U.S. GOVERNMENT ACCOUNTABILITY OFFICE
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July 23, 2015

The Honorable Lamar Alexander
Chairman
The Honorable Patty Murray
Ranking Member
Committee on Health, Education, Labor, and Pensions
United States Senate

The Honorable Fred Upton
Chairman
The Honorable Frank Pallone, Jr.
Ranking Member
Committee on Energy and Commerce
House of Representatives

Subject: *Department of Health and Human Services, Food and Drug Administration: Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products*

Pursuant to section 801(a)(2)(A) of title 5, United States Code, this is our report on a major rule promulgated by the Department of Health and Human Services, Food and Drug Administration (FDA) entitled "Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products" (RIN: 0910-AG88). We received the rule on July 7, 2015. It was published in the *Federal Register* as a final rule on July 8, 2015. 80 Fed. Reg. 38,915.

The final rule implements certain drug shortages provisions of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Food and Drug Administration Safety and Innovation Act (FDASIA). According to FDA, the rule requires all applicants of covered approved drugs or biological products—including certain applicants of blood or blood components for transfusion and all manufacturers of covered drugs marketed without an approved application—to notify FDA electronically of a permanent discontinuance or an interruption in manufacturing of the product that is likely to lead to a meaningful disruption in supply (or a significant disruption in supply for blood or blood components) of the product in the United States.

Enclosed is our assessment of FDA's compliance with the procedural steps required by section 801(a)(1)(B)(i) through (iv) of title 5 with respect to the rule. Our review of the procedural steps taken indicates that FDA complied with the applicable requirements.

If you have any questions about this report or wish to contact GAO officials responsible for the evaluation work relating to the subject matter of the rule, please contact Shirley A. Jones, Assistant General Counsel, at (202) 512-8156.

signed

Robert J. Cramer
Managing Associate General Counsel

Enclosure

cc: Kenneth Cohen
Director, Regulations Policy and Management Staff
Food and Drug Administration
Department of Health and Human Services

ENCLOSURE

REPORT UNDER 5 U.S.C. § 801(a)(2)(A) ON A MAJOR RULE
ISSUED BY THE
DEPARTMENT OF HEALTH AND HUMAN SERVICES,
FOOD AND DRUG ADMINISTRATION
ENTITLED
"PERMANENT DISCONTINUANCE OR INTERRUPTION
IN MANUFACTURING OF CERTAIN DRUG OR
BIOLOGICAL PRODUCTS"
(RIN: 0910-AG88)

(i) Cost-benefit analysis

The Food and Drug Administration (FDA) states that the rule imposes annual reporting costs of up to $16,827 on applicants affected by the rule, and up to $441,000 on FDA in review costs. Undertaking mitigation strategies, as measured by labor resources, is estimated to cost FDA between $1.85 and $5.94 million, and industry between $2.97 and $9.55 million. FDA also estimates annual costs for industry between $9.57 and $30.97 million associated with increasing production. Estimated total annual costs of the interactions between industry and FDA range between $14.54 and $46.92 million. Discounting over 20 years, annualized quantified benefits from avoiding the purchase of alternative products, managing product shortages, and life-years gained, would range from $30.45 million to $98.65 million using a 3 percent discount rate, and from $30.39 million to $98.42 million using a 7 percent discount rate. According to FDA, the public health benefits, mostly nonquantified, include the value of information that would assist FDA, manufacturers, health care providers, and patients in evaluating, mitigating, and preventing shortages of drugs and biological products that could otherwise result in delayed patient treatment or interruption in clinical trial development. FDA included a table in the final rule summarizing the benefits, costs, and distributional effects of the final rule.

(ii) Agency actions relevant to the Regulatory Flexibility Act (RFA), 5 U.S.C. §§ 603-605, 607, and 609

The Regulatory Flexibility Act requires agencies to analyze regulatory options that would minimize any significant impact of a rule on small entities. According to FDA, the estimated per notification cost for small business entities, $227, represents a small percentage of average annual sales (up to 0.10 percent). Although the final rule does not require specific mitigation strategies for firms that choose to implement mitigation or prevention strategies, it is possible that additional costs of $113,000 associated with implementing mitigation strategies could be significant: 2 to 7.8 percent of average annual sales for companies with fewer than 20 employees. Based on FDA's experience, as noted in the final rule, 4 to 5 small businesses per year have been affected by a shortage. FDA certified that the final rule will not have a significant economic impact on a substantial number of small entities.

(iii) Agency actions relevant to sections 202-205 of the Unfunded Mandates Reform Act of 1995, 2 U.S.C. §§ 1532-1535

FDA states that 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 $144 million, using the most current (2014) Implicit Price Deflator for the Gross Domestic Product. FDA stated that it does not expect this final rule to result in any 1-year expenditure that would meet or exceed this amount.

(iv) Other relevant information or requirements under acts and executive orders

Administrative Procedure Act, 5 U.S.C. §§ 551 et seq.

On November 4, 2013 (78 Fed. Reg. 65,904), FDA published a proposed rule to implement certain drug shortages provisions of the Federal Food, Drug, and Cosmetic Act (the FD&C Act), as amended by the Food and Drug Administration Safety and Innovation Act (FDASIA). Section 506C(i)(4) of the FD&C Act specifies that in promulgating a regulation to implement the FD&C Act's drug shortages provisions, FDA must issue a notice of proposed rulemaking that includes the proposed rulemaking and provide a period of no less than 60 days for public comment on the proposed rule. FDA provided 60 days for public comment on the proposed rule.

Based on the comments received and FDA's experience to date receiving notifications, maintaining public lists of drug and biological product shortages, and working with manufacturers and stakeholders to prevent and mitigate drug and biological product shortages, FDA finalized the rule as proposed. FDA received comments from 34 commenters, including public health associations, the pharmaceutical industry, hospital groups, consumer groups, and individuals. FDA summarized the comments contained in the submissions received and responded to them in the final rule.

Paperwork Reduction Act (PRA), 44 U.S.C. §§ 3501-3520

The final rule contains information collection requirements that are subject to review by the Office of Management and Budget (OMB) under PRA. The title, description, and respondent description of the information collection provisions are shown in the final rule with an estimate of the total reporting burden. According to FDA, 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. The final rule requires that applicants with an approved new drug application or abbreviated new drug application for a covered drug product, manufacturers of a covered drug product marketed without an approved application, and applicants with an approved biologics license application 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.

Based on the number of drug and biological product shortage related notifications FDA has seen during the past 12 months, FDA estimates that annually a total of approximately 75 respondents will notify FDA 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 under the final rule.

FDA estimated that these respondents will submit annually a total of approximately 305 notifications as required under sections 310.306, 314.81(b)(3)(iii), and 600.82. Approximately 80 of these notifications are notifications that FDA currently receives under OMB control number 0910–0699 for the interim final rule, and FDA expects to receive approximately 225 new notifications under the final rule. FDA estimated three notifications per respondent, because, according to FDA, a respondent may experience multiple discontinuances or interruptions in manufacturing in a year that require notification. FDA also estimated that preparing and submitting these notifications to FDA will take approximately 2 hours per respondent for a total of 450 hours. A table estimating the annual reporting burden associated with notifications required is included in the rule.

FDA states that in compliance with PRA, the information collection provisions of this final rule have been submitted to OMB for review. FDA stated that prior to the effective date of this final rule, FDA will publish a notice in the *Federal Register* announcing OMB's decision to approve, modify, or disapprove the information collection provisions in this final rule. FDA explained that it may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

Statutory authorization for the rule

FDA states that it is amending its regulations to implement sections 506C and 506E of the FD&C Act as amended by FDASIA, and that FDA's authority for this rule also derives from section 701(a) of the FD&C Act (21 U.S.C. § 1(a)).

Executive Order No. 12,866 (Regulatory Planning and Review)

FDA concluded that the final rule is an economically significant regulatory action as defined by Executive Order 12,866.

Executive Order No. 13,132 (Federalism)

FDA 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, FDA 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 was not required.