

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2008-D-0339]

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Draft Guidance for Industry on Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled "Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices." The Food and Drug Administration Amendments Act of 2007 (FDAAA) includes a requirement that FDA identify and periodically update susceptibility test interpretive criteria for antibacterial drug products and make those findings publicly available. This draft guidance informs industry of how FDA intends to comply with the FDAAA requirement. Specifically, the draft guidance describes procedures and responsibilities for updating information on susceptibility test interpretive criteria, susceptibility test methods, and quality control parameters in the labeling for systemic antibacterial drug products for human use. This draft guidance also describes procedures for making corresponding changes to susceptibility test interpretive criteria for antimicrobial susceptibility testing (AST) devices.

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DATES: Although you can comment on any guidance at any time (see 21 CFR 10.115(g)(5)), to ensure that the agency considers your comments on this draft guidance before it begins work on the final version of the guidance, submit written or electronic comments on the draft guidance by [*insert date 60 days after date of publication in the Federal Register*]. Submit written comments on the proposed collection of information by [*insert date 60 days after date of publication in the Federal Register*].

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, rm. 2201, Silver Spring, MD 20993-0002 or the Division of Small Manufacturers Assistance (HFZ-220), Center for Devices and Radiological Health, Food and Drug Administration, 1350 Piccard Dr., Rockville, MD 20850-4307. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance, including comments regarding proposed collection of information, to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.regulations.gov>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT:

Regarding antibacterial drug products: Edward Cox, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 6414, Silver Spring, MD 20993-0002, 301-796-1300, or

Regarding AST devices: Freddie Poole, Center for Devices and Radiological

Health (HFZ-440), Food and Drug Administration, 2098 Gaither Rd.,
Rockville, MD 20850, 240-276-0712.

SUPPLEMENTARY INFORMATION:

I. Background

Antibacterial susceptibility testing is used to determine if bacteria that are isolated from a patient with an infection are likely to be killed or inhibited by a particular antibacterial drug product at the concentrations of the drug that are attainable at the site of infection using the dosing regimen(s) indicated in the drug product's labeling. The results from antibacterial susceptibility testing generally categorize bacteria as "susceptible," "intermediate," or "resistant" to each of the antibacterial drugs that are tested. When available, culture and susceptibility testing results are one of the factors that physicians consider when selecting an antimicrobial drug product for treating a patient.

The numerical values generated by susceptibility testing to determine whether a particular microorganism is susceptible to a particular antimicrobial drug—the antimicrobial susceptibility test interpretive criteria—are commonly referred to as breakpoints. These breakpoints are specified in the antimicrobial drug product's label. The antimicrobial susceptibility test interpretive criteria can be used to interpret results from either manual or automated AST devices.

On September 27, 2007, the President signed FDAAA (Public Law 110-85) into law. Section 1111 of FDAAA requires FDA to identify and periodically update susceptibility test interpretive criteria for antibacterial drug products and to make those findings publicly available. By enacting section 1111 of FDAAA, Congress recognized the importance of maintaining updated susceptibility test interpretive criteria.

FDA is announcing the availability of a draft guidance for industry entitled “Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices” to inform industry of how FDA intends to comply with section 1111 of FDAAA. The draft guidance explains the importance of making available to health care providers the most current information regarding susceptibility test interpretive criteria for antibacterial drug products. The draft guidance describes procedures for FDA, drug application holders, and AST device manufacturers to ensure that updated susceptibility test information is available to health care providers for the following reasons: (1) To address concerns about antibacterial drug product labeling with out-of-date information on susceptibility test interpretive criteria, quality control parameters, and susceptibility test methods and (2) to comply with the new requirements of section 1111 of FDAAA. Where appropriate, FDA intends to identify susceptibility test interpretive criteria, quality control parameters, and susceptibility test methods by recognizing annually, in a **Federal Register** notice, standards developed by one or more nationally or internationally recognized standard development organizations. Drug application holders of approved antibacterial drug products will then have the option of relying on FDA recognized standards to update their product labeling.

The draft guidance describes possible approaches that holders of new drug applications (NDAs) and those abbreviated new drug applications (ANDAs) that are designated as a reference listed drug can use to meet their responsibilities to update their product labeling for systemic antibacterial drug products. Application holders can use the following approaches:

- Submit a labeling supplement that relies upon a standard recognized by the agency.
- Submit a labeling supplement that includes data supporting a proposed change to the microbiology information in the labeling that differs from the agency's recognized standard.

