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PUBLIC INTEREST COMMENT

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

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INTRODUCTION

The Regulatory Studies Program of the Mercatus Center at George Mason University is dedicated to advancing knowledge about the effects of regulation on society. As part of its mission, the program conducts careful and independent analyses that employ contemporary economic scholarship to assess rulemaking proposals and their effects on the economic opportunities and the social well-being available to all members of American society.

This comment addresses the efficiency and efficacy of this proposed reconsideration from an economic point of view. Specifically, it examines how the relevant rule may be improved by more closely examining the societal goals the rule intends to achieve and whether this reconsideration will successfully achieve those goals. In many instances, regulations can be substantially improved by choosing more effective regulatory options or more carefully assessing the actual societal problem.

SUMMARY

The Food and Drug Administration (FDA) has proposed a new regulatory rulemaking covering shortages of drugs and related treatment components. The proposed rule requires covered makers of drugs and biological products, such as blood components for transfusions, to give notice of any significant interruption in manufacturing likely to disrupt their supply in the United States. Interruption includes total discontinuance. The FDA believes that increasing the information flow over discontinuances helps them to intervene in the supply chain with the aim of maintaining the supply of treatment components. Manufacturers must give notice to the FDA electronically; failure to do so leads to naming and shaming by the FDA. The FDA focuses unduly on information flows while ignoring other policy objectives, such as sustaining competition between manufacturers. The FDA's analysis suffers from poor quantification that provides little guidance for citizens.

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PROPOSED RULEMAKING

The FDA's proposed new rulemaking is designed to implement provisions of the Federal Food, Drug, and Cosmetic Act (the FD&C Act)[1] covering shortages of drugs and biological products. The proposed rulemaking will require all makers of drugs and biological products (other than blood-transfusion components) that are covered by the legislation and subject to an approved application to give notice of any significant interruption in manufacturing likely to disrupt supply of their product within the United States. The rulemaking will also extend the reporting requirement to manufacturers of blood components for transfusions who supply at least 10 percent of the market, and to manufacturers of drugs covered by the legislation but marketed without an approved application. The statute defines a covered product as a drug or biological product that is a prescription item that is "life supporting, life sustaining, or intended for use in the prevention or treatment of a debilitating disease or condition, including any such drug used in emergency medical care or during surgery."[2] In the case of blood transfusion supplies, significant interruptions are defined as arising when a manufacturer serves 10 percent or more of a market and experiences difficulty in meeting demand.[3]

The rulemaking requires covered manufacturers to report anticipated disruption of supplies six months in advance or as soon as is practicably possible. If the requirement is not met, the FDA will issue publicly available letters on noncompliance to the firm concerned.[4] The penalty appears to be one of naming and shaming rather than the imposition of fines. The FDA claims that it has increased the number of avoided discontinuations of covered products through its activities over the past two years and that the reporting requirements will assist it further in this regard.[5]

THE COSTS AND BENEFITS OF THE PROPOSAL

As required by Executive Order 12866, the FDA assessed the regulatory proposal as an economically significant regulatory action, in this case because it is likely to have an annual effect on the economy of $100 million or more through the financial impact of the reporting requirements. The FDA therefore carried out a benefit-cost analysis of the proposed rulemaking. The FDA claims the benefits of the reporting requirements come from the way the information flow leads to the FDA having a greater ability to intervene in the market and maintain supplies of drugs and biological materials. The FDA argues that avoiding disruption of normal supply channels saves treatment- and supplier-switching costs.[6]

The FDA claims that benefits arise from avoiding the purchase of more expensive alternative products, managing product shortages, and life years gained because treatment of patients is less disrupted. These benefits are estimated to be as high as $86.77 million using a three-percent discount rate.[7] The upper estimate for quantified annualized net benefits is estimated at a shade over $39 million. To these net benefits, the FDA would add qualitative estimates of public health benefits, including the value of information assisting the FDA, manufacturers, and others in mitigating the effects of shortages of drug and biological products.

The costs of reporting are borne by the covered firms and could be as much as $39.34 million a year.[8] Commendably, the FDA recognizes that there are annual costs of up to $8.29 million attached to its interven-

1. Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 30 (1938).
2. Permanent Discontinuance or Interruption in Manufacturing of Certain Drug or Biological Products, 78 Fed. Reg. 213 (November 4, 2013), 65905..
3. Ibid., 65913.
4. Docket No. FDA-2011-N-0898, 4.
5. Ibid.
6. Ibid.
7. Trivially less at seven percent.
8. FDA figures are annualized over a 20-year period using three-percent or seven-percent discount rate and are reported in detail in Docket No. FDA-2011-N-0898..

tions, although neither the interventions nor their costs are outlined in detail. The maximum annual costs of the dealings between the FDA and industry interests therefore add up to $47.63 million.

