SUPPORTING STATEMENT A

Applications for Food and Drug Administration Approval to Market a New Drug; Revision of Postmarketing Reporting Requirements—Discontinuance

A. Justification

1. Circumstances Making the Collection of Information Necessary

Sections 314.81(b)(3)(iii) and 314.91 of the Code of Federal Regulations ("section 314.81(b)(3)(iii)" and "section 314.91", respectively) implement section 506C. Section 314.81(b)(3)(iii) requires entities who are the sole manufacturers of certain drug or biologic products to notify us at least 6 months before discontinuing the manufacture of the product. For the rule to apply, a product must meet the following three criteria:

1. The product must be life supporting, life sustaining, or intended for use in the prevention of a serious disease or condition;
2. The product must have been approved by FDA under section 505(b) or 505(j) of the act; and
3. The product must not have been originally derived from human tissue and replaced by a recombinant product.

Section 314.91 allows us to reduce the 6-month notification period if we find good cause for the reduction. A manufacturer may request that we reduce the notification period by certifying that good cause for the reduction exists. Under section 314.91, we will also publicly disclose information about the drugs that are discontinued.

In the Federal Register of October 18, 2007, FDA published a final rule adding §§ 314.81(b)(3)(iii) and 314.91 to our regulations. Sections 314.81(b)(3)(iii) and 314.91 require two new reporting requirements to FDA that are subject to OMB approval under the PRA:

Notification of Discontinuance and Certification of Good Cause. This interim final rule adds two new definitions to § 314.81(b)(3)(iii): "Sole Manufacturer" and "Discontinuance." This Paperwork Reduction Act (PRA) analysis covers the information collection resulting from the October 18, 2007, final rule and also includes estimates of how the number of Notifications of Discontinuance and Certifications of Good Cause may increase as a result of the interim final rule.

A. Notification of Discontinuance

Under § 314.81(b)(3)(iii), at least 6 months before a sole manufacturer intends to discontinue manufacture of a drug product subject to section 506C, the manufacturer must send us notification of the discontinuance. The notification of discontinuance generally contains the name of the manufacturer, the name of the product to be discontinued, the reason for the discontinuance, and the date of discontinuance.

For drugs regulated by CDER or CBER, manufacturers must send notifications of discontinuance to the following designated offices: (1) The CDER Drug Shortage Coordinator at the address of the Director of CDER; (2) the CDER Drug Registration and Listing Team, Division of Compliance Risk Management and Surveillance in CDER; and (3) the director of either the CDER division or the CBER office that is responsible for reviewing the application. FDA requires that the notification be sent to these offices to ensure that the efforts regarding the discontinuation of the product are commenced in a timely manner.

FDA will work with relevant manufacturers during the 6-month notification period to help minimize the effect of the discontinuance on patients and health care providers, and to distribute appropriate information about the discontinuance to physician and patient

organizations.

The interim final rule adds definitions of sole manufacturer and discontinuance to section 314.81(b)(3)(iii). The inclusion of these definitions expands notification requirements under § 314.81(b)(3)(iii) to additional discontinuance circumstances and clarifies the scope of manufacturers who must report discontinuances. The interim final rule also requires that notifications of discontinuance be submitted either electronically or by telephone according to instructions on FDA's Drug Shortage Website at http://www.fda.gov/Drugs/DrugSafety/DrugShortages. This change ensures that the appropriate offices are timely notified of all relevant discontinuances. It also reflects existing practice for submitting notices of discontinuance, and reduces the burden on industry to submit multiple copies of the notification.

B. Certification of Good Cause

FDA may reduce the 6-month notification period if it finds good cause for the reduction. As described in section 314.91, a manufacturer can request a reduction in the notification period by submitting written certification that good causes exists to the following designated offices: (1) The CDER Drug Shortage Coordinator at the address of the Director of CDER; (2) the CDER Drug Registration and Listing Team, Division of Compliance Risk Management and Surveillance in CDER; and (3) the director of either the CDER division or the CBER office that is responsible for reviewing the application. The following circumstances may establish good cause:

- A public health problem may result from continuation of manufacturing for the 6-month period (§ 314.91(d)(1));

- A biomaterials shortage prevents the continuation of manufacturing for the 6-month period (§ 314.91(d)(2));
- A liability problem may exist for the manufacturer if the manufacturing is continued for the 6-month period (§ 314.91(d)(3));
- Continuation of the manufacturing for the 6-month period may cause substantial economic hardship for the manufacturer (§ 314.91(d)(4));
- The manufacturer has filed for bankruptcy under chapter 7 or 11 of title 11, United States Code (§ 314.91(d)(5));
- The manufacturer can stop making the product but still distribute it to satisfy existing market need for 6 months (§ 314.91(d)(6)); or
- Other good cause exists for a reduction in the notification period (§ 314.91(d)(7)).

