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PUBLIC INTEREST COMMENT

ELECTRONIC DISTRIBUTION OF PRESCRIBING INFORMATION FOR HUMAN PRESCRIPTION DRUGS, INCLUDING BIOLOGICAL PRODUCTS

Todd M. Nesbit

Agency: Food and Drug Administration, Department of Health and Human Services
Proposed: December 18, 2014
Comment period closes: May 18, 2015
Submitted: May 18, 2015
21 C.F.R. Parts 201, 606, and 610
RIN: 0910-AG18; Docket No.: FDA-2007-N-0363

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

For more information, contact
Robin Bowen, Director of Regulatory Outreach,
703-993-8582 (o), 703-801-1344 (m), rbowen@mercatus.gmu.edu
Mercatus Center at George Mason University
3434 Washington Boulevard, 4th Floor, Arlington, VA 22201

SUMMARY

The proposed rule titled "Electronic Distribution of Prescribing Information for Human Prescription Drugs, Including Biological Products"[1] would require that prescribing information intended for medical professionals no longer be distributed in paper form. Instead, this information would be disseminated electronically, except in limited circumstances. Prescribing information is intended to help health care professionals make more informed decisions concerning prescriptions and thereby improve the safety of their patients. Prescribing information distributed in paper form may not be current because it may have been printed before more recent labeling changes. The Food and Drug Administration (FDA) argues that requiring electronic dissemination of prescribing information will allow for real-time updates and improve the safety and effectiveness of prescription medications. In addition, the FDA argues that the electronic distribution of prescribing information will lead to substantial cost savings in the form of reduced printing costs.

The FDA's claim that access to up-to-date information on prescription drugs can help both physicians and pharmacists avoid dangerous prescribing errors is not contested here. However, this comment argues that the agency fails to adequately make the case that the proposed regulation is needed and that it best accomplishes the goals of improved patient health and lower costs of distributing prescribing information. This argument is founded on three observations.

First, in order to present the case in favor of the proposed regulation, the agency must establish that there exists a systemic failure owing to either market imperfections or ineffective past policies or regulations. The analysis presented in the proposed regulatory impact analysis (PRIA)[2] falls far short of doing so. Beyond discussing printing costs, the PRIA includes no assessment of the status quo. Specifically, it makes no attempt to determine the extent to which the risk to patient health is increased owing to the potentially outdated prescribing information inserts. Given that "most physicians do not use the paper form of the prescribing information but instead use compendiums containing information supplied by third parties,"[3] the risks may be negligible, particularly if the information provided by third parties is up to date. Unfortunately, the PRIA makes no attempt to assess current risk exposure. Instead it assumes the risk to patient health to be substantial, and uses this assumption as justification for regulatory action.

Second, the FDA's assessment of the net benefits of the proposed regulation is incomplete. The FDA makes no attempt to measure the benefits of the proposed regulation beyond the potential savings related to reduced paperwork costs if prescribing information were no longer required

1. Electronic Distribution of Prescribing Information for Human Prescription Drugs, Including Biological Products (Food and Drug Administration, Department of Health and Human Services), 21 C.F.R. pts. 201, 606, and 610 (proposed December 18, 2014).
2. Department of Health and Human Services, Food and Drug Administration, proposed regulatory impact analysis for "Electronic Distribution of Prescribing Information for Human Prescriptions Drugs, Including Biological Products" (hereafter cited as "PRIA").
3. Ibid., 21.

in paper form. It is unclear how many prescribing errors could be prevented by the electronic distribution of prescribing information on a centralized FDA webpage.

Third, the PRIA does not consider any substantial alternatives to the proposed regulatory action. The one alternative presented is to effectively eliminate the six-months-after-publication-of-final-rule effective date in the proposed rule, delaying the implementation of the rule until two years after the publication of the final rule. If the agency had assessed the net benefits of approaches other than the proposed command-and-control option, the public could have more confidence in the proposed regulation's merits. For example, if the adoption of the proposed regulation does not lead to reduced health risks relative to the status quo—in which health professionals rely on third-party compendiums, including many electronic ones—then the appropriate action may be to eliminate the existing paper-form requirement and not dictate any specific centralized repository of prescribing information.

