sides.

HardyDisk AST Disks are supplied in plastic cartridges containing 50 disks each. They are also packaged as one cartridge per vial with desiccant or five cartridges per vial with desiccant.

### 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. Mueller Hinton agar is recommended for agar diffusion testing of non-fastidious organisms and Mueller Hinton with 5% Sheep Blood is recommended for *Streptococcus* spp. 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 make contact with the agar surface. Agar plates are incubated in an ambient air incubator at 35±2°C for 16 - 18 hours. Fastidious organisms are tested using appropriate media incubated in an atmosphere enriched with 5% CO2, as recommended in the CLSI M02 approved standard document.

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):

Hardy Disk Ast Tigecycline 15 Ug

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

K062245

## C Comparison with Predicate(s):

| Device & Predicate Device(s): | Device K191931 | Predicate K062245 |
|---|---|---|
| Device Trade Name | HardyDisk AST Imipenem/Relebactam 10/25µg | Hardy Disk AST Tigecycline 15 µg |
| **General Device Characteristic Similarities** | | |
| Test Method | Antimicrobial Susceptibility Testing using paper disks impregnated with an antimicrobial agent | Same |
| Intended Use/Indications For Use | Antimicrobial Susceptibility Test Disks are used for *in vitro* susceptibility testing by standardized agar diffusion test procedures. | 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 colonies to match the turbidity equivalent of a 0.5 McFarland in Tryptic Soy Broth. | Same |
| Inoculation 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 are dependent on the organism tested. | Same |
| Reading Method | The user will interpret the zone diameters according to established interpretive criteria for the drug. | Same |

| General Device Characteristic Differences | | |
|---|---|---|
| Product Name | HardyDisk AST Imipenem/Relebactam 10/25µg (IMR10/25) | Hardy Disk AST Tigecycline 15 µg |
| Antimicrobial Agent | Imipenem/Relebactam | Tigecycline |
| Antimicrobial Concentration | 10/25µg | 15 µg |

## VI Standards/Guidance Documents Referenced:

- CLSI M100, "Performance Standards for Antimicrobial Susceptibility Testing"; Twenty-ninth Edition (January 2019)

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

Descriptive characteristics were sufficient for the HardyDisk AST Imipenem/Relebactam 10/25µg (IMR10/25) disk based on extensive data from several microbiology disk studies evaluated by CDER which were used to generate the breakpoints and quality control (QC) expected ranges used for this subject device. The disk data used to support this submission included data from testing organisms shown to be active *in vitro* and in clinical infections within the spectrum of activity of Imipenem/Relebactam and as noted in the device's intended use. Data obtained from disk quality control and disk-to-MIC correlation studies was 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 interpretative criteria are applied broadly to the *Enterobacteriaceae* family and *Pseudomonas aeruginosa* according to the FDA STIC website. Testing has been expanded to include members of the family and is not limited only to the indicated species. To address the unknown clinical utility of Imipenem/Relebactam to organisms outside of the drug's indication for use, the following statement is included in the *Precautions* section of the HardyDisk AST Imipenem/Relebactam 10/25µg 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 Imipenem/Relebactam are listed below.

**FDA-Identified Disk Diffusion Interpretive Criteria (zone diameter in mm) for Imipenem/Relebactam 10/25 µg (IMR 10/25)[a]**

| Organisms | S | I | R |
|---|---|---|---|
| *Enterobacteriaceae* | ≥ 25 | 21 - 24 | ≤ 20 |
| *Pseudomonas aeruginosa* | ≥ 23 | 20 - 22 | ≤ 19 |

[a] According to FDA STIC Website:

**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.