

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

I Background Information:

A 510(k) Number

K192326

B Applicant

Hardy Diagnostics

C Proprietary and Established Names

HardyDisk AST Lefamulin 20µg (LMU20)

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 Lefamulin (LMU20) Antimicrobial Susceptibility Test Disk

B Measurand:

Lefamulin 20µg

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 Lefamulin 20µg (LMU20) for in vitro agar diffusion susceptibility testing is indicated when there is the need to determine the susceptibility of bacteria to Lefamulin.

HardyDisk AST Lefamulin at concentration 20µg can be used to determine the zone diameter (mm) of Lefamulin against the following bacteria for which Lefamulin has been shown to be active both clinically and *in vitro*:

Streptococcus pneumoniae
Staphylococcus aureus (methicillin-susceptible isolates)
Haemophilus influenzae

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

For *S. pneumoniae*, *H. influenzae*, and *S. aureus*, the current absence of resistant isolates precludes defining any results other than "Susceptible". No resistance or intermediate interpretive criteria have been established. Isolates yielding MIC results other than "Susceptible" should be submitted to a reference laboratory for further testing.

D Special Instrument Requirements:

N/A

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 20µg Lefamulin. The disks are marked with the code LMU20, 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 µg

B Predicate 510(k) Number(s):

K062245

C Comparison with Predicate(s):

Table 1: Comparison with Predicate

Device & Predicate Device(s):	<u>Device:</u> K192326	<u>Predicate:</u> K062245
Device Trade Name	HardyDisk AST Lefamulin 20µg (LMU20)	HardyDisk Tigecycline 15µg
General Device Characteristic Similarities		
Intended Use/Indications For Use	Semi-quantitative <i>in vitro</i> susceptibility testing by the agar diffusion test procedure (Kirby-Bauer) of rapidly growing and certain fastidious bacterial pathogens.	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
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. Incubate the agar plate agar side up in a 35 ± 2°C incubator for 16-18 hours.	Same
Reading Method	The user will interpret the zone diameters	Same

	according established interpretive criteria for the drug.	
General Device Characteristic Differences		
Antimicrobial Agent	Lefamulin	Tigecycline
Concentration	20µg	15µg

VI Standards/Guidance Documents Referenced:

CLSI M100-29th ed. *Performance Standards for Antimicrobial Susceptibility Testing* (January 2019).

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

N/A

2. Linearity:

N/A

3. Analytical Specificity/Interference:

N/A

4. Assay Reportable Range:

N/A

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

N/A

6. Detection Limit:

N/A

7. Assay Cut-Off:

N/A

B Comparison Studies:

1. Method Comparison with Predicate Device:

Descriptive characteristics were sufficient for the HardyDisk Lefamulin 20µg (LMU20) disk based on extensive data from several microbiology disk studies evaluated by CDER which were used to generate the breakpoints. In addition, CDER concurred with the QC ranges that were established by CLSI of which QC data obtained for this subject device were deemed acceptable. 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 Lefamulin 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 interpretative criteria are applied to *S. aureus* (methicillin-susceptible), *S. pneumoniae*, and *H. influenzae* according to the FDA [STIC](#) website. Testing has been expanded to include isolates of similar genus or organism group and is not limited only to the indicated species. To address the unknown clinical utility of lefamulin for organisms outside of the drug's indication for use, the following statements are added as footnotes to the Lefamulin 20µg interpretative criteria table in the HardyDisk AST 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.*

2. Matrix Comparison:

N/A

C Clinical Studies:

1. Clinical Sensitivity:

N/A

2. Clinical Specificity:

N/A

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

N/A

D Clinical Cut-Off:

N/A

E Expected Values/Reference Range:

The Lefamulin interpretative criteria for disk diffusion is shown in Table 2 below.

**Table 2: FDA Identified Disk Diffusion Interpretative Criteria
(Zone diameter in mm for Lefamulin)**

Organism(s)	Susceptible*	Intermediate	Resistant
<i>Staphylococcus. aureus</i> (methicillin-susceptible isolates)	≥23	-	-
<i>Streptococcus pneumoniae</i>	≥17	-	-
<i>Haemophilus influenzae</i>	≥17	-	-

*The current absence of resistant isolates precludes defining any results other than "Susceptible". Isolates yielding MIC results other than "Susceptible" should be submitted to a reference laboratory for further testing.

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.