United States Food and Drug Administration

Permanent Discontinuance or Interruption in Manufacturing of
Certain Drug or Biological Products

OMB Control No. 0910-0759

SUPPORTING STATEMENT **Part A: Justification**

1. Circumstances Making the Collection of Information Necessary

This information collection supports Food and Drug Administration (FDA, us or we) regulations. As amended by the Food and Drug Administration Safety and Innovation Act (FDASIA), (Pub. Law 112-144), the Federal Food, Drug, and Cosmetic Act (FD&C Act) requires all manufacturers of certain drugs to notify FDA of a permanent discontinuance or an interruption in manufacturing of these drugs 6 months in advance of the permanent discontinuance or interruption in manufacturing, or as soon as practicable. FDASIA also added section 506E to the FD&C Act (21 U.S.C. 356e), requiring FDA to maintain a current list of drugs that are determined by FDA to be in shortage in the United States and to include on that public list certain information about those shortages. Finally, FDASIA permits FDA to apply section 506C to biological products by regulation and implement certain drug shortages provisions.

Accordingly we established regulations in 21 CFR Parts 310.306, 314.81, and 600.82 to implement these provisions. Under the regulations, applicants with an approved new drug application (NDA) or abbreviated new drug application (ANDA) for a covered drug product, manufacturers of a covered drug product marketed without an approved application, and applicants with an approved biologics license application (BLA) for a covered biological product (including certain applications of blood or blood components) must notify FDA in writing of a permanent discontinuance of the manufacture of the drug or biological product or an interruption in manufacturing of the drug or biological product that is likely to lead to a meaningful disruption in the applicant's supply (or a significant disruption for blood or blood components) of that product. The notification is required if the drug or biological product is life supporting, life sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition, including use in emergency medical care or during surgery, and if the drug or biological product is not a radiopharmaceutical drug product.

The regulations prescribe the collection of the following information: (1) The name of the drug or biological product subject to the notification, including the NDC (or, for a biological product that does not have an NDC, an alternative standard for identification and labeling that has been recognized as acceptable by the Center Director); (2) the name of each applicant of the drug or biological product; (3) whether the notification relates to a permanent discontinuance of the drug or biological product or an interruption in manufacturing of the product; (4) a description of the reason for the permanent discontinuance or interruption in manufacturing; and (5) the estimated duration of the interruption in manufacturing.

As previously stated, notifications must be submitted to FDA electronically at least 6 months prior to the date of the permanent discontinuance or interruption in manufacturing. If 6 months' advance notice is not possible because the permanent discontinuance or interruption in manufacturing was unanticipated 6 months in advance, the applicant must notify FDA as soon as practicable, but in no case later than 5 business days after the permanent discontinuance or interruption in manufacturing occurs.

We therefore request OMB approval of the information collection provisions found in the following regulations:

- 21 CFR 310.306 – *notification of a permanent discontinuance or an interruption in manufacturing of marketed prescription drugs for human use without approved new drug applications*;
- 21 CFR 314.81(b)(3)(iii) – *permanent discontinuance or interruption in manufacturing of approved prescription drugs*; and
- 21 CFR 600.82 – *permanent discontinuance or interruption in manufacturing of prescription biological products*.

2. Purpose and Use of the Information Collection

Respondents to the information collection are applicants of approved NDAs, ANDAs, and BLAs, as well as manufacturers of prescription drug products marketed without an approved ANDA or NDA if the product is life supporting, life sustaining, or intended for use in the prevention or treatments of a debilitating disease or condition, including use in emergency medical care or during surgery, and is not a radiopharmaceutical product. Finally, BLA applicants of blood or blood components manufacturing a significant percentage of the Nation's blood supply are also subject to the applicable regulations. The information collection was established to help prevent and reduce current and future disruptions in the supply of lifesaving medicines, as well as to ensure that both FDA and the public receive adequate advance notice of shortages whenever possible. Shortages can involve critical drugs used to treat cancer, to provide required parenteral nutrition, or to address other serious medical conditions and can delay or deny needed care for patients. Shortages can also result in providers prescribing second-line alternatives, which may be less effective or higher risk than first-line therapies. Early notifications of potential shortages enables us to work with manufacturers and other stakeholders to help prevent such shortages.