Given the potential impact a prescribing error can have on a patient's health, this issue deserves a more thoughtful and rigorous analysis than has thus far been offered. Before the FDA takes any regulatory action, it must make a convincing argument establishing the existence of a systemic problem, one that causes patients to face an avoidable risk from prescribing errors. If a systemic problem does exist, then the FDA must present a more comprehensive assessment of the net benefits of the proposed regulation relative to the status quo and then compare and contrast the merits of the proposed regulation with those of other reasonable alternatives. Only after addressing these concerns is it possible to make an educated decision regarding the appropriateness of the proposed rule.

FAILURE TO ESTABLISH REGULATORY NEED

In order to establish the need for regulatory action, a regulator must identify a systemic failure. The FDA attempts to apply a public goods argument to support regulatory action: "A single electronic labeling repository for prescribing information accessible to all users is a public good."[4] Standard economics textbooks define public goods as goods which are both nonrival in consumption—meaning that multiple users can consume the same unit of production without reducing the benefits enjoyed by other users—and nonexcludable—meaning that once the good is provided, it is prohibitively costly to prevent nonpaying consumers from obtaining the good. While a repository of prescribing information is nonrival in consumption, it does not meet the conditions of nonexcludability. Indeed, prescribing information is already provided by private, for-profit organizations to those who pay a subscription fee. Prescribing information is excludable and is therefore a mixed good.

Because prescribing information is a mixed good, economic theory cannot predict whether it would be more efficiently provided privately or publicly. Answering this question demands a comprehensive analysis to determine how an information repository is best produced. Instead, the FDA simply assumes that there is a market failure requiring regulatory action, though

4. Ibid., 4.

its justification for the proposed rule ironically highlights the failure of regulatory action to evolve seamlessly with technology. On the other hand, entrepreneurs have thrived, creating third-party compendia of prescribing information in more accessible formats than the government-provided information.[5] Significant numbers of third-party compendia even offer applications for mobile devices.

The fact that the FDA-mandated paper-form prescribing information may be out of date is not sufficient to warrant new regulation that prohibits issuing the information in paper form. Given that pharmacies reported that they rely on corporately curated prescribing information and manufacturer websites[6] while physicians and nurses generally rely on third-party compendia,[7] the relevant questions are whether the privately provided sources of prescribing information are out of date and how frequently prescribing errors occur owing to out-of-date prescribing information. The FDA should assess the degree to which commonly referenced third-party sources of prescribing information are out of date and the frequency of resulting prescribing errors. While determining the causes of prescribing errors may not be feasible, it is certainly possible to assess the degree to which third-party sources are out of date. One method is to track new boxed warnings and contraindications and determine the average number of days before the information on the most common third-party sources is updated. Another method is to select a number of medications and determine what percentage of common third-party sources are out of date in ways that are likely to lead to prescribing errors.

The FDA admits the difficulty of determining "how often health care professionals rely on the prescribing information as well as different information sources."[8] Yet the FDA refers to results of an industry survey that suggest such information has already been collected. The FDA reports that "pharmacists refer to product labeling less than 1 percent of the time when filling prescriptions."[9] Given the FDA's assessment that physicians and nurses rely on third-party compendia and pharmacists rely almost exclusively on third-party sources of prescribing information, the fact that current FDA-mandated paper-form prescribing information is out-of-date may be irrelevant. The relevant questions are the following: (1) How often is the third-party prescribing information out-of-date? (2) What percentage of the out-of-date information is relevant to boxed warnings and contraindications? and (3) What are the primary sources for the information collected by the third-party sources?

If third-party information is rarely out of date or rarely concerns boxed warnings and contraindications, then prescribing errors may not be a systemic problem and there may be no need for additional command-and-control action. If third-party sources are out of date in ways that are likely to lead to prescribing errors, then policymakers must understand *why* this occurs in order to prescribe an adequate solution.

