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**REVIEW CRITERIA FOR ASSESSMENT
OF
ANTIMICROBIAL SUSCEPTIBILITY TEST DISCS**

This document is intended to provide guidance in the preparation of a regulatory submission. It does not bind the FDA or the regulated industry in any manner.

Microbiology Branch, Division of Clinical Laboratory Devices
Office of Device Evaluation

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While this guidance document represents a final document, comments and suggestions may be submitted at any time for Agency consideration by writing to Sharon L. Hansen, Ph.D., 2098 Gaither Road, (HFZ-440), Rockville, MD 20850. For questions regarding the use or interpretation of this guidance, contact Sharon L. Hansen, Ph.D. at (301) 594-2096.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration
Center for Devices and Radiological Health

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OF
ANTIMICROBIAL SUSCEPTIBILITY TEST DISCS**

PREMARKET NOTIFICATIONS

I. INTRODUCTION

A. GUIDANCE INTRODUCTION AND PURPOSE

This document reflects the current review guidance for antimicrobial susceptibility discs devices. It is based on 1) current scientific knowledge, 2) clinical experience, 3) previous submissions by manufacturers to the Food and Drug Administration (FDA), and 4) the Safe Medical Devices Act of 1990 and FDA regulations in the Code of Federal Regulations (CFR). As advances are made in science and medicine, and changes occur in implementation of Congressional legislation, these review criteria will be evaluated and revised as necessary.

This document is an adjunct to the CFR and other FDA Guidance documents for the preparation and review of 510(k) submissions. It does not supersede those publications, but provides additional clarification on what is necessary before FDA can clear a device for marketing. The submission must provide evidence that the device is safe, effective, and substantially equivalent to a predicate device legally marketed in the United States. In some cases, the performance of the device can be established by comparison of the standardized reference method.

The primary reference for the information required in a premarket notification (510(k)) for a medical device is found in 21 CFR 807.87. Substantial equivalence to a legally marketed device is to be established with respect to, but not limited to, intended use, design, energy used/delivered, materials, performance, safety, effectiveness, labeling, and other applicable characteristics.

B. PRODUCT INTRODUCTION

An Antimicrobial Susceptibility Test Disc is described in the FDA regulation, 21 CFR 866.1620(a) as a “device that consists of antimicrobial-impregnated paper discs used to measure by a disc agar diffusion technique or a disc broth elution technique the *in vitro* susceptibility of most clinically important bacterial pathogens to antimicrobial agents. In the disc agar diffusion technique, bacterial susceptibility is ascertained by directly

devices with this generic type include: 1) Becton Dickinson's Sensi-Discs which are prepared by impregnating paper discs with a specific antimicrobial. Each disc is marked on both sides with the agent and content and are furnished in cartridges of 50 discs each. 2) Difco's Dispens-O-Discs which are furnished in dispenser cartridges of 50 discs each.

C. REGULATORY BACKGROUND

In the Federal Register dated November 9, 1982 (47 CFR 50814), the Final Rule classified antimicrobial susceptibility test discs (21 CFR §866.1620) into Class II. This means that these devices are subject to class II controls. In May, 1991, FDA released the document "Review Criteria for Assessment of Antimicrobial Susceptibility Devices" which describes Antimicrobial Susceptibility Test Discs in the development of antimicrobial susceptibility systems. The document also further states that FDA performs only a labeling review because the scientific evaluation of these discs are completed during the review process of the antimicrobial drug (21 CFR §430, 431, 460) by the Center for Drug Evaluation and Research (CDER). Interpretive criteria and quality control procedures are based on those breakpoints established by the FDA (CDER) during the antimicrobial drug review. The FDA also encourages the use of the National Committee for Clinical Laboratory Standards (NCCLS) M2-A5 (1) and M100-S5 (2) for details of disk susceptibility testing (M2-A5) and interpretive criteria (M100-S5).

