K993577

DEC - 1 1999

510(k) SUMMARY

SUBMITTED BY:	BECTON DICKINSON MICROBIOLOGY SYSTEMS 7 LOVETON CIRCLE SPARKS, MD 21152
CONTACT:	Monica E. Giguere Regulatory Affairs Associate
TELEPHONE:	(410) 316-4287
PREPARED:	October 18, 1999
DEVICE NAME:	Cefotaxime/Clavulanic Acid, 30/10μg, BBL™ Sensi-Disc™ and Ceftazidime/Clavulanic Acid, 30/10μg, BBL™ Sensi-Disc™.
PREDICATE DEVICE:	Other BBL™ Sensi-Disc™ such as Cefotaxime, 30μg, BBL™ Sensi-Disc™ and Ceftazidime, 30μg, BBL™ Sensi-Disc.
INTENDED USE:	Antimicrobial susceptibility test discs are used for semi-quantitative susceptibility testing of bacteria by standardized agar diffusion. Cefotaxime/Clavulanic Acid, BBL™ Sensi-Disc™ and Ceftazidime/Clavulanic Acid BBL™ Sensi-Disc™ are intended for use for confirmatory tests for organisms that secrete Extended-spectrum β-lactamases (ESBL)s as indicated in the Results section of the package insert and indicated below.
INDICATIONS FOR USE	Use of Cefotaxime/Clavulanic Acid, BBL™ Sensi-Disc™ and Ceftazidime/Clavulanic Acid BBL™ Sensi-Disc™ together with Cefotaxime and Ceftazidime susceptibility discs for *in vitro* agar diffusion susceptibility testing are indicated when there is a need to perform a confirmatory test for ESBLs in *Klebsiella spp.* and *Escherichia coli.*

DEVICE DESCRIPTION:

Cefotaxime/Clavulanic Acid and Ceftazidime/Clavulanic Acid susceptibility test discs are prepared by impregnating high quality absorbent paper with accurately determined amounts of Cefotaxime, supplied by Marion Roussel, Inc., Kansas City, MO, and Ceftazidime, supplied by Glaxo Wellcome Operations, Cumbria, UK, respectively. Both discs are also impregnated with specific amounts of Clavulanic Acid supplied by SmithKline Beecham Pharmaceuticals, Piscataway, NJ.

The disks are clearly marked with the agents: CTX/CLA and CAZ/CLA. Cefotaxime/Clavulanic Acid and Ceftazidime/Clavulanic Acid susceptibility test discs are provided in cartridges of 50 disks each and packaged separately.

Agar diffusion methods employing dried filter paper discs impregnated with specific concentrations of antimicrobial agents were developed in the 1940's. In order to eliminate or minimize variability in the testing, Bauer et al. developed a standardized procedure in which Mueller Hinton Agar was selected as the test medium.

Various regulatory agencies and standards-writing organizations subsequently published standardized reference procedures based on the Bauer-Kirby method. Among the earliest and most widely accepted of these standardized procedures were those published by the U. S. Food and Drug Administration (FDA) and the World Health Organization (WHO). The procedure was adopted as a consensus standard by the National Committee for Clinical Laboratory Standards (NCCLS) and is periodically updated. The latest NCCLS documents are M2-A6[1] (1/97) and M100-S9[2] (1/99).

Disks containing an antimicrobial agent are applied to the surface of Mueller Hinton Agar plates inoculated with pure cultures of clinical isolates. Following incubation, the plates are examined and the zones of inhibition surrounding the discs are measured and compared with established zone size ranges for the antimicrobial agents in order to determine which is most suitable for use in therapy. The determination as to whether the organism is susceptible (S), intermediate (I), or resistant (R) to an antimicrobial agent is made by comparing zone sizes to the interpretive criteria defined in the tables of NCCLS document M100-S9.

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[1] National Committee for Clinical Laboratories Standards, 1997 NCCLS document M2-A6. (Performance Standards for Antimicrobial Disk Susceptibility tests" – Sixth Edition, Approved Standard, 1/97. NCCLS, Wayne, PA.