With each certification described previously, the manufacturer must describe in detail the basis for its conclusion that such circumstances exist. FDA will require that the written certification that good cause exists be submitted to the offices identified previously to ensure that our efforts regarding the discontinuation take place in a timely manner. The interim final rule makes no changes to the requirements or process for certification of good cause.

2. Purpose and Use of the Information Collection

As explained above, the requirements of sections 314.81(b)(3)(iii) and 314.91, as amended by the interim final rule, are designed to implement section 506C of the FD&C Act.

3. Use of Improved Information Technology and Burden Reduction

Sections 314.81(b)(3)(iii) and 314.91do not specify the format of the submissions. However, FDA has encouraged manufacturers to use email or any other electronic communication in order to expedite notifications of potential drug shortages.

4. Efforts to Identify Duplication and Use of Similar Information

The information collection under sections 314.81(b)(3)(iii) and 314.91, as amended by the interim final rule, would not duplicate any other information collection.

5. Impact on Small Businesses or Other Small Entities

Section V. of the Interim Final Rule, Analysis of Impacts, analyzes this impact as follows:

> FDA has examined the economic implications of the interim final rule as required by the Regulatory Flexibility Act. If a rule will have a significant economic impact on a substantial number of small entities, the Regulatory Flexibility Act requires the Agency to analyze regulatory options that would lessen the economic effect of the rule on small entities. This analysis serves as the final Regulatory Flexibility Analysis as required under the Regulatory Flexibility Act.
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> The Small Business Administration (SBA) uses different definitions of what a small entity is for different industries. Using SBA size standard definitions, a firm categorized in NAICS code 315412 (Pharmaceutical Preparations) or NAICS code 325414 (Biological Products) is considered small if it employs fewer than 750 or 500 people, respectively. The most currently available data from the 2007 Economic Census show that at least 92 percent of these establishments would be considered small by SBA

standards.[1] FDA notes that using data at the establishment level implicitly assumes that the typical manufacturing establishment is roughly equivalent to the typical small manufacturing firm.

FDA estimates that the cost per response as a percent of average sales for manufacturers in NAICS code 325412 could represent up to 0.002 percent of sales. The greatest impact is on establishments hiring fewer than 10 employees, where the cost per response as a percent of average sales ranges from 0.029 percent to 0.235 percent. The analysis of the effect on small versus large entities for NAICS 312314 is limited by data restrictions imposed to safeguard the confidentially of some establishments.

Consequently, for NAICS code 312314 the average value of shipments is only presented for all establishments. FDA estimates that the cost per response as a percent of average sales in this industry is between 0.001 percent and 0.004 percent (see the following table).

The Agency concludes that this rule will have a significant impact on a substantial number of small entities, but the impact is small and uncertain.

ESTIMATED ECONOMIC IMPACT OF INTERIM FINAL RULE ON SMALL ENTITIES

Number of Employees	Number of Establishments	Total Value of Shipments ($000)	Average Value of Shipments ($1000)	Cost per Response as a Percent of Average Sales	
				($234 per response—Notification of Discontinuance)	($1,872 per response—Certification of Good Cause)
NAICS Code 325412					
0-9	408	$324,604	$796	0.029%	0.235%
10-19	77	$317,551	$4,124	0.006%	0.045%
20-99	249	$8,377,347	$33,644	0.001%	0.006%
100-499	182	$32,516,961	$178,665	0.000%	0.001%

1 For NAICS code 325412, total value of shipments data are not available for establishments employing fewer than 750 employees. The estimated percent of small establishments (92 percent) is based on the total number of establishments with fewer than 500 employees. For NAICS code 324514 the percent of establishments with fewer than 750 employees is 96 percent.

