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

A. 510(k) Number:

K181700

B. Purpose for Submission:

Addition of Plazomicin Antimicrobial Susceptibility Test Disk

C. Measurand:

Plazomicin 30µg

D. Type of Test:

Antimicrobial Susceptibility Test Disks

E. Applicant:

Hardy Diagnostics

F. Proprietary and Established Names:

HardyDisk AST Plazomicin 30µg (PLZ30)

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.1620 Antimicrobial Susceptibility Test Disc

2. Classification:

   Class II

3. Product code:

   JTN

4. Panel:

   83, Microbiology

H. Intended Use:

1. 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*.

2. Indication(s) for use:

   Use of HardyDisk AST Plazomicin 30µg (PLZ30) for *in vitro* agar diffusion susceptibility testing is indicated when there is need to determine the susceptibility of bacteria to Plazomicin.

   Plazomicin has been shown to be active against susceptible isolates of the following bacteria both *in vitro* and in clinical infections:
   Escherichia coli
   Klebsiella pneumoniae
   Proteus mirabilis
   Enterobacter cloacae

   Plazomicin has been shown to be active *in vitro* against susceptible isolates of the following bacteria:
   Citrobacter freundii
   Citrobacter koseri
   Enterobacter aerogenes
   Klebsiella oxytoca
   Morganella morganii
   Proteus vulgaris
   Providencia stuartii
   Serratia marcenscens

   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*.

3. Special conditions for use statement(s):

   For prescription use only

4. Special instrument requirements:

   N/A

I. 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 30µg Plazomicin. The disks are marked with the code PLZ30 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.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   HardyDisk Tigecycline 15µg

2. Predicate 510(k) number(s):

   K062245

3. Comparison with predicate:

Table 1: Comparison with the Predicate

Similarities		
Item	**Device K181700 HardyDisk Plazomicin 30µg**	**Predicate K062245 HardyDisk Tigecycline 15µg**
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 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. 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 according established interpretive criteria for the drug.	Same

Differences		
Item	Device	Predicate
Product Name	HardyDisk Plazomicin 30µg (PLZ30)	HardyDisk Tigecycline
Antimicrobial Agent	Plazomicin	Tigecycline
Concentration	30µg	15µg

K. Standard/Guidance Document Referenced (if applicable):

CLSI M100 28th Edition, Performance Standards for Antimicrobial Susceptibility Testing

L. Test Principle:

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% CO_2, 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.

M. Performance Characteristics (if/when applicable):

Descriptive characteristics were sufficient for the HardyDisk Plazomicin 30µg (PLZ30) 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 within the spectrum of activity of plazomicin. Data was obtained from reproducibility, quality control and disk to MIC correlation studies and 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 include the *Enterobacteriaceae* family. The list of bacterial species has been expanded and is not limited only to the indicated species.

The following statements are added as footnotes to the plazomicin interpretative criteria table for *Enterobacteriaceae* in the HardyDisk AST package insert:

The statement below is added to the package insert and is consistent with the FDA STIC website:

- *The safety and efficacy of plazomicin in treating clinical infections due to organisms other than Escherichia coli, Klebsiella pneumoniae, Proteus mirabilis, and Enterobacter cloacae may not have been established in adequate and well-controlled clinical trials. The clinical significance of susceptibility information in such instances is unknown.*

Regarding resistance marker/enzyme characterization, *Enterobacteriaceae* isolates harboring extended spectrum βeta-Lactamases (ESBL) including CTX-M, SHV, TEM; AmpC; carbapenemases (KPC, NDM, OXA, VIM); aminoglycoside modifying enzymes (AMEs) including AAC, AAD, ANT, APH; 16S rRNA methyltransferases (plazomicin resistant RMTB and armA) were tested with the HardyDisk Plazomicin. Information regarding the performance of Plazomicin with isolates that exhibit overexpression of efflux pumps or lower expression of porins is provided in the following footnote:

- *The performance of HardyDisk AST Plazomicin 30µg (PLZ30) is unknown for Enterobacteriaceae with the following resistance mechanisms: overexpression of efflux pumps (e.g., acrAB-tolC) or lower expression of porins (e.g., ompF or ompK36).*

1. Analytical performance:

   a. *Precision/Reproducibility:*

      Not applicable

   b. *Linearity/assay reportable range:*

      Not applicable

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

      Not applicable

   d. *Detection limit:*

      Not applicable

   e. *Analytical specificity:*

      Not applicable

   f. *Assay cut-off:*

      Not applicable

2. Comparison studies:

   a. *Method comparison with predicate device:*

      Not applicable

   b. *Matrix comparison:*

Not applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable

b. Clinical specificity:

Not applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

The plazomicin interpretative criteria for disk diffusion in the approved pharmaceutical drug package insert is located at the FDA STIC website and shown in Table 2 below.

Table 2: Interpretative Criteria for Plazomicin Disk

Indications For Use Organism(s)	Interpretative Criteria		
	Zone Diameter (mm)		
	R	I	S
Enterobacteriaceae	≤13	14-15	≥16

The QC isolates and expected ranges are the same as recommended by the current (28th) edition of CLSI M100.

N. Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.