[2] National Committee for Clinical Laboratories Standards, 1999. NCCLS document M100-S9. Performance standards for antimicrobial susceptibility testing, 9th informational supplement, NCCLS, Wayne, PA

Strains of *Klebsiella* spp. and *E. coli* that produce extended spectrum beta-lactamases (ESBLs) may be clinically resistant to therapy with penicillins, cephalosporins or aztreonam, despite in vitro susceptibility to some of these agents. Some of these strains will show zones of inhibition below the normal susceptible population but above the standard breakpoints for certain extended-spectrum cepahlosporins or aztreonam; such strains may be screened for potential ESBL production by using screening breakpoints. Other strains may test intermediate or resistant by standard breakpoints to one or more of those agents. In all strains with ESBLs the zone diameters should increase in the presence of clavulanic acid. (A ≥5mm increase in zone diameter for either cefotaxime or ceftazidime tested in combination with clavulanic acid versus its zone when tested alone means the organism is an ESBL-producing strain.)

For all ESBL-producing strains the test interpretation should be reported as resistant for all penicillins, cephalosporins, and aztreonam.

DEVICE COMPARISON

Cefotaxime/Clavulanic Acid, BBL™ Sensi-Disc™ and Ceftazidime/Clavulanic Acid BBL™ Sensi-Disc™ are substantially equivalent[3] to all of the other susceptibility discs that have been manufactured and marketed by Becton, Dickinson and Company for over twenty years.

These Sensi-discs are comprised of clavulanic acid and a drug agent, either cefotaxime or ceftazidime, and is used in a manner analogous to discs used for these and other antimicrobics.

Table 1: Summary of Substantially Equivalent Components

	Cefotaxime/Clavulanic Acid, BBL™ Sensi-Disc™ and Ceftazidime/ Clavulanic Acid BBL™ Sensi-Disc™	**Other BBL™ Sensi-Disc™ such as Cefotaxime BBL Sensi-Disc and Ceftazidime BBL Sensi-Disc**
Intended Use	Antimicrobial susceptibility test disks are used for semi-quantitative *in vitro* susceptibility testing of bacteria by standardized agar diffusion. These discs are used as confirmatory tests for organisms that secrete Extended-spectrum β-lactamases (ESBLs).	Antimicrobial susceptibility test discs are used for semi-quantitative *in vitro* susceptibility testing of bacteria by standardized agar diffusion. These tests are used for a wide variety of gram-negative and gram-positive bacteria.
Result	Qualitative –Interpretation based on the difference in zone size between these disks and disks with the drug alone. (≥5mm increase in zone diameter for either = ESBL)	Qualitative – S/I/R interpretation based on zone size.
Sample	Test organism grown in pure culture.	Test organism grown in pure culture.
Procedure	Disks are placed on the surface of an inoculated plate; after incubation zones are read and compared to the zone size for the appropriate drug. ESBL-producing strains are reported as resistant for all penicillins, cephalosporins, and aztreona per NCCLS criteria.	Disks are placed on the surface of an inoculated plate; after incubation, zones are read and compared to S/I/R categories determined per NCCLS criteria.

[3] The term "substantial equivalence" as used in this 510(k) notification is limited to the definition of substantial equivalence as found in the Federal Food, Drug and Cosmetic Act, as amended and as applied under 21 CFR 807, Subpart E under which a device can be marketed without pre-market approval or reclassification. A determination of substantial equivalency under this notification is not intended to have any bearing whatsoever on the resolution of patent infringement suits or any other patent matters. No statements related to, or in support of substantial equivalence herein shall be construed as an admission against interest under the US Patent Laws or their application by the courts.

Summary of Performance Studies

A Reproducibility Study was performed at three sites to determine the reproducibility of the product using the NCCLS recommended negative and positive Quality Control organisms. The study was performed in triplicate at three test sites for ten days using three lots of disks. Zone sizes formed around the test disks were examined, recorded and compared to the zone sizes achieved with disks containing the Cefotaxime and Ceftazidime alone. Average zone sizes and the standard deviation for each single and combination disk and the difference between the two were calculated. Expected results were obtained in all cases.

An internal reproducibility study was performed to determine the reproducibility of results between different individuals performing the test. This test used ten organism strains of various resistance mechanisms. Three individuals tested the ten strains on three different days in triplicate, using one lot of test disks. All zones of inhibition were recorded. Variability between individual tests by the same person and between participants was examined. All results met the acceptance criteria.

Testing was also performed to determine the performance of the product using the Jacoby challenge set of organisms. The study followed the procedure described in the NCCLS M100-S9 document. Expected results were obtained in all cases.

Accuracy testing was performed to compare the performance of production Cefotaxime/Clavulanic Acid and Cetazidime/Clavulanic Acid BBL™ Sensi-Discs to disks prepared in the laboratory as described in the NCCLS M100-S9 document, for confirmatory tests for organisms secreting Extended-spectrum β-lactamases. Both the screening and confirmatory tests were performed as described in the document. Organisms tested included genotypic and phenotypic ESBL strains and non-ESBL strains. QC organisms were run each day of testing. Results from the production disks were compared to results obtained with disks made in the laboratory.

QC testing over the course of the study was acceptable. All expected outcomes were achieved during the screening test. All production disks results correlated with laboratory disks with 100% equivalency in performance. Expected outcomes were met for all of the genotypic and non-ESBL strains. The phenotypic strains performed as expected with the exception of four *K. oxytoca* strains. These four strains were not detected as ESBL by the reference or test disks. Overall performance accuracy was 95% and meets the acceptance criteria as outlined in the study protocol.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC - 1 1999

Ms. Monica E. Giguere, RAC
Regulatory Affairs Specialist
Becton Dickinson Microbiology Systems
7 Loveton Circle
Sparks, Maryland 21152

Re: K993577
Trade Name: Cefotaxime/Clavulanic Acid, 30/10µg, BBL™ Sensi-Disc™ and
Ceftazidime/Clavulanic Acid, 30/10µg, BBL™ Sensi-Disc™
Regulatory Class: II
Product Code: JTN
Dated: October 20, 1999
Received: October 21, 1999

Dear Ms. Giguere:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). You may, therefore, market the device, subject to the general controls provisions of the Act. 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.

If your device is classified (see above) into either class II (Special Controls) or class III (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770)488-7655.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll free number (800) 638-2041 or at (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsmamain.html"

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and Radiological Health

Enclosure

510(k) Number (if known) K993577

Device Name: Cefotaxime/Clavulanic Acid, 30/10µg ,BBL™ Sensi-Disc™ and Ceftazidime/Clavulanic Acid, 30/10µg, BBL™ Sensi-Disc™

Indications For Use:

Antimicrobial susceptibility test discs are used for semi-quantitative susceptibility testing by standardized agar diffusion. Cefotaxime/Clavulanic Acid, BBL™ Sensi-Disc™ and Ceftazidime/Clavulanic Acid,BBL™ Sensi-Disc™ are intended for use for confirmatory tests for organisms that secrete Extended-spectrum β-lactamases (ESBLs) as indicated in the Results section of the package insert and indicated below.

Use of Cefotaxime/Clavulanic Acid, BBL™ Sensi-Disc™ and Ceftazidime/Clavulanic Acid, BBL™ Sensi-Disc™ together with Cefotaxime and Ceftazidime susceptibility discs for *in vitro* agar diffusion susceptibility testing are indicated when there is a need to perform a confirmatory test for ESBLs in *Klebsiella spp.* and *Escherichia coli.*

(PLEASE DO NOT WRITE BELOW THIS LINE–CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluations (ODE)

Prescription Use ✓
Per 21 CFR 801.109

OR

Over –The Counter-Use
(Optional Format 3-10-98)

Woody Dubois
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K993577

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