500 and over	75	$68,162,155	$908,829	0.000%	0.000%
All	991	$109,698,618	$110,695	0.000%	0.002%
NAICS Code 325414					
All	350	$16,112,435	$46,036	0.001%	0.004%

6. Consequences of Collecting the Information Less Frequently

As explained above, sections 314.81(b)(3)(iii) and 314.91, as amended by the interim final rule, sets forth procedures for applicants who are the sole manufacturers of certain drug or biologic products to notify us at least 6 months before discontinuing manufacture of the product. Sections 314.81(b)(3)(iii) and 314.91, as amended by the interim final rule, also describes procedures for an applicant to request that we reduce the 6-month notification period.

7. Special Circumstances Relating to the Guidelines of 5 C.F.R. § 1320.5

There is no inconsistency with the guidelines.

8. Efforts to Consult Outside the Agency

In the Federal Register of November 7, 2000 (65 FR 66665), we published a proposed rule to implement section 506C of the FD&C Act. The proposed rule requested public comment. We published a final rule in the Federal Register of October 7, 2007 (72 FR 58993), which included a summary of and our responses to the public comments we received on the proposed rule.

9. Remuneration of Respondents

FDA has not provided and has no intention to provide any payment or gift to respondents

under sections 314.81(b)(3)(iii) and 314.91, as amended by the interim final rule.

10. Assurance of Confidentiality Provided to Respondents

Confidentiality of the information submitted under drug approval applications is protected under 21 CFR 314.430 and under 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under Section 310(j) of the FD&C Act.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

Description of Respondents: An applicant that is the sole manufacturer and who discontinues manufacture of a drug product that meets the following criteria: (1) Is life supporting, life sustaining, or intended for use in the prevention of a serious disease or condition; (2) was approved by FDA under section 505(b) or (j) of the act; and (3) was not originally derived from human tissue and replaced by recombinant product.

Burden Estimate: The table below provides an estimate of the annual reporting burden for notification of product discontinuance and certification of good cause under sections 314.81(b)(3)(iii) and 314.91, as amended by this interim final rule.

Notification of Discontinuance: Based on data collected from the CDER Drug Shortage Coordinator since December 17, 2007, when §§ 314.81(b)(3)(iii) and 314.91 went into effect, one manufacturer during each year reported to FDA a discontinuance of one drug product meeting the criteria of section 506C and its implementing regulations (i.e., the drug product was approved under section 505(b) or (j) of the Federal Food, Drug, and Cosmetic Act, the drug product was "life-supporting, life-sustaining or intended for use in the prevention of a debilitating disease or condition," the drug product was produced by a sole manufacturer, and the drug product was permanently discontinued). CDER's Drug Shortages Coordinator tracked 220 drug shortages between January and October of 2011. The Agency estimates that 30 percent (66) of these shortages would relate to discontinuances subject to mandatory reporting under section 506C as a result of the interim final rule. Adjusting to include an additional two months of reporting (November and December), we estimate that FDA will receive a total of 80 notifications of a discontinuance per year under section 506C, as amended by the interim final rule. Based on experience, a manufacturer submits only one notification of a discontinuance per year, thus the total number of manufacturers who would be required to notify us of a discontinuance would be 80. Therefore, the number of respondents is estimated to be 80. The hours per response is the estimated number of hours that a respondent would spend preparing the information to be submitted with a notification of product discontinuance, including the time it takes to gather and copy the statement. Based on experience in working with manufacturers to submit notifications under § 314.81(b)(3)(iii), we estimate that approximately 2 hours on average are needed per response. We do not expect the changes in the interim final rule to affect the number of hours per response. Therefore, we estimate that respondents will spend 160 hours per

year notifying us of a product discontinuance under these regulations.

