June 7, 2023

Becton, Dickinson and Company
Katherine Cicala
Regulatory Affairs Specialist
7 Loveton Circle
Sparks, Maryland 21152-0999

Re: K230651
Trade/Device Name: BD BBL Sensi-Disc Lefamulin 20µg (LMU-20)
Regulation Number: 21 CFR 866.1620
Regulation Name: Antimicrobial Susceptibility Test Disc
Regulatory Class: Class II
Product Code: JTN
Dated: March 8, 2023
Received: March 9, 2023

Dear Katherine Cicala:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's

requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801 and Part 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Ribhi Shawar -S

Ribhi Shawar, Ph.D. (ABMM)
Chief
General Bacteriology and Antimicrobial
Susceptibility Branch
Division of Microbiology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K230651

Device Name
BD BBL Sensi-Disc Lefamulin 20µg (LMU-20)

Indications for Use *(Describe)*
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 Lefamulin Disc 20 µg (LMU-20) can be used to determine susceptibility to Lefamulin against the following bacteria, as described in the FDA-approved package insert for this antimicrobial agent.

Active in vitro and in Clinical Infections Against:
Gram-positive Bacteria
Streptococcus pneumoniae
Staphylococcus aureus (methicillin-susceptible isolates)

Gram-negative Bacteria
Haemophilus influenzae

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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510(k) Summary

Summary Preparation Date:
June 06, 2023

I Background Information

A 510(k) Number

K230651

B Applicant

BD Diagnostic Systems
Becton, Dickinson and Company
7 Loveton Circle
Sparks, Maryland 21152
Establishment Registration Number: 1119779

C Proprietary and Established Name

BD BBL Sensi-Disc Lefamulin 20 µg (LMU-20)

D Regulatory Information

Product Code	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 Lefamulin Antimicrobial Susceptibility Test Disc.

B Measurand:

Lefamulin Disc 20 µg (LMU-20)

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 Lefamulin Disc 20 µg (LMU-20) can be used to determine susceptibility to Lefamulin against the following bacteria, as described in the FDA-approved package insert for this antimicrobial agent.

Active *in vitro* and in Clinical Infections Against:

Gram-positive Bacteria
Streptococcus pneumoniae
Staphylococcus aureus (methicillin-susceptible isolates)

Gram-negative Bacteria
Haemophilus influenzae

C Special Conditions for Use Statement(s):

- Rx – For Prescription Use Only
- 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.
- Limitations
  - The current absence of resistant isolates precludes defining any results other than "Susceptible." Isolates yielding results other than "Susceptible" should be submitted to a reference laboratory for further testing.

D Special Instrument Requirements:

Not applicable.

IV Device/System Characteristics:

A Device Description:

The BD BBL Sensi-Disc Lefamulin 20 µg (LMU-20) device is a 6 mm disc prepared by impregnating high quality absorbent paper with accurately determined amounts of Lefamulin. Discs are clearly marked on both sides with the code LMU-20. The code designates the agent Lefamulin (LMU) and the drug content (20 µg).

BD BBL Sensi-Disc Antimicrobial Susceptibility Test Discs are furnished 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:

A suitable therapeutic agent can be determined using filter paper discs impregnated with specified concentrations of antimicrobial agents placed on the surface of a suitable test medium. The test is performed by inoculating pure cultures of clinical isolates onto the test 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:

HardyDisk AST Lefamulin 20µg (LMU20)

B Predicate 510(k) Number:

K192326

C Comparison with Predicate:

Device & Predicate Device:	**Device: K230651**	**Predicate: K192326**
Device Trade Name	BD BBL Sensi-Disc Lefamulin 20 µg (LMU-20)	HardyDisk AST Lefamulin 20 µg (LMU20)
General Device Characteristic Similarities		
Regulation	866.1620	Same
Product Code	JTN	Same
Intended Use	See Indications for Use below.	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*.

