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

0910-0638

Supporting Statement

A. Justification

1. Circumstances Making the Information Collection Necessary

Section 1111 of 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 guidance informs industry of how FDA will comply with the FDAAA requirement.

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 antibacterial drug 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 (AST) interpretive criteria can be used to interpret results from either manual or automated AST devices.

In the Federal Register of December 23, 2010 (75 FR 80823), FDA issued a draft guidance entitled "Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices." The draft guidance described procedures for FDA, drug application holders, and AST device manufacturers to ensure that updated susceptibility test information is available to health care providers. The draft guidance explained that where appropriate, FDA intends to identify susceptibility test interpretive criteria, quality control parameters, and susceptibility test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. The draft guidance described, for holders of applications for approved antibacterial drug products, the option of relying on FDA-recognized standards to update their product labeling. The draft guidance explained that the Agency intends to 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 described, for manufacturers of in vitro diagnostic AST devices, the process for updating the susceptibility test information in their labeling to incorporate an FDA recognized standard or a change in labeling for a relevant antibacterial drug product. FDA is now issuing a finalized version of this guidance.

2. Purpose and Use of the Information Collection

Section 1111 of 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 guidance informs industry of how FDA will comply with the FDAAA requirement.

3. Use of Improved Information Technology and Burden Reduction

Application holders can use one of the following approaches to meet their responsibilities to update their product labeling under the 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.

In the Federal Register of December 11, 2003, FDA issued a final rule amending FDA regulations governing the format in which certain labeling is required to be submitted for review with New Drug Applications (NDAs), certain Biologic License Applications (BLAs), Abbreviated New Drug Applications (ANDAs), supplements, and annual reports. The final rule requires the electronic submission of the content of labeling (i.e., the content of the package insert or professional labeling, including all text, tables, and figures) in NDAs, certain BLAs, ANDAs, supplements, and annual reports electronically in a form that FDA can process, review, and archive.

The following guidances for industry have been developed to improve the use of information technology in the submission of marketing applications for human drugs and related reports:

- “Indexing Structured Product Labeling.”
- "Providing Regulatory Submissions in Electronic Format - Content of Labeling."
- "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and related Submissions Using the eCTD Specifications.”
- "Providing Regulatory Submissions in Electronic Format - General Considerations."
- "Providing Regulatory Submissions in Electronic Format – Postmarketing Individual Case Safety Reports."
- "Providing Regulatory Submissions in Electronic Format - Prescription Drug Advertising and Promotional Labeling."
- "Providing Regulatory Submissions in Electronic Format – Receipt Date."
- "SPL Standard for Content of Labeling Technical Qs and As."

These guidance documents and others are available at FDA's Web site http://www.fda.gov/cder/guidance/index.htm.

4. Efforts to Identify Duplication and Use of Similar Information

This information collection does not duplicate any other information collection.

5. Impact on Small Businesses or Other Small Entities

Under the Regulatory Flexibility Act, FDA analyzes regulatory options that would minimize any significant impact on small entities. FDA also assists small businesses in complying with regulatory requirements. FDA only expects two applicants to be subject to this information collection.

6. Consequences of Collecting the Information Less Frequently

Section 1111 of 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 guidance informs industry of how FDA will comply with the FDAAA requirement.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

There are no special circumstances for this collection.

8. Comments in Response to the Federal Register Notice and Efforts of Information to Consult Outside the Agency

8a. In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of December 23, 2010 (75 FR 80823). No comments were received.

9. Explanation of Any Payment or Gift to Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents under this guidance.

10. Assurance of Confidentiality Provided to Respondents

Confidentiality of information submitted under marketing applications is protected under 21 CFR 314.430 and 21 CFR Part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under Section 310(j) of the FDAAA.

11. Justification for a Sensitive Nature

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden and Costs

12a. Annualized Hour Burden Estimate

Application holders can use one of the following approaches to meet their responsibilities to update their product labeling under the 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. For human drugs, 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 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 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 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 two applicants will submit the written justification described above and in the guidance, and 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 Burden

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

12b. Annualized Cost Burden Estimate

Type of Respondent	Total Burden Costs	Hourly Wage Rate	Total Respondent Costs
Application Holders	32	$50.00	$1,600

FDA has estimated an average industry wage rate of $50.00 per hour for preparing and submitting the information collection under the guidance. Using this rate, and multiplied times the annual burden hours estimated in the tables above, the total cost burden to respondents is $ 1,600 (32 hours x $50).

13. Estimates of Other Total Annual Costs to Respondents and/or Recordkeepers/Capital Costs

There are no capital, start-up, operating, or maintenance costs associated with this information collection.

14. Annualized Cost to the Federal Government

Because we only expect two responses as a result of the guidance, the additional application reviewer time would be negligible and would be covered by our general estimate of FDA reviewer time for all marketing submissions under Part 314 (i.e., 835 Full Time Employees).

15. Explanation for Program Changes or Adjustments

There are no changes in this collection of information.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no publications.

17. Reasons(s) Display of OMB Expiration Date is Inappropriate

The agency is not seeking to display the expiration date for OMB approval of the information collection.

18. Exceptions to Certification for Paperwork Reduction Act Submission

There are no exceptions to the certification.