The FDA admits that its estimates are surrounded by considerable uncertainty and recognizes that it is not possible to be confident in the resulting assessment of costs and benefits attached to the reporting requirement.

THE UNDERLYING ANALYSIS

The current move to expand the early notification requirements for discontinuances arises because the FDA must implement the new provisions or very similar rules since the Food and Drug Administration Safety and Innovation Act (FDASIA)[9] altered the drug-shortage provisions of the FD&C Act in 2012. Nonetheless, it is still a valid criticism of the proposals that they are narrowly drawn. The FDA does not consider the costs and benefits of alternatives to its proposed rulemaking to any significant degree. It merely describes possible alternatives.[10] Such alternatives need to be properly included in a thorough benefit-cost comparison.

If the proposed regulation increases availability of drugs or components by "naming and shaming," then there is a compliance cost in addition to the notification cost. Manufacturers incur costs in altering their behavior to avoid being publicly shamed. Such compliance costs do not appear to be considered in the analysis.

There is no true focus in the rulemaking on the fundamental question of whether or not discontinuation of a specific treatment represents a systemic problem justifying regulatory intervention. The FDA is also apparently willing to ignore other significant economic issues in pursuing the narrow regulatory target of increasing an information flow. This narrowness leads to a conflict between policy objectives. The crux of the matter surfaces in the FDA's description of steps it takes when presented with information on shortages:

> Various activities can result from FDA's efforts to prevent or mitigate shortages. These activities—some of which would violate antitrust rules if pursued by manufacturers in the absence of FDA's intervention—include notifying and encouraging manufacturers of the same or similar products to increase their production, finding another manufacturer to begin production of the product, using regulatory discretion with regard to selective release of product when accompanied by appropriate warnings or remedies . . .[11]

There are several difficulties with the approach indicated in the quotation. One problem is the creation of an incentive for firms to behave strategically in threatening shortages to induce the authorities to loosen safety rules covering product certification.[12] Another is that no oversight is in place balancing out antitrust policy against policy over prescription drugs and biological products. The implied violation of antitrust policy would probably be the sharing of information about production among firms as a way of increasing production. Although it is not clear that these actions would actually harm consumers, the FDA really should analyze cases to see if its actions have created any anticompetitive effects before claiming that the actions have been beneficial.

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9. Food and Drug Administration Safety and Innovation Act (FDASIA), Pub. L. No. 112-144, 126 Stat. 993 (2012).
10. Docket, ibid.
11. Docket, 11.
12. Strategic behavior by pharmaceutical companies is well recognized. See G. Ellison and S. Fisher Ellison, "Strategic Entry Deterrence and the Behavior of Pharmaceutical Incumbents Prior to Patent Expiration," *American Economic Journal: Microeconomics* 3, no. 1 (2011): 1–36 and M. Paich, C. Peck, and J. Valant, "Pharmaceutical Market Dynamics and Strategic Planning: A System Dynamics Perspective," *System Dynamics Review* 27, no. 1 (2011): 47–63.

POOR QUANTIFICATION

Many calculations in the analysis supporting the proposed rulemaking are so poorly carried out that they are misleading. The regulatory impact analysis[13] relies on a series of assumptions extrapolating crudely estimated costs and benefits over populations of patients and firms. This is one worrying example of the troubling methodology:

> Using estimates of the average annual increase in off-contract purchases of $35,380, we estimate the rule-induced savings from avoiding purchasing alternative products could be between $17.07 million (=$35,380*20*(5754/239)) and $53.77 million (=$35,380*63*(5754/239)). Part of this estimate includes mitigation costs that must be excluded from the benefits because they could not be avoided as a result of the rule. . . . We are unable to disentangle these two estimates and as a conservative measure we adjust the benefits down by 50 percent. . . . We seek comments on this approach.[14]

Frankly, calculations of this caliber do nothing to increase the information flows needed by citizens, including patients, if they are to be able to assess the value of the proposed rulemaking.

CONCLUSION

This is an important area of regulation concerning life-saving drugs and biological products. The FDA is constrained by earlier legislation in formulating its proposed regulatory rulemaking. Unfortunately, the claimed net benefit for the requirement to report discontinuances in production of these products is predicated on weakly constructed data, reflecting uses of the data that conflict with antitrust policy. It is simply impossible to conclude that the rulemaking is of net benefit. As this is at a proposal stage, we can hope that public discussion between now and January 2014 will encourage the FDA to carry out a more detailed analysis and recognize a need to be more careful in avoiding conflicts with other areas of public policy.

13. Docket, ibid.
14. Docket, 13.