Device & Predicate Device:	**Device: K230651**	**Predicate: K192326**
Indications 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 Lefamulin Disc 20 µg (LMU-20) can be used to determine susceptibility to Lefamulin against the following bacteria, as described in the FDA-approved package insert for this antimicrobial agent. **Active *in vitro* and in Clinical Infections Against:** Gram-positive Bacteria *Streptococcus pneumoniae* *Staphylococcus aureus* (methicillin-susceptible isolates) Gram-negative Bacteria *Haemophilus influenzae*	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*
Antimicrobial Agent	Lefamulin	Same
Antimicrobial Agent Concentration	20 µg	Same

Device & Predicate Device:	Device: K230651	Predicate: K192326
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*. 33rd ed. CLSI supplement M100. Clinical and Laboratory Institute; 2023.
- CLSI. *Performance Standards for Antimicrobial Disk Susceptibility Tests*. 13th ed. CLSI standard M02. Clinical and Laboratory Standards Institute; 2018.
- CLSI. *Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria*. 9th ed. CLSI standard M11. Wayne, PA: 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 organisms, tested in triplicate with two disc lots on three separate days using one lot of appropriate media (Mueller Hinton agar (MHA) for *Staphylococcus aureus*, Haemophilus Test Medium for *Haemophilus influenzae*, and MHA with 5% Sheep Blood for *Streptococcus pneumoniae*). Each test was visually read by three independent readers with results masked, resulting in 270 data points for evaluation (15 organisms x 2 disc lots x 1 media lot x 3 days x 3 independent readers = 270 data points).

The reproducibility study included 5 *Haemophilus influenzae*, 5 *Staphylococcus aureus*, and 5 *Streptococcus pneumoniae*. Reproducibility was calculated as the percent of results which were within ±3 mm difference in zone diameter comparing test results with the modal or median, if no mode is present, zone diameter value. Summary results between disk lots and across readers are shown in **Table 1** below.

Table 1: Reproducibility Summary

Between Disc Lots			Across Readers			
Lot #1	**Lot #2**	**All Lots**	**Reader #1**	**Reader #2**	**Reader #3**	**All Readers**
100.00% (135/135)	100.00% (135/135)	100.00% (270/270)	96.67% (87/90)	100.00% (90/90)	100.00% (90/90)	98.89% (267/270)

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, *Haemophilus influenzae* (ATCC 49247), *Staphylococcus aureus* (ATCC 25923), and *Streptococcus pneumoniae* (ATCC 49619), were tested a sufficient number of times (i.e., a minimum of 20 replicates per lot per reader). One Comparator disk lot and two BD disc lots were used. Each test was visually read by three independent readers, resulting in 129 data points (69 and 60 data points for Lot A and B, respectively) and 69 Comparator disk data points. The performance is shown in **Table 2** below.

Table 2: Quality Control Performance

QC Organism	Zone Diameter (mm)	BD Lot 1[1] (*N*)	BD Lot 2[1] (*N*)	Comparator disk[2] (*N*)
Haemophilus influenzae ATCC 49247 Expected Range: 22-28 mm	19			
	20			
	21			
	22			6
	23			14
	24	1		21
	25	9	4	24
	26	33	30	4
	27	25	25	
	28	1	1	
	29			
	30			
	31			

QC Organism	Zone Diameter (mm)	BD Lot 1[1] (*N*)	BD Lot 2[1] (*N*)	Comparator disk[2] (*N*)
Staphylococcus aureus ATCC 25923 Expected Range: 26-32 mm	23			
	24			
	25			1
	26			3
	27	11	6	15
	28	17	16	31
	29	30	31	21
	30	13	7	
	31			
	32			
	33			
	34			
	35			
Streptococcus pneumoniae ATCC 49619 Expected Range: 19-27 mm	16			
	17			
	18			
	19			
	20			
	21			1
	22			7
	23	3		26
	24	21	16	24
	25	33	28	8
	26	10	16	3
	27	2		
	28			
	29			
	30			

ATCC = American Type Culture Collection
[1]Two BD disc lots were tested (Lot A and Lot B).
[2]One Comparator disk lot was tested.

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

Inoculum Density Check:
Colony counts were conducted for all QC and reproducibility isolates, as well as 14.0% of 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 Lefamulin 20 µg (LMU-20) was compared with an FDA cleared disk of the same antimicrobial, mass/concentration, and content. The study was conducted at one 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 discs from each test manufacturer (BD and comparator FDA-cleared disk), utilizing appropriate media following the method outlined in CLSI M02 and M100. An equivalent procedure to CLSI M11 was utilized for conducting colony counts.

Clinical:
Clinical testing was performed at one U.S. site with both the BD BBL Sensi-Disc Lefamulin disc and the comparator FDA cleared disk using a total of 270 clinical isolates including 90 *Haemophilus influenzae*, 90 *Staphylococcus aureus* (methicillin-susceptible isolates), and 90 *Streptococcus pneumoniae.*

Challenge:
Challenge testing was performed at one U.S site. A total of 66 challenge isolates were tested which included 22 *Haemophilus influenzae*, 22 *Staphylococcus aureus* (methicillin-susceptible isolates), and 22 *Streptococcus pneumoniae.*

Performance results for the total 336 clinical and challenge isolates are shown in **Table 3**. Performance of 39 MRSA isolates is not included in this table due to the lack of FDA-recognized breakpoints for Lefamulin when testing MRSA.

Table 3: Overall Performance of the BD BBL Sensi-Disc Lefamulin Disc vs. Comparator disk

	Total	**CA#**	**CA%**	**S (#)**	**NS (#)**	**VMJ***	**MAJ**
Haemophilus influenzae							
Clinical	90	89	98.9	90	0	0	1
Challenge	22	19	86.4	13	9	3	0
Combined	112	108	96.4	103	9	3	1
Staphylococcus aureus (methicillin-susceptible isolates)							
Clinical	90	90	100.0	90	0	0	0
Challenge	22	22	100.0	10	12	0	0
Combined	112	112	100.0	100	12	0	0
Streptococcus pneumoniae							
Clinical	90	89	98.9	89	1	1	0
Challenge	22	22	100.0	19	3	0	0
Combined	112	111	99.1	108	4	1	0
Overall							
Clinical	270	268	99.3	269	1	1	1
Challenge	66	63	95.5	42	24	3	0
Combined	336	331	98.5	311	25	4	1

*Due to the lack of an interpretive category other than susceptible and considering that a 3 mm disk zone diameter is equivalent to one MIC doubling dilution, because all potential VMJ errors had disk zone diameter measurement differences

	Total	CA#	CA%	S (#)	NS (#)	VMJ*	MAJ

≤3 mm compared to the FDA-cleared comparator disk and were ≤ an MIC doubling dilution-equivalent compared to the historical MIC result, the adjusted potential VMJ error rate is 0%.

CA – Category Agreement
S – Susceptible isolates
NS – Nonsusceptible isolates
MAJ – major errors
VMJ – very major errors

Category Agreement (CA) is when the BD result interpretation agrees exactly with the FDA cleared comparator result interpretation. The overall performance of the BD BBL Sensi-Disc Lefamulin disc as compared to the Comparator disk for *Haemophilus influenzae* group (**Table 3**) was acceptable with 96.4% (108/112) CA. There were 3 very major errors and 1 major error.

The overall performance of the BD BBL Sensi-Disc Lefamulin disc as compared to the Comparator disk for *Staphylococcus aureus* (methicillin-susceptible isolates) group (**Table 3**) was acceptable with 100.0% (112/112) CA. There were no very major or major errors.

The overall performance of the BD BBL Sensi-Disc Lefamulin disc as compared to the Comparator disk for *Streptococcus pneumoniae* group (**Table 3**) was acceptable with 99.1% (111/112) CA. There was 1 very major error and no 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."*

Resistant Isolates:

A total of 336 clinical and challenge isolates were tested when the BD BBL Sensi-Disc Lefamulin was compared to the FDA cleared comparator disk. However, an insufficient number of resistant isolates were available for testing. The following limitation was added in the device labeling:

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

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 interpretive criteria for Lefamulin are listed in **Table 4.**

Table 4: Interpretive Categories and Breakpoints for Lefamulin[1]

	Minimum Inhibitory Concentration (µg/mL)			Disk Diffusion (zone diameter in mm)		
Pathogen	**S**	**I**	**R**	**S**	**I**	**R**
Staphylococcus aureus (methicillin-susceptible isolates)	≤0.25	-	-	≥23	-	-
Streptococcus pneumoniae	≤0.5	-	-	≥19	-	-
Haemophilus influenzae	≤2	-	-	≥18	-	-

[1] According to the **FDA STIC Website**, which recognizes CLSI M100-Ed33.
Note: 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.
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/development-resources/antibacterial-susceptibility-test-interpretive-criteria**). 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 Lefamulin 20µg (LMU-20) when revised breakpoints for Lefamulin 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 Lefamulin 20µg 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.