3. Use of Improved Information Technology and Burden Reduction

Sections 310.306, 314.81(b)(3)(iii), and 600.82 provide that the notifications must be provided to FDA electronically, in a format that FDA can process, review, and archive. We anticipate that manufacturers will email us the submissions.

4. Efforts to Identify Duplication and Use of Similar Information

This is the first extension request of an information collection established through agency rulemaking (0910-AG88). Now that regulatory requirements have been codified and the effective date realized, we intend to consolidate the information collection elements into existing and approved collections as appropriate. Specifically, we believe burden attributed under this collection may be accounted for under related collections (see OMB Control Nos. 0910-0308, 0910-0230, and 0910-0645), and we are therefore reviewing our inventory. Upon ensuring that information collection requirements associated with the permanent discontinuance or interruption in manufacturing of certain drug or biological products as prescribed under 21 CFR §§ 310.306, 314.81(b)(3)(iii), and 600.82 are included elsewhere in our inventory, we will discontinue this information collection.

5. Impact on Small Businesses or Other Small Entities

While new drug and biological product development is typically an activity completed by large multinational drug firms, we do not believe the information collection poses undue burden on small entities. At the same time, we provide assistance to small businesses in complying with our regulations. We offer assistance from both scientific and administrative staffs within the agency and have provided a Small Business Guide on our website at http://www.fda.gov/ForIndustry/SmallBusinessAssistance/default.htm.

6. Consequences of Collecting the Information Less Frequently

The regulations implement a statutory 6-month notification period before permanent discontinuance or interruption in manufacturing of applicable products, or, if that is not possible, as soon as practicable thereafter. We believe this information collection schedule is necessary to help prevent and reduce current and future disruptions in the supply of lifesaving medicines.

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

There are no special circumstances for this collection of information.

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

In accordance with 5 CFR 1320.8(d), we published a notice in the Federal Register of April 13, 2018 (83 FR 16108) soliciting public comment on the information collection. No comments were received in response to the notice.

9. Explanation of Any Payment or Gift to Respondents

No payments or gifs are provided to respondents to the information collection.

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. In addition, information is protected under §§ 314.81(b)(3)(iii)(d), and 600.82(d).

11. Justification for Sensitive Questions

There are no questions of a sensitive nature associated with the information collection.

12. Estimates of Annualized Burden Hours and Costs

12a. Annualized Hour Burden Estimate

We estimate the burden of the information collection as follows:

Table 1.--Estimated Reporting Burden[1]

21 CFR Section	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Notifications required under §§ 310.306 (unapproved drugs), 314.81(b)(3)(iii) (products approved under an NDA or ANDA), and 600.82 (products approved under a BLA)	75	4.7	352.5	2	705

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

Based on the number of drug and biological product shortage related notifications we have received in the past 12 months, we estimate that annually 75 respondents ("No. of Respondents" in table 1) will notify us of a permanent discontinuance of the manufacture of a drug or biological product or an interruption in manufacturing of a drug or biological product that is likely to lead to a meaningful disruption in the respondent's supply of that product. Cumulatively we estimate these respondents will submit 352.5 notifications annually as required under §§ 310.306, 314.81(b)(3)(iii), and 600.82. We estimate 4.7 notifications per respondent, because a respondent may experience multiple discontinuances or interruptions in manufacturing in a year that require notification ("No. of Responses per Respondent" in table 1). We also estimate that preparing and submitting these notifications to FDA will take approximately 2 hours per respondent ("Average Burden per Response" in table 1).

12b. Annualized Cost Burden Estimate

Based on previous analysis in support of agency rulemaking (0910-AG88), we retain an estimated annual cost to respondents of $16,827. This estimate assumes industry costs associated with the reporting requirements as prescribed in the regulations.

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

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

14. Annualized Cost to the Federal Government

Based on FTE allocations for review of information submitted and associated administrative activities, we estimate a cost of $441,000 annually to the Federal government.

15. Explanation for Program Changes or Adjustments

This information collection reflects adjustments since the previous OMB approval. The current burden is based on the number of actual new notifications received including notifications that were counted previously under the OMB approval for the interim final rule entitled "*Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products*" (80 FR 38915, July 8, 2015) (OMB control number 0910-0699). This results in an increase of 128 responses and 255 burden hours.

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 display of the expiration date of OMB approval.

18. Exception to Certification for Paperwork Reduction Act Submissions

There are no exceptions to the certification.