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5. Examples of user-friendly third-party sources of prescribing information include Epocrates, Medscape, and Lexicomp, among many others.
6. Electronic Distribution of Prescribing Information, 21 C.F.R., at 75512.
7. PRIA, 21.
8. Ibid., 5.
9. Ibid., 6.

FAILURE TO PROPERLY ASSESS BENEFITS

Physicians' and pharmacists' access to updated information on prescription drugs can surely assist in minimizing the occurrence of prescribing errors and, in the process, lead to improved patient care. Unfortunately, the FDA does not assess the potential benefits the proposed regulation might have for patient health.

Such an assessment should include two steps. First, it should calculate the potential number of prescribing errors caused by out-of-date prescribing information. The baseline could be an estimate of the total number of prescribing errors during a typical year as an upper limit to the number of errors that could be prevented. Estimates of medical errors because of out-of-date package inserts indicate that they are quite rare, accounting for only 0.3 percent of all medication errors.[10] Currently, the PRIA includes no such assessment of the potential size of the problem.

Second, the assessment should calculate the number of prescribing errors that could be eliminated by means of a centralized repository. If third-party sources of prescribing information are rarely out of date in ways that are likely to lead to prescribing errors, then there may be little benefit to be gained from a centralized repository provided by the FDA. If third-party boxed warnings and contraindications information is out of date, then further analysis is required. First, what percentage of physicians and pharmacists will choose to directly access the repository, and in what percentage of decisions? Second, will the repository improve the speed at which third-party sources of prescribing information update their systems? Given the third-party development of accessible and easily searchable mobile applications, it may be reasonable to conclude that few health care professionals will directly access the FDA repository. If that is the case, it is vital for regulators to determine how the repository would affect the information provided by third parties in order to ascertain its impact on the number of prescribing errors. To do so, the FDA will need to involve the third-party information providers in the regulatory impact analysis process.

Even ignoring the role of third-party compendia, the FDA-claimed benefits of the electronic repository are very likely exaggerated. In a 2013 report, the Government Accountability Office (GAO) states that relying on electronic labeling as a complete substitute for paper labeling "could adversely impact public health by limiting the availability of drug labeling for some physicians, pharmacists, and patients by requiring them to access drug labeling through a medium with which they might be uncomfortable, they might find inconvenient, or that might be unavailable."[11] The GAO mentions Internet availability in rural areas and during power outages as particularly concerning to stakeholders. For instance, in a 2012 report the Federal Communications Commission notes that roughly 14 million Americans lack adequate broadband capabilities.[12] Further, stakeholders reported to the GAO that many pharmacies, "in order

10. Maria R. Thomas, Carol Holquist, and Jerry Phillips, "Med Error Reports to FDA Show a Mixed Bag," FDA Safety Page, *Drug Topics*, October 1, 2001.
11. United States Government Accountability Office, *Electronic Drug Labeling: No Consensus on the Advantages and Disadvantages of Its Exclusive Use*, GAO-13-592, July 2013, 10.
12. Federal Communications Commission, *Connecting America: The National Broadband Plan*, 2010.

to protect their systems from potential threats like computer viruses, do not have Internet access."[13] Indeed, 27 percent of pharmacists surveyed by NERA Economic Consulting report that they either do not have Internet access or cannot browse the Internet and 82 percent of those with access report having experienced a loss of Internet connectivity during business hours.[14] Internet connectivity issues have the potential, at least in certain regions and during power outages, to erode if not entirely dissipate the advantages a centralized electronic repository has over paper-form information. Accordingly, only 25 percent of surveyed pharmacists agree that electronic labeling would provide more accurate information than the status quo.[15]

Lastly, the net benefits of the proposed and alternative solutions must be evaluated with the understanding that medicine is constantly evolving toward ever more individualized care based on genetic markers. As indicated by Peter Huber, such advancements have important implications for the usefulness of the FDA-mandated labeling:

> But the FDA-approved label is history, or soon will be. That scrap of paper is Washington's attempt to tell you and your doctor whether your body is bioequivalent to other bodies in which the drug has performed well in the past. Except in the simplest cases, paper can't convey even a tiny fraction of the information that we should be using to fit drugs to patients. The accurate fitting will emerge from pattern-matching search engines powered by constantly growing databases. They will contain far more information than is currently collected in FDA-scripted clinical trials.[16]

If the proposed regulation were an advancement toward the development and distribution of more patient-centered prescribing information, then it would be a step in the right direction—toward improving patient health. Unfortunately, the proposed regulation may stifle innovation involving patient-centered prescribing information, since individualized information would not be offered on the repository without another rulemaking authorizing such information.

Given the competition for subscribers in the market for third-party compendia, the incentives to develop patient-centered prescribing information may still exist. However, the proposed centralized repository would, at best, lag behind competing third-party compendia in providing individualized information, making it of diminished value relative to the third-party compendia. As such, it is unlikely that individualized information can adequately be offered in a centralized repository. If it cannot, then any FDA repository—whether it be in paper or electronic form—will soon become obsolete, as prescribers and pharmacists access the information distributed via third-party compendia instead. If this is the case, the long-run benefits of a centralized repository are highly limited.

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13. GAO, *Electronic Drug Labeling*, 15.
14. Sarah Butler, "Pharmacy Practice: A Report on Pharmacists' Use of Printed Package Inserts," NERA Economic Consulting, January 2015, 7.
15. Ibid., 10.
16. Peter Huber, *The Cure in the Code: How 20th Century Law Is Undermining 21st Century Medicine* (New York: Basic Books, 2013), 188.

NO CONSIDERATION OF ALTERNATIVES

The proposed rule has been deemed to be "an economically significant regulatory action under Executive Order 12866."[17] As such, the regulatory analysis must follow the guidelines set forth in that executive order. These guidelines state that "each agency shall identify and assess available alternatives to direct regulation, including providing economic incentives to encourage the desired behavior, such as user fees or marketable permits, or providing information upon which choices can be made by the public."[18] Unfortunately, the PRIA fails to consider any alternatives other than an 18-month difference in the regulation's effective date.

To assure the public of the merits of the proposed regulation, the FDA needs to explore other alternatives. In this case, the FDA has ignored at least one alternative that is very likely better than the proposed regulation: simply removing the paper requirement. Manufacturers and repackagers would still be required to disseminate minimum standard content of prescribing information. The requirement could be to include the information in the packaging or to refer the user to an online resource that, similarly to the requirement in the proposed regulation, must be updated within a specified amount of time after FDA label approval. This would give manufacturers and repackagers the flexibility to determine the lowest-cost means of providing assessable information that third-party sources can reference without involving the extra administrative step of interacting with an FDA office.

The analysis included in the PRIA presents a stronger argument for the above-described alternative than for the proposed regulation. Both alternatives would reduce the cost of printing the currently mandated paper-form prescribing information. The FDA-proposed regulation is only preferable if it can be shown to lead to quicker updates to prescribing information provided by third parties at a reasonable cost. The FDA does not provide such evidence. Since the FDA demonstrates only that the proposed regulation would reduce printing costs—an effect that would also follow the removal of the current in-print requirement—the less restrictive alternative that would allow third-party firms the greatest degree of flexibility to adjust to medical and technological advancements may be preferable.

CONCLUSIONS

For the reasons discussed above, the argument in favor of implementing the "Electronic Distribution of Prescribing Information for Human Prescription Drugs, Including Biological Products" is flawed and incomplete. The FDA does not demonstrate that the regulation solves a significant problem, and it fails to estimate the benefits of the regulation for patient health. Ultimately, a more complete analysis of both the costs and, particularly, the benefits of the proposed regulation and of reasonable alternatives is needed before the FDA can claim that this particular regulation is in the best interests of the public.

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17. Electronic Distribution of Prescribing Information, 21 C.F.R., at 75524.
18. Exec. Order No. 12866, 58 Fed. Reg. 51736 (October 4, 1993).