**SUPPORTING STATEMENT**

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

A. Justification

1. Circumstances of Information Collection

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

In the *Federal Register* of June 12, 2008 (73 FR 33438), FDA issued a draft guidance entitled "Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices." The draft guidance described procedures for FDA, drug application holders, and AST device manufacturers to ensure that updated susceptibility test information is available to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 The draft guidance explained that where appropriate, FDA intends to identify susceptibility test interpretive criteria, quality control parameters, and susceptibility test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 Information

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

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 NDAs, certain BLAs, 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

This information collection does not duplicate any other information collection.

5. Involvement of 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 2 applicants to be subject to this information collection.

6. Consequences If Information Collected 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. Consistency with the Guidelines in 5 CFR 1320.5(d)(2)

There is no inconsistency resulting from these regulations.

8. Consultation Outside the Agency

In the Federal Register of June 12, 2008 (73 FR 33438), FDA announced 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." FDA received no comments that pertained to the information collection analysis in the Federal Register notice.

9. Remuneration of Respondents

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

10. Assurance of Confidentiality

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 Act.

11. Questions of a Sensitive Nature

There are no questions of a sensitive nature.

12. Estimated Reporting Burden

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 2 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[1]

| Reporting Burden | Number Of Respondents | Number 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 information collection.

13. Estimates of Total Cost Burden to Respondents

1

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).

14. Estimates of Annualized Cost Burden to the Government

Because we only expect 2 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 FTEs).

15. Changes In Burden

This is a new collection.

16. Time Schedule, Publication, and Analysis Plans

There are no publications.

17. Displaying of OMB Expiration Date

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

18. Exception to the Certification Statement - Item 19

There are no exceptions to the certification statement identified in Item 19, "Certification for Paperwork Reduction Act Submission," of OMB Form 83-I.

# PAPERWORK REDUCTION ACT SUBMISSION

Please read the instructions before completing this form. For additional forms or assistance in completing this form, contact your agency's Paperwork Clearance Officer. Send two copies of this form, the collection instrument to be reviewed, the supporting statement, and any additional documentation to: Office of Information and Regulatory Affairs, Office of Management and Budget, Docket Library, Room 10102, 725 17th Street NW, Washington, DC 20503.

1. Agency/Subagency originating request

FDA

2. OMB control number b. [ x ] None

a. 0910 -

3. Type of information collection (*check one*)

a. [X ] New Collection

b. [ ] Revision of a currently approved collection

c. [ ] Extension of a currently approved collection

d. [ ] Reinstatement, without change, of a previously approved collection for which approval has expired

e. [ ] Reinstatement, with change, of a previously approved collection for which approval has expired

f. [ ] Existing collection in use without an OMB control number

For b-f, note Item A2 of Supporting Statement instructions

4. Type of review requested (*check one*)
a. [x] Regular submission
b. [ ] Emergency - Approval requested by at close of comment period
c. [ ] Delegated

5. Small entities
Will this information collection have a significant economic impact on a substantial number of small entities? [ ] Yes [ x ] No

6. Requested expiration date
a. [X ] Three years from approval date b. [ ] Other Specify:_____/

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

8. Agency form number(s) (*if applicable*)

9. Keywords: antibacterial drugs, labeling

10. Abstract. The 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.

11. Affected public (*Mark primary with "P" and all others that apply with "x")*
a. ___ Individuals or households d. ___ Farms
b. _x__ Business or other for-profit e. ___ Federal Government
c. ___ Not-for-profit institutions f. ___ State, Local or Tribal Government

12. Obligation to respond (*check one*)
a. [ X ] Voluntary- (guidance document)
b. [ ] Required to obtain or retain benefits
c. [ ] Mandatory

13. Total Reporting burden
a. Number of respondents 2
b. Total responses 2
1. Percentage of these responses collected electronically approximately 75 %
c. Total hours requested 32__
d. Current OMB inventory 0_____
e. Difference _____
f. Explanation of difference
1. Program change _____
2. Adjustment _____

14. Annual reporting and recordkeeping cost burden *(in thousands of dollars)*
a. Total annualized capital/startup costs ____0_____
b. Total annual costs (O&M) ____0_____
c. Total annualized cost requested ____0_____
d. Current OMB inventory ____0_____
e. Difference ____0_____
f. Explanation of difference
1. Program change _____
2. Adjustment _____

15. Purpose of information collection (*Mark primary with "P" and all others that apply with "X"*)
a. __ Application for benefits e.__ Program planning or management
b. __ Program evaluation f.__ Research
c. __ General purpose statistics g._x_ Regulatory or compliance
d. __ Audit

16. Frequency of recordkeeping or reporting *(check all that apply)*
a. [ ] Recordkeeping b. [ ] Third party disclosure
c. [x ] Reporting
1. [x ] On occasion 2. [ ] Weekly 3. [ ] Monthly
4. [ ] Quarterly 5. [ ] Semi-annually 6. [ ] Annually
7. [ ] Biennially 8. [ ] Other (describe) _____

17. Statistical methods
Does this information collection employ statistical methods
[ ] Yes [x ] No

18. Agency Contact (person who can best answer questions regarding the content of this submission)

Name: Elizabeth Berbakos

| | |
|---|---|
| | Phone: _____ |