Alternatively, in the event that application holders do not believe that any labeling changes are necessary, they should provide written justification in support of the current information in the *Microbiology* subsection of the product labeling.

The agency will make the updated information available by publicly posting changes to the product labeling within 30 days of approval of a supplement that includes a change to the *Microbiology* subsection of the product labeling.

The draft guidance also describes how manufacturers of in vitro diagnostic AST devices should update the susceptibility test information in their labeling to incorporate an FDA recognized standard or a change in labeling for a relevant antibacterial drug product.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments regarding this document. Submit a single copy of electronic comments or two paper copies of any mailed

comments, except that individuals may submit one paper copy. Comments are to be identified with the docket number found in brackets in the heading of this document. Received comments may be seen in the Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

Please note that on January 15, 2008, the FDA Division of Dockets Management Web site transitioned to the Federal Dockets Management System (FDMS). FDMS is a Government-wide, electronic docket management system. Electronic comments or submissions will be accepted by FDA only through FDMS at <http://www.regulations.gov>.

III. Paperwork Reduction Act of 1995

Under the Paperwork Reduction Act of 1995 (the PRA) (44 U.S.C. 3501–3520), Federal agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information that they conduct or sponsor. “Collection of information” is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal agencies to provide a 60-day notice in the **Federal Register** for each proposed collection of information before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing this notice of the proposed collection of information set forth in this document.

With respect to the collection of information associated with this draft guidance, FDA invites comments on the following topics: (1) Whether the proposed collection of information is necessary for the proper performance of FDA’s functions, including whether the information will have practical utility; (2) the accuracy of FDA’s estimated burden of the proposed collection of

information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

Application holders can use one of the following approaches to meet their responsibilities to update their product labeling under the draft guidance and FDA regulations: Submit a labeling supplement that relies upon a standard recognized by FDA in a **Federal Register** notice, or submit a labeling supplement that includes data supporting a proposed change to the microbiology information in the labeling. In addition, application holders should include in their annual report an assessment of whether the information in the *Microbiology* subsection of their product labeling is current or changes are needed. This information collection is already approved by OMB under control number 0910-0572 (the requirement in 21 CFR 201.56(a)(2) to update labeling when new information becomes available that causes the labeling to become inaccurate, false, or misleading) and control number 0910-0001 (the requirement in 21 CFR 314.70(b)(2)(v) to submit labeling supplements for certain changes in the product's labeling, and the requirement in 21 CFR 314.81(b)(2)(i) to include in the annual report a brief summary of significant new information from the previous year that might affect the labeling of the drug product).

In addition, under the draft guidance, if the information in the applicant's product labeling differs from the standards recognized by FDA in the **Federal Register** notice, and the applicant believes that changes to the labeling are not needed, the applicant should provide written justification to FDA. This

justification should explain why the recognized standard does not apply to its drug product and why changes are not needed to the *Microbiology* subsection of the product's labeling. This justification should also be submitted as general correspondence to the product's application, and a statement indicating that no change is currently needed and the supporting justification should be included in the annual report. Based on our knowledge of the need to update information on susceptibility test interpretive criteria, susceptibility test methods, and quality control parameters in the labeling for systemic antibacterial drug products for human use, we estimate that, annually, only 2 applicants will submit the written justification described previously and in the draft guidance. We also estimate that each justification will take approximately 16 hours to prepare and submit to FDA as general correspondence and as part of the annual report.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN¹

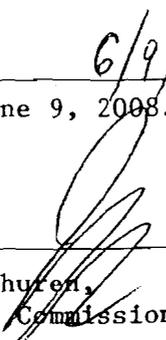
	No. of Respondents	No. of Responses per Respondent	Total Responses	Hours Per Response	Total Hours
Justification submitted as general correspondence and in the annual report	2	1	2	16	32

¹ There are no capital costs or operating and maintenance costs associated with this collection of information.

IV. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/cder/guidance/index.htm> or <http://www.regulations.gov>.

Dated: 6/9/08
June 9, 2008.



Jeffrey Shuren,
Associate Commissioner for Policy and Planning.

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