II. DESCRIPTION OF THE DEVICE

Antimicrobial Susceptibility Discs are paper discs or strips impregnated with a specific antimicrobial agent and are usually marked with the drug concentration and the disk code. The test procedure is based on the Kirby-Bauer method. Discs are placed on the surface of an agar plate that is inoculated with pure colonies of the organism to be tested then incubated overnight. Clinically the *in vitro* antimicrobial susceptibility is useful as a guide for determining antimicrobial agent of choice whenever the susceptibility of a bacterial pathogen is unpredictable or when a patient's infection has not responded to therapy that otherwise appears appropriate.

III. CLASSIFICATION AND TIER OF THE DEVICE

This device has been placed in class II under section 513 of the Federal Food, Drug, and Cosmetic Act. This device is Tier II. The appropriate panel is Microbiology (MI 83), the product code is JTN..

IV. POSSIBLE PREDICATE DEVICES

Possible predicate devices that are legally marketed in the U.S. are Becton Dickinson's Cefepime 30 mcg Sensi-Discs and Difco's Cefepime 30 mcg Dispens-O-Discs.

V. REQUIRED 510 (k) INFORMATION

The information needed to evaluate the 510(k) submission can be found in the FDA document "Premarket Notification (510(k)) Checklist for Acceptance Decision. This document is available from the Division of Small Manufacturer's Assistance (DSMA) which can be contacted at (800) 638-2041 or (301) 443-6597

The 510(k) must include a statement that the submitter believes, to the best of his/her knowledge that all data and information submitted are truthful and accurate, and that no material fact has been omitted as set forth in 21 CFR §807.87 (j). An Indication for use Statement, on a separate form, is also required and available through DSMA.

The Safe Medical Devices Act of 1990 (SMDA) requires all persons submitting a premarket notification submission to include either (1) a summary of safety and effectiveness information in the 510(k) submission upon which an equivalence determination could be based (510k summary) OR (2) a statement that safety and effectiveness information will be made available to interested persons upon request (510k statement).

A Summary of Equivalence comparing similar devices legally in commercial distribution in the United States must be provided. This statement should include the name of the device, the manufacturer, and the 510(k) number if known.

VI. LABELING REVIEW

The attached checklist was developed to facilitate the review of antimicrobial susceptibility test discs and to ensure consistency in the review process. The completed checklist must be inserted into the 510(k) by the reviewer.

A. Preliminary Evaluation

If the antimicrobial drug for the particular submission has not been approved, the review can not proceed. The submitter should be notified that until FDA (CDER) approves the antimicrobial drug, the submission should be withdrawn. The submitter should include the new drug application (NDA) number of the drug application. With the NDA number, CDRH (Microbiology Branch) can be contacted for the approval status. New drug approvals are also available on the Internet, (<http://www.fda.gov/cder/da/adp.htm>), and for drugs approved in the previous year, the product label is in the current Physicians Desk Reference (PDR). (3)

The intended use statement in the antimicrobial susceptibility disc product labeling should not include any organisms not found in the "Approved Indications for Use" Section of the drug package insert.

The Disk Code and Drug Concentration on the antimicrobial susceptibility disc should be the same as that stated in the "Susceptibility Testing" section of the drug product insert. The approved Disc code and concentration can also be found in the World Health Organization (WHO) annual publication "WHO Technical Report Series-Requirements for Antimicrobial Susceptibility Tests" (4); or Becton Dickinson's Antimicrobial Susceptibility Disc Charts. If the Disk Code and Concentration are different from the FDA's and WHO's, the submitter must correct this before the review can proceed.

B. Interpretive Criteria

The FDA approved interpretative criteria and recommended Quality Control organisms and acceptable ranges must be included in each disc manufacturers package insert. The NCCLS Performance Standard M100-A5 for Antimicrobial Disk Susceptibility Testing usually contains the same values. The FDA approved product insert supersedes the NCCLS Standards . Additional NCCLS recommended Quality Control organisms or interpretative criteria may be used if the FDA approved product labeling does not contraindicate the use for this indication.

The checklist should include the manufacturer's suggested criteria, and FDAs criteria. NCCLS breakpoints can be included if available. The FDA breakpoints and ranges will be listed in the "Microbiology" Section of the drug product label, under the Diffusion Techniques Section (the zone diameters in mm). The recommended Quality Control Organisms and acceptable zone diameters are also listed. Contraindications for testing of certain organism groups if indicated will be listed here also.

C. Data

Because data evaluation was completed by CDER, no performance data is requested from the manufacturer unless the manufacturer claims different interpretive criteria. If this occurs, refer the manufacturer to the FDA document "Review Criteria for the Assessment of Antimicrobial Susceptibility Devices" for appropriate performance data.

If submitted, stability data is reviewed for consistency with the drug package insert. The manufacturer should have this data available for GMP inspections, but it is not required in the 510(k).

D. Labeling Considerations

The product labeling must conform to 21 CFR §809.10. All the information required must be included following the format of §809.10.

Guidance on labeling issues is described in the ODE Bluebook Memo G91-1 "Device Labeling Guidance (3/18/91)". A copy may be obtained from the Center for devices and Radiological Health's DSMA.

The Interpretive (S-I-R) breakpoints and recommended quality control organisms must appear in the product labeling. The manufacturer can not refer user to the NCCLS standards document.

FOR MORE INFORMATION

For more information refer to the FDA document "Review Criteria for the Assessment of Antimicrobial Susceptibility Devices" or contact Sharon L. Hansen, Ph.D., Chief Microbiology Branch, Division of Clinical Laboratory Devices, (301) 594-2096.

Literature Cited:

1. National Committee for Clinical Laboratory Standards, Approved Standard. M2-A5. Performance Standards for Antimicrobial Disk Susceptibility Tests. Fifth Edition. NCCLS, Villanova, PA.:1995.
2. National Committee for Clinical Laboratory Standards, Approved Standard. M100-S5 Performance Standards for Antimicrobial Susceptibility Testing. Fifth Edition. NCCLS, Villanova, PA:1994.
3. Physicians Desk Reference. 49th ed. Oradell, NJ: Medical Economics Company, Inc., 1995.
4. World Health Organization Expert Committee on Biological Standardization. WHO Technical Report Series. Requirements for Antimicrobial Susceptibility Tests: I. Agar diffusion tests using antimicrobial susceptibility disks. 42nd rpt.:1992.

AST REVIEW CRITERIA FOR SUSCEPTIBILITY DISKS

Manufacturer.....Antimicrobial.....K.....

FDA/CDER approved this antimicrobial: Yes.....No.....NDA#.....
 (If NO, review can not proceed. Manufacturer must withdraw.)

APPROVED INDICATIONS FOR USE.....
 (See drug package insert for approved indications).

DISK CODE and CONCENTRATION: MFR.....WHOBBL
 (Disk Code and Concentration must be the same as WHO recommended or listed on BBL chart.)

INTERPRETIVE CRITERIA (zone sizes)

	SUSCEPTIBLE	INTERMEDIATE	RESISTANT
Manufacturer's			
FDA			
NCCLS			

QUALITY CONTROL RANGES

Q.C. ORGANISM	MANUFACTURER	FDA	NCCLS
E. coli ATCC 25922			
P aeruginosa ATCC27853			
E. coli ATCC 35218			
S. aureus ATCC 29213			
E. faecalis ATCC 29212			
S. pneumoniae ATCC49619			
H.influenzae ATCC 49247			
(Others)			

LABELING CONSIDERATIONS

Interpretive (S-I-R) Breakpoints in Labeling: Yes.....No.....
 Q.C. organisms and ranges in labeling: Yes.....No.....
 Indications for Use stated in labeling: Yes.....No.....

SUBSTANTIALLY EQUIVALENT.....PREDICATE DEVICE.....