Certification of Good Cause: Based on data collected from the CDER drug shortage coordinator since 2007, one manufacturer each year reported a discontinuance of one product meeting the criteria of section 506C and its implementing regulations. Each manufacturer has the opportunity under section 314.91 to request a reduction in the 6-month notification period by certifying to us that good cause exists for the reduction. The Agency has received no certifications of good cause since 2007. Although FDA expects to receive an increase in the number of reports of discontinuances as a result of the changes in the interim final rule, because of the limited circumstances under which good cause can be requested or would be appropriately granted, FDA does not expect a correspondingly large increase in the number of manufacturers requesting a certification of good cause. FDA estimates that only 5 manufacturers will request a certification of good cause each year. Therefore, the number of respondents is estimated to be 5. The total annual responses are the total number of certifications of good cause that are expected to be submitted to FDA in a year. FDA estimates that the total annual responses will remain small, averaging one response per respondent. The hours per response is the estimated number of hours that a respondent spends preparing the detailed information certifying that good cause exists for a reduction in the notification period, including the time it takes to gather and copy the documents. FDA estimates that approximately 16 hours on average are needed per response. Therefore, FDA estimates that 80 hours will be spent per year by respondents certifying that good cause exists for a reduction in the 6- month notification period under § 314.91.

ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	No. of Responses per	Total Annual Responses	Hours per Response	Total Hours

		Respondent			
Notification of Discontinuance (314.81(b)(3)(iii))	80	1	80	2	160
Certification of Good Cause (314.91)	5	1	5	16	80
Total					240

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

12b. Annualized Cost Burden Estimate

Section V. of the Interim Final Rule, Analysis of Impacts, calculates the industry costs of this rulemaking as follows:

From a baseline of current levels of reporting and shortages, FDA estimates that the total number of manufacturers who would be required to notify us of discontinuance under the interim final rule would be 80 per year.[2] However, the impact of the interim final rule represents the incremental impact, which is the difference between the total number of reports required by the interim final rule and the baseline, i.e., the estimated number of reports that we would receive without the interim final rule. FDA estimates that as a result of the interim final rule, we will receive an additional 9 to 24 notifications of section 506C discontinuances (both temporary and permanent discontinuances) and 2 to 5 associated certifications of good cause. FDA estimates that it will take longer to prepare a certification of good cause than a notification of discontinuance because preparing a certification of good cause requires a detailed narrative justifying a reduction in the notification period, which is more labor intensive than the simpler notification of discontinuance.

2 The total is estimated based on 220 shortages tracked by FDA's CDER Drug Shortages Coordinator from January through October of 2011, of which we estimate 30 percent would relate to discontinuances subject to mandatory reporting under section 506C and this interim final rule. The estimated number of discontinuances subject to mandatory reporting (220 x 30 percent) is then adjusted to include two additional months of reporting.

FDA estimates that it will take two hours to prepare a notification of discontinuance and 16 hours to prepare a certification of good cause (72 FR at 58999, October 18, 2007).

Notifications are generally prepared and submitted by a regulatory affairs manager. Thus, labor hours are valued using the median hourly wage for Management Occupations (occupation code 11-0000) in Pharmaceutical and Medicine Manufacturing (North American Industry Notification, NAICS, code 32400) as reported by the Bureau of Labor Statistics 2010 Employment Occupational Statistics. The median hourly wage is $117, which is adjusted for benefits and overhead.

The estimated cost is $234 ($117 x 2) per notification of discontinuance, and $1,872 ($117 x 16) per certification of good cause. The cost of submitting both a notification of discontinuance and certification of good cause is the sum of each individual response ($234 + $1,872, or $117 per hour x 18 hours). In the table below we present a range of the estimated costs. The estimated annual cost of the interim final rule is between $5,850 and $15,064.

Estimated Additional Annual Reporting Costs of the Interm Final Rule

Type of Response	Number of Additional Responses	Hours per Response	Cost per Response	Total Estimated Cost
Notification of Discontinuance (§ 314.81(b)(3)(iii))	9-24	2	$234	$2,106-$5,704
Certification of Good Cause (§ 314.91)	2-5	16	$1,872	$3,744-9,360
Total				$5,850-$15,064

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

There are no other costs, including capital costs or operating and maintenance costs, associated with this information collection.

14. Annualized Cost to the Federal Government

FDA estimates that there will be no additional costs associated with the receipt/review by FDA of the information submitted under §§ 314.81(b)(3)(iii) and 314.91 as amended by the interim final rule.

15. Explanation for Program Changes or Adjustments

This is a new approval request.

16. Plans for Tabulation and Publication and Project Time Schedule

There are no tabulated results to publish for this information collection.

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

FDA is not seeking approval to exempt the display of the expiration date of the OMB approval.

18. Exception to Certification for Paperwork Reduction Act Submissions

There are no exceptions to Section 19 of OMB Form 83-I.