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# Proposed FDA Generic Drug Regulation: Higher Prices, No Public Health Benefit

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**Key points in this *Outlook*:**

- A new regulation proposed by the Food and Drug Administration will compel generic drug makers to update their drug labels to reflect purported "new" safety issues.
- The regulation will result in increased drug prices and leave generic drug firms vulnerable to "failure to warn" tort suits, but produce no public health benefit.
- It would be far more efficient and effective for the FDA to review generic drug labels itself. Alternatively, generic drug makers could undertake additional responsibilities without additional liability.

The generic drug industry won two decisive Supreme Court cases in the last two years over the question of whether generic firms can be subject to the same type of product liability suits that are routinely brought against brand drug manufacturers. At issue was whether generic firms could be accused of failing to warn consumers of side effects of older generic medicines. While the legal wrangling turned on the issue of torts, beneath the litigation is a broader public health question: what is the best way to keep multisource drug labels up-to-date with the latest and most-appropriate warning information?

For a multisource drug (a typically older drug that is available as both a generic and brand medicine) an average of eight manufacturers will make the generic version.[1] The question is whether each drug maker should bear independent responsibility for updating its label. Now, responsibility for making sure the label on an older medicine is kept up-to-date falls primarily to the Food and Drug Administration (FDA) and the branded company that first introduced the medicine. However, a new regulation proposed by the FDA will compel generic drug makers to unilaterally update their drug labels to reflect purported "new" safety issues.

While there may be merit in changing the existing law to enable generic firms to play a more-active role in making sure labels reflect the most current information, the proposed FDA regulation would not achieve this purpose. Instead, the regulation seems carefully crafted to invalidate the recent Supreme Court decisions that protect generic drug makers from a vast swath of product liability suits.

By allowing generic drug makers to unilaterally change their labels without FDA review and

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approval—which they are currently prohibited from doing—the FDA's new regulation would expose generic firms to massive torts. This may make for good politics in Washington, but the agency's action may also undermine some of the key public health benefits that generic drugs provide and that both parties have pursued over several decades. These include wider access to medicines and lower-cost health care options for consumers.

Moreover, the FDA's proposed rule will fail to achieve its ostensible purpose, which is to make sure generic labels accurately reflect the most-current information. There are better policies to achieve that end.

With this proposed change, the agency implies an urgency to label changes for multisource drugs that is simply misplaced. In the vast majority of label changes after a drug has gone generic, the updates are not newly discovered safety concerns. Instead, they are typically well-known side effects that are judged to require more prominence on drug labels. Often this is a reflection of new clinical norms that change in response to new therapies that allow certain medical conditions to be treated more safely with newer therapeutics.

If the FDA's concern is how to keep generic labels up-to-date—to make sure that they incorporate new safety information and properly reflect known risks—there are far more efficient vehicles than the framework the FDA has proposed. But this is not the FDA's true purpose. Rather, the agency is attempting to circumvent the recent Supreme Court decisions that denied tort claims against generic drug makers. That is why its new policy is so misguided and unmanageable.

## Background

**Generic Drug Approval Process.** A generic drug is identical—or bioequivalent—to a brand-name drug (often referred to as the reference listed drug, or RLD) in dosage form, safety, strength, route of administration, quality, performance characteristics, and intended use. Although generic drugs are chemically identical to their branded counterparts, they are typically sold at substantial discounts from the brand-name price. On average, generic drug prices are 80–85 percent lower than brand drug prices.[2]

This is possible because a 1984 law, known as the Hatch-Waxman Act after the bill's principal sponsors, created an abbreviated approval process for generic drugs to encourage competition and, in turn, drive down drug prices. In 2012 alone, generic drugs generated $217 billion in savings over the cost of their brand counterparts in the United States.[3]

To gain approval for a generic drug, companies must submit an abbreviated new drug application (ANDA) with the FDA, asking the agency for permission to market the generic medicine. Through the ANDA process, the generic drug maker is freed from repeating costly animal and clinical research on drugs already approved for safety and effectiveness. The generic drug needs only to demonstrate that it is bioequivalent to the brand drug—in other words, that it is the same.[4]

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This abbreviated process allows the cost of developing a generic drug to be very low. This low economic barrier, in turn, enables the entry of multiple generic competitors that each compete to drive down generic drug prices. This low development cost, and the competition it facilitates, is the primary way that generic drugs save consumers so much money.

**FDA Protocol for Label Changes.** Under Hatch-Waxman, generic drugs have to exactly reproduce the labels of their branded counterparts since the generic drugs are the same and can generally be substituted for their respective reference product, depending on state law. While a generic drug maker can petition the FDA to change a label should the drug maker become aware of new safety information, under Hatch-Waxman, a generic firm cannot unilaterally change a label on its own.

The FDA maintains tight control over brand drug label information, not allowing these drug makers to add superfluous warnings. But the agency has created an avenue for brand-name drug makers to change drug labels, under very specific circumstances, before the FDA has formally reviewed the new language. This is accomplished with a "changes being effected" (CBE-0) supplement.[5]

A downside of this process is that it exposes brand-name drug firms to product liability claims. These cases typically proceed on allegations that brand drug firms knowingly failed to warn consumers of certain drug risks. Tort lawyers argue that brand-name drug makers should be held liable for failing to warn of potential risks because the CBE-0 process gives them the ability to change the

safety information on a label without seeking explicit permission from the FDA.

These suits proceed notwithstanding the fact that the FDA still maintains tight control over the label and quickly reviews any change made under the CBE-0 process. Moreover, changes can be made only in narrowly prescribed circumstances. Even after a brand drug maker submits a CBE-0 supplement, it could face failure-to-warn suits claiming the firm should have made the change sooner.

A crucial question is whether the FDA has the legal authority to extend its regulatory control in this manner.

**Proposed Generic Drug Labeling Rule.** The FDA's new proposed regulation would effectively extend the brand drug CBE-0 provision to generic firms, conferring on them a similar obligation to make independent changes to their drug labels. In so doing, it would expose generic firms to the same type of product liability suits that plague brand-name drug firms and likely lead to multiple, differing labels for the same product.[6]

Opening up generic firms to these same sorts of claims is undeniably one of the motivations behind the FDA's new regulation. The agency says that its aim is to make sure generic labels are kept up-to-date. But other, more-efficient vehicles can achieve those ends.

In the agency's "Preliminary Regulatory Impact Analysis" that accompanied the proposed regulation in November 2013, the FDA prominently acknowledges its primary motivation under the heading "Need for Regulation": "As a result of [two recent] Supreme Court decisions, an individual can bring a product liability action for failure to warn against an NDA [new drug application] holder, but generally not an ANDA holder, and thus access to the courts is dependent on whether an individual is dispensed a 'brand name' or generic drug."[7]

**Supreme Court Cases on Generic Drug Labeling.** Because generic firms are not free to change their own labels, state torts that claim that a drug maker failed to warn of a particular risk are currently preempted. This argument has been tested in two recent Supreme Court cases. The Supreme Court first ruled on these matters in its 2011 decision in *Pliva v. Mensing*, when it affirmed the limitation on the ability of generic firms to adapt their drug labels in ways that deviate from the RLD.[8]

The plaintiff's argument in *Pliva v. Mensing* was that generic drug makers could be held liable in state torts because generic labels need only to conform to brand labels at the time of approval—later, generic drug makers are free to change their labels. The Supreme Court rejected that reasoning, holding that generic firms do not have freedom under law to change their labels at will. In a separate but related case decided last summer (*Mutual Pharmaceutical Co. v. Bartlett*), the Supreme Court solidified this precedent.

The FDA's proposed generic labeling regulation would try to reverse this precedent by obligating generic drug makers to unilaterally change their drug labels to reflect whatever safety issues they do not believe have sufficient prominence on the existing label.[9]

## Legality of the FDA's Actions

A crucial question is whether the FDA has the legal authority to extend its regulatory control in this manner. In the proposed rule, the FDA attempts to preclude doubts about the legality of its actions: "Nothing in the Hatch-Waxman Amendments or subsequent amendments to the FD&C [Federal Food, Drug and Cosmetic] Act limits the Agency's authority to revise the CBE-0 supplement regulations to apply to ANDA holders to help ensure that generic drugs remain safe and effective under the conditions of use prescribed, recommended, or suggested in the labeling throughout the life cycle of the generic drug product."[10]

But legal experts have taken issue with the FDA's analysis.[11] Critics argue that nothing in Hatch-Waxman allows deviations from the "sameness" requirements of the law on the scale that the FDA has proposed. Congress has raised similar questions. In a sharply worded letter sent to FDA Commissioner Margaret Hamburg on January 22, 2014, Republican members of the House Energy and Commerce Committee and Senate Health, Education, Labor, and Pensions Committee said the rule "would conflict directly with the statute, thwart the law's purposes and objectives, and impose significant costs on the drug industry and healthcare consumers."[12]

The FDA tried to justify its regulatory grab by arguing that the Supreme Court decisions reduced the incentive of generic drug makers to conduct postmarket surveillance and make sure their labels are up-to-date. On top of the fact that the FDA cited no evidence to support this claim,

the court decisions merely affirmed the widely believed legal status quo when it comes to generic firms and their liability under state tort law.[13]

## Consequences of the FDA's Proposed Rule

**Increased Costs.** According to the FDA, "The proposed rule is expected to generate little cost."[14] The agency estimates a paltry amount based only on the compliance and paperwork burden of the regulation. However, there are good reasons to believe the rule will in fact carry a substantial cost.

The largest impact of the proposed FDA regulation would be in generic drug affordability and health care costs. Exposing generic drug makers to the kind of costly litigation that burdens brand-name drug makers would add to generic drug costs directly, through the expense of fighting and settling the resulting torts, along with the expense of the steps that generic drug makers would have to take to reduce their liability. Because the generic drug industry is highly competitive, manufacturers would be forced to pass on liability expenses to consumers. As the Government Accountability Office noted in a report on medical liability costs, "Manufacturers pass on their liability costs . . . in their products' prices. Their liability costs include insurance and liability-related production and marketing costs."[15]

In a February 2014 analysis of the proposed FDA rule sponsored by the Generic Pharmaceutical Association, Brill estimates that—should the rule be finalized—generic drug maker spending on product liability insurance alone would increase US spending on generic drugs substantially. That analysis conservatively estimates that brand product liability spending was roughly $1.16 per prescription in 2012. Given that generics account for 84 percent of all prescriptions in the United States, roughly 3.4 billion prescriptions in total, total generic liability is expected to be $4 billion annually. Government health programs would bear $1.5 billion of this total, while private insurance companies and the uninsured would have to pay $2.5 billion.[16]

On top of these price increases, product liability exposure would add to costs indirectly through reduced competition. Small generic firms, in particular—because they are less able than larger firms to face the uninsurable risks the rule would create—would be forced to exit the market as a consequence of the regulation, reducing the competition that facilitates lower prices. The FDA's own analysis shows that it is often only after five or more generic firms enter the market for a particular drug that prices decline substantially.[17]

It is also a certainty that generic drug firms would each have to hire additional professional staff to comply with the obligations imposed by the new regulation.

**Label Confusion and Overwarning.** The FDA's policy change likely would have the opposite effect of the agency's stated goal of improving the utility of generic drug labels. The provision is likely to lead to confusing, conflicting generic labels that are cluttered with superfluous safety information. This, in turn, would undermine the interchangeability and substitutability of generic drugs both for the RLD and for one another.

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The existing CBE-0 process limits brand-name drug makers to updates that involve significant safety information and good scientific evidence to support a link between the safety issue and the drug. The proposed generic drug rule leaves more ambiguity for generic label updates.

Brand drug makers also have commercial reasons to make more judicious use of the CBE-0 process. If they load their labels with superfluous safety information not tethered to science but merely intended to shield themselves from lawsuits, competing drug makers with similar medicines could use any labeling discrepancies in competitive marketing. So brand drug makers have reason to make sure that any warnings they add are clinically relevant and based on sound science.

Generics typically do not have the same constraints. In most cases, they do not market their products competitively against other generic versions of the same drug based on the product's profile or label. While there are exceptions not relevant here, generic firms usually compete solely on distribution and price.[18] This means that they will have ample reason to load their drug labels with as many warnings as possible. Facing torts for "failure to warn" and having no competitive reason to limit labels only to clinically pertinent risks, generic firms will be driven by considerations of torts. There is every reason to assume that generic drug labels will become cluttered with

safety information as generic firms try to use the labels' warning section to reduce risk of torts.

The FDA has on many occasions addressed concerns about overwarning.[19] For example, in testimony before Congress in 2008, the agency's deputy commissioner for policy stated, "Including warnings in the labeling without a determination by FDA that they are well-grounded in science can have the effect of over warning and confusion as well as deterring use of a beneficial drug. Thus, FDA interprets and implements its responsibility under the act as establishing both a 'floor' and a 'ceiling' for risk information."[20]

In FDA regulatory guidance dating back as far as the mid-1970s, the agency also expressed concern about overwarning.[21] For example, in 2001, the FDA wrote:

> Including too many warnings and precautions, over-warning, dilutes the strength of all of the hazard alerts. We recommend that writers use care in what is designated as a warning or precaution. Careless designation can have the same diluting effect as over-warning. . . . Repeated exposure to unnecessary hazard alerts (not relevant or already known) reduces the effectiveness of the important warnings and precautions.[22]

## The Public Health Case

If we are to take the FDA at its word about the purported purpose of the regulation—keeping generic labels updated with the most-recent safety information— the key issue is one of public health.[23] Therefore, policymakers must ask the fundamental question: will the proposed regulation improve public health? We argue that it will not.

The FDA is unable to identify a single quantifiable benefit from imposing CBE-0 obligations on generic drug makers. The most the agency can claim is that communication of drug safety information "could be improved" by the proposed regulation.[24] The FDA also cites no evidence that the absence of a CBE-0 process prevents new safety information from being incorporated into generic drug labels. Indeed, the FDA cites no relevant data to demonstrate that generic drug labels do not incorporate pertinent safety information in a reasonable fashion when it becomes available.

Our review of label changes made for drugs after generic versions were available shows that the vast majority of these updates were for known safety risks, which simply received more prominent placement on the labels. As we mentioned, the submission of a CBE-0 supplement often triggers failure-to-warn suits. According to the FDA's analysis of the proposed rule, drugs with generic equivalents available represent 48 percent of these CBE-0 supplements.[25] This means that the proposed regulation would expose generic drug makers to tort liability without even facilitating the communication of new safety warnings in most cases. In short, the FDA's rule is a poor tool for keeping generic drug labels up-to-date, and it will come at a significant cost to consumers.

## Better Policy Options for Updating Generic Drug Labels

There are far more effective and efficient ways of keeping generic drug labels up-to-date and ensuring that generic firms continue to engage in an equivalent or higher level of postmarket safety surveillance. The following two policy options are preferable to the proposed regulation.

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First, the FDA could assume responsibility for reviewing and updating old drug labels. One way of going about this is through the agency's Sentinel Initiative, currently in development. Sentinel assembles a massive database of drug safety information that the FDA can use to engage in postmarket drug safety monitoring. At a time when the FDA is preaching the value of consolidated data sets like Sentinel as the optimal tool for postmarket pharmacovigilance (and the need for resources to make this program fully operational), the agency's new generic labeling regulation relies on a suboptimal approach to postmarket drug safety. The agency could instead use Sentinel as the cornerstone of a monitoring program designed to ensure that generic drug labels reflect the full complement of observable risks.

This approach would enable more uniform changes to labels, with new warnings simultaneously introduced across all generic versions of a drug. This would be far more efficient than under the proposed regulation, which is likely to result in the FDA's being deluged with CBE-0 supplements from generic firms looking to mitigate torts.

If the FDA were to assume responsibility for updating generic labels, it could fund this enterprise from the

generic drug user fee program. Fees for the postmarket program could be apportioned based on volume of sales to make sure the burdens of the new system are evenly distributed. Right now, the approach the FDA has taken with the CBE-0 process is going to disproportionately harm small generic drug firms. As we have explained, many may fold or be acquired, reducing the amount of competition in the market and inevitably leading to higher generic drug costs.

A second alternative could place label change updates in the hands of generic drug makers but would do so through prior approval supplements (PAS) rather than CBE-0 supplements. The PAS process would accomplish the same public health goals that the FDA maintains are behind its proposed CBE-0 regulation, but with two important refinements.

First, it would not create incentives for generic drug makers to issue potentially conflicting labels because the FDA must review a PAS before a label change occurs. This review would be expedited, occurring in 30 days. If the information merits the immediate attention of patients and providers, the FDA can use the same established channels it has relied on for years—public health advisories and "Dear Doctor" letters sent to health care providers. Second, because the FDA is involved in the PAS process prior to a label change, generic firms would not be exposed to the same magnitude of costly failure-to-warn litigation that they would face with CBE-0 supplements.

## Conclusion

From a patient safety perspective, allowing generic drug labels to deviate from the RLD labels could create confusion among patients and providers. It also would likely undermine the principle that most generic drugs are freely substitutable—with not only the RLD, but also different generic versions of the same drug.

On top of this, the FDA's proposed regulation could induce enormous liability costs for generic drug makers: $4 billion annually, according to Brill's estimate. Imposing the same kind of litigation costs on generic firms that brand drug firms face today will force generic drug prices higher.

For decades, generic drug makers never had the ability to unilaterally change their drug labels. The FDA seemed comfortable with, if not sympathetic to, this labeling framework. There is no evidence that new safety issues with generic drugs were not being surfaced in a reasonable fashion. There also is no evidence that generic firms have not collected safety data and made this information available to the FDA.

If the FDA believes generic labels should undergo more-regular review, it would be far more efficient and effective for the agency to assume this task itself. This is especially true since the FDA has not articulated what kind of safety information it believes is not being incorporated into generic labels. The FDA just successfully implemented a user fee for its generic drug program. Commensurate with these fees is an obligation for the FDA to use its new resources to take greater responsibility for modernizing its generic drug program.

What prompted the change in the FDA's regulatory approach was not a consideration of public health, but court rulings that firmly foreclosed generic drug product liability suits. As a consequence, the proposed rule largely misses any pertinent public health goals while creating huge, unnecessary burdens. If public health is the true imperative for this change, the FDA can address the generic labeling issues that are purportedly at the root of this regulation in far better ways.

## Notes

1. US Food and Drug Administration, "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products" (analyses), Docket no. FDA-2013-N-0500, November 2013, www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Reports/EconomicAnalyses/UCM375128.pdf.

2. US Food and Drug Administration, "Facts about Generic Drugs," September 19, 2012, www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/understandinggenericdrugs/ucm167991.htm.

3. Generic Pharmaceutical Association, *Generic Drug Savings in the US*, 5th ed., 2013, www.gphaonline.org/media/cms/2013_Savings_Study_12.19.2013_FINAL.pdf.

4. *Drug Price Competition and Patent Term Restoration Act*, Public Law 98-417 (September 24, 1984); *Federal Food, Drug, and Cosmetic Act*, Section 505(j), 21 US Code 355(j) (2010).

5. See "Supplements and Other Changes to an Approved Application," *Code of Federal Regulations*, Title 21, §§ 314.70(c)(6)(iii) (April 1, 2013); and "Changes to an Approved Application," *Code of Federal Regulations,* Title 21, 601.12(f)(2) (April 1, 2013).

6. The current regulations provide that application holders may submit CBE-0 supplements for the following types of changes

to product labeling: (1) To add or strengthen a contraindication, warning, precaution, or adverse reaction for which the evidence of a causal association satisfies the standard for inclusion in the labeling under § 201.57(c); (2) To add or strengthen a statement about drug abuse, dependence, psychological effect, or overdosage; (3) To add or strengthen an instruction about dosage and administration that is intended to increