

DDM

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 314

Display Date 9-26-08
Publication Date 9-29-08
Certifier A. Corbin

[Docket No. FDA-2008-N-0341]

Applications for Food and Drug Administration Approval to Market a New Drug;
Postmarketing Reports; Reporting Information About Authorized Generic Drugs; Companion
Document to Direct Final Rule

AGENCY: Food and Drug Administration, HHS.

ACTION: Proposed rule.

SUMMARY: The Food and Drug Administration (FDA) is publishing this companion proposed rule to the direct final rule, published elsewhere in this issue of the FEDERAL REGISTER, which is intended to amend our regulations to require that the holder of a new drug application (NDA) submit certain information in an annual report regarding authorized generic drugs. We are taking this action as part of our implementation of the Food and Drug Administration Amendments Act of 2007 (FDAAA). FDAAA requires that FDA publish a list of all authorized generic drugs included in an annual report since 1999, and that the agency update the list quarterly.

DATES: Submit written or electronic comments on the proposed rule by [insert date 75 days after date of publication in the FEDERAL REGISTER]. If FDA receives any significant adverse comments, the agency will publish a document withdrawing the direct final rule within 30 days after the comment period ends. FDA will then proceed to respond to comments under this proposed rule using the usual notice and comment procedures. Submit comments on information collection issues under the Paperwork Reduction Act of 1995 by [insert date 30 days

FDA.2008.N.0341

NPR

after date of publication in the FEDERAL REGISTER] (see the "Paperwork Reduction Act of 1995" section of this document).

ADDRESSES: You may submit comments, identified by Docket No. FDA-2008-N-0341, by any of the following methods, except that comments on information collection issues under the Paperwork Reduction Act of 1995 must be submitted to the Office of Regulatory Affairs, Office of Management and Budget (OMB) (see the "Paperwork Reduction Act of 1995" section of this document).

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: <http://www.regulations.gov>. Follow the instructions for submitting comments.

Written Submissions

Submit written submissions in the following ways:

- FAX: 301-827-6870.
- Mail/Hand delivery/Courier (for paper, disk, or CD-ROM submissions): Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

To ensure more timely processing of comments, FDA is no longer accepting comments submitted to the agency by e-mail. FDA encourages you to continue to submit electronic comments by using the Federal eRulemaking Portal, as described previously, in the ADDRESSES portion of this document under Electronic Submissions.

Instructions: All submissions received must include the agency name and docket number for this rulemaking. All comments received may be posted without change to

<http://www.regulations.gov>, including any personal information provided. For additional information on submitting comments, see the “Request for Comments” heading of the SUPPLEMENTARY INFORMATION section of this document.

Docket: For access to the docket to read background documents or comments received, go to <http://www.regulations.gov> and insert the docket number, found in brackets in the heading of this document, into the “Search” box and follow the prompts and/or go to the Division of Dockets Management, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT:

Michelle D.D. Bernstein,
Center for Drug Evaluation and Research,
Food and Drug Administration,
10903 New Hampshire Ave.
Bldg. 51, rm. 6223,
Silver Spring, MD 20993-0002,
301-796-3601.

SUPPLEMENTARY INFORMATION:

I. Background

As described more fully in the direct final rule, FDAAA requires that FDA take the following actions: (1) Publish on its Internet site a complete list of all authorized generic drugs included in an annual report submitted to the agency after January 1, 1999; (2) update the list quarterly; and (3) notify relevant Federal agencies that the list has been published and will be updated quarterly. For purposes of publishing the list, section 505(t)(3) of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355(t)) defines the term “authorized generic drug”

as a “listed drug (as that term is used in [section 505(j) of the act]) that has been approved [under section 505(c) of the act] and is marketed, sold, or distributed directly or indirectly to retail class of trade under a different labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark than the listed drug.”

We are proposing to amend § 314.3 (21 CFR 314.3) of our regulations by adding a definition of “authorized generic drug.” To allow FDA to accurately report a complete list of all authorized generic drugs included in annual reports and to update the list in a timely fashion, we are proposing to amend § 314.81 (21 CFR 314.81) by adding paragraph (b)(2)(ii)(b), which would require that annual reports specifically and clearly include the information we are required to report. In addition, we propose to require that the NDA holder report the date the authorized generic drug ceased being distributed to ensure that the list is as accurate and up-to-date as possible. The first annual report submitted after implementation of this regulation must provide information regarding any authorized generic drug that was marketed during the time period covered by an annual report submitted after January 1, 1999. When information is included in an annual report about an authorized generic drug, we would require that a copy of that portion of the annual report be sent to a central office in the agency that will compile the list and update it quarterly. This proposed rule assumes that the copy of the relevant portion of the annual report may currently be submitted in any number of formats (e.g., a paper copy, a PDF document on a computer disc). Current capabilities do not permit direct electronic submission through a Web-based system. However, FDA is committed to adapting its business practices to evolving technology, including using the significant advancements in Web-based, electronic systems. We anticipate that, in future rulemakings, Web-based submission of annual reports will

eventually be required. In anticipation of that future change, this proposed rule provides that once an electronic submission format is adopted for annual reports, the submission to the agency of the information required under this regulation will also be required in that electronic format. We anticipate that when such a change is implemented, future guidance will address any technical questions related to such submissions.

II. Additional Information

This proposed rule is a companion to the direct final rule published elsewhere in this issue of the FEDERAL REGISTER. This companion proposed rule and the direct final rule are identical in substance. This companion proposed rule will provide the procedural framework to proceed with standard notice-and-comment rulemaking in the event the direct final rule receives significant adverse comment and is withdrawn. The comment period for the companion proposed rule runs concurrently with the comment period of the direct final rule. Any comments received under the companion proposed rule will be treated as comments regarding the direct final rule and vice versa.

A significant adverse comment is one that explains why the rule would be inappropriate, including challenges to the rule's underlying premise or approach, or would be ineffective or unacceptable without change. A comment recommending a rule change in addition to this rule will not be considered a significant adverse comment unless the comment states why this rule would be ineffective without the additional change.

If no significant adverse comment is received in response to the direct final rule, no further action will be taken related to the companion proposed rule. Instead, we will publish a confirmation notice within 30 days after the comment period ends. We intend the direct final rule to become effective 30 days after publication of the confirmation notice.

If we receive significant adverse comments, we will withdraw the direct final rule. We will proceed to respond to all the comments received regarding the direct final rule, treating those comments as comments to this proposed rule. The agency will address the comments in the subsequent final rule. We will not provide additional opportunity for comment. If we receive a significant adverse comment which applies to part of the rule and that part may be severed from the remainder of the rule, we may adopt as final those parts of the rule that are not the subject of significant adverse comment.

For additional background information, see the corresponding direct final rule published elsewhere in this issue of the FEDERAL REGISTER. All persons who may wish to comment should review the complete rationale for this amendment set out in the preamble of the direct final rule.

III. Environmental Impact

We have carefully considered, under 21 CFR part 25, the potential environmental effects of this action. We have concluded that this action will not have a significant impact on the human environment and that an environmental impact statement is not required.

IV. Analysis of Impacts

FDA has examined the impacts of the proposed rule under Executive Order 12866 and the Regulatory Flexibility Act (5 U.S.C. 601-612), and the Unfunded Mandates Reform Act of 1995 (Public Law 104-4). Executive Order 12866 directs agencies to assess all costs and benefits of available regulatory alternatives and, when regulation is necessary, to select regulatory approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity). The agency

believes that this proposed rule is not a significant regulatory action as defined by the Executive order.

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. Because this proposed rule imposes only minimal regulatory obligations, the agency certifies that the proposed rule will not have a significant economic impact on a substantial number of small entities.

Section 202(a) of the Unfunded Mandates Reform Act of 1995 requires that agencies prepare a written statement, which includes an assessment of anticipated costs and benefits, before proposing "any rule that includes any Federal mandate that may result in the expenditure by State, local, and tribal governments, in the aggregate, or by the private sector, of \$100,000,000 or more (adjusted annually for inflation) in any one year." The current threshold after adjustment for inflation is \$130 million, using the most current (2007) Implicit Price Deflator for the Gross Domestic Product. FDA does not expect this proposed rule to result in any 1-year expenditure that would meet or exceed this amount.

The only costs of this proposed rule are associated with the Paperwork Reduction Act burden, described in section V of this document. If we assume an average hourly wage plus benefits of \$56 for the reporting personnel, the annual cost is about \$29,000 (\$56 per hour x 520 hours).

V. The Paperwork Reduction Act of 1995

This proposed rule contains information collection provisions that are subject to review by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501-3520). A description of these provisions is given with an estimate of the annual reporting and recordkeeping burden in Table 1 of this document. Included in the

estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

FDA invites comments on the following: (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 estimate of the 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.

Title: Applications for FDA Approval to Market a New Drug; Postmarketing Reports; Reporting Information About Authorized Generic Drugs.

Description: This rulemaking requires the holder of an NDA to notify the agency if an authorized generic drug is marketed by clearly including this information in annual reports in an easily accessible place and by sending a copy of the relevant portion of the annual reports to a central office. We are taking this action as part of our implementation of FDAAA, which requires that FDA publish a list of all authorized generic drugs included in an annual report after January 1, 1999, and that the agency update the list quarterly. We plan to publish this list on the Internet and to notify relevant Federal agencies that the list has been published and will be updated.

Description of Respondents: Current holders of an NDA under which an authorized generic drug was marketed during the time period covered by an annual report submitted after January 1, 1999.

Table 1.--Estimated Annual Reporting Burden¹

21 CFR 314.81(b)(2)(ii)(b)	Number of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Authorized generic drug information in the first annual report submitted after the implementation of § 314.81(b)(2)(ii)(b)	60	6.7	400	1 hour	400
Authorized generic drug information submitted in each subsequent annual report	60	6.7	400	15 minutes	100
The submission of a copy of that portion of each annual report containing authorized generic drug information	60	6.7	400	3 minutes	20

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

During the past several years, FDA has reviewed a small sample of annual reports it has received under § 314.81(b)(2) to discern whether an authorized generic drug is being marketed by the NDA holder. Based on information learned from this review and based on the number of annual reports the agency currently receives under § 314.81(b)(2),¹ we estimate that, after the implementation of § 314.81(b)(2)(ii)(b), we will receive approximately 400 annual reports containing the information required under § 314.81(b)(2)(ii)(b) for authorized generic drugs that were marketed during the time period covered by an annual report submitted after January 1, 1999. Based on the number of sponsors that currently submit all annual reports, we estimate that approximately 60 sponsors will submit these 400 annual reports with authorized generics. As indicated in Table 1 of this document, we are estimating that the same number of annual reports will be submitted each subsequent year from the same number of sponsors containing the information required under § 314.81(b)(2)(ii)(b), and that the same number of copies of that

¹ During fiscal year 2006, the Center for Drug Evaluation and Research received 2,569 annual reports under § 314.81(b)(2) from 374 sponsors.

portion of each annual report containing the authorized generic drug information will be submitted from the same number of sponsors. Concerning the hours per response, based on our estimate of 40 hours to prepare each annual report currently submitted under § 314.81(b)(2),² we estimate that sponsors will need approximately 1 hour to prepare the information required under § 314.81(b)(2)(ii)(b) for each authorized generic drug that was marketed during the time period covered by an annual report submitted after January 1, 1999, approximately 15 minutes to prepare the information required under § 314.81(b)(2)(ii)(b) for each subsequent annual report, and approximately 3 minutes to submit to FDA a copy of that portion of each annual report containing the authorized generic drug information.

The information collection provisions of this proposed rule have been submitted to OMB for review. Interested persons are requested to fax comments regarding information collection by [insert date 30 days after date of publication in the FEDERAL REGISTER], to the Office of Information and Regulatory Affairs, OMB. To ensure that comments on information collection are received, OMB recommends that written comments be faxed to the Office of Information and Regulatory Affairs, OMB, Attn: FDA Desk Officer, FAX: 202-395-6974.

VI. Legal Authority

The Federal Food, Drug, and Cosmetic Act (the act), as amended by the Food and Drug Administration Amendments Act of 2007 (FDAAA), provides authority for FDA to issue this proposed rule. Section 505(t) of the act (21 U.S.C. 355(t); FDAAA section 920) requires that FDA publish a complete list of all authorized generic drugs included in an annual report submitted to the agency after January 1, 1999, and to update that list quarterly. In addition, section 701(a) of the act (21 U.S.C. 371(a)) provides general authority for FDA to issue

² See the FEDERAL REGISTER of January 4, 2008 (73 FR 865).

regulations for the efficient enforcement of the act. This proposed rule would amend FDA's existing regulations regarding annual reports in order to ensure that the information necessary for the agency to fulfill its obligation under section 505(t) is clearly reported.

VII. Federalism

FDA has analyzed this proposed rule in accordance with the principles set forth in Executive Order 13132. FDA has determined that the rule does not contain policies that have substantial direct effects on the States, on the relationship between the National Government and the States, or on the distribution of power and responsibilities among the various levels of government. Accordingly, the agency has concluded that the rule does not contain policies that have federalism implications as defined in the Executive order and, consequently, a federalism summary impact statement is not required.

VIII. Request for Comments

Interested persons may submit to the Division of Dockets Management (see ADDRESSES) written or electronic comments regarding this document. This comment period runs concurrently with the comment period for the direct final rule; any comments received will be considered as comments regarding the direct final rule. 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>.

List of Subjects in 21 CFR Part 314

Administrative practice and procedure, Confidential business information, Drugs, Reporting and recordkeeping requirements.

Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs, it is proposed that 21 CFR part 314 be amended as follows:

PART 314—APPLICATIONS FOR FDA APPROVAL TO MARKET A NEW DRUG

1. The authority citation for 21 CFR part 314 continues to read as follows:

Authority: 21 U.S.C. 321, 331, 351, 352, 353, 355, 356, 356a, 356b, 356c, 371, 374, 379e.

2. Section 314.3 is amended in paragraph (b) by adding the following definition for authorized generic drug in alphabetical order:

§ 314.3 Definitions.

* * * * *

(b) * * *

Authorized generic drug means a listed drug, as defined in this section, that has been approved under section 505(c) of the act and is marketed, sold, or distributed directly or indirectly to retail class of trade with labeling, packaging (other than repackaging as the listed drug in blister packs, unit doses, or similar packaging for use in institutions), product code, labeler code, trade name, or trade mark that differs from that of the listed drug.

* * * * *

3. Section 314.81 is amended by redesignating paragraph (b)(2)(ii) as paragraph (b)(2)(ii)(a) and by adding new paragraph (b)(2)(ii)(b) as follows:

§ 314.81 Other postmarketing reports.

* * * * *

(b) * * *

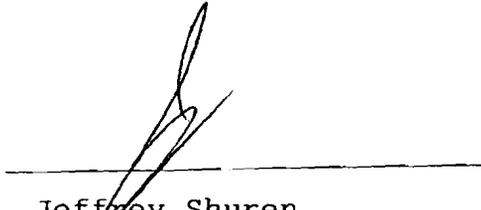
(2) * * *

(ii) * * *

(b) Authorized generic drugs. If applicable, the date each authorized generic drug (as defined in § 314.3) entered the market, the date each authorized generic drug ceased being distributed, and the corresponding trade or brand name. Each dosage form and/or strength is a different authorized generic drug and should be listed separately. The first annual report submitted on or after [insert date 135 days after date of publication in the FEDERAL REGISTER], must include the information listed in this paragraph for any authorized generic drug that was marketed during the time period covered by an annual report submitted after January 1, 1999. If information is included in the annual report with respect to any authorized generic drug, a copy of that portion of the annual report must be sent to the Food and Drug Administration, Center for Drug Evaluation and Research, Office of Pharmaceutical Science, 10903 New Hampshire Ave., Bldg. 51, rm. 4183, Silver Spring, MD 20993-0002 and marked "Authorized Generic Submission" or, if FDA has required that annual reports be submitted in an electronic format, the information required by this section must also be submitted in the electronic format.

* * * * *

Dated 9/16/08
September 16, 2008.



Jeffrey Shuren,
Associate Commissioner for Policy and Planning.

[FR Doc. 08-????? Filed ??-??-08; 8:45 am]
BILLING CODE 4160-01-S

**CERTIFIED TO BE A TRUE
COPY OF THE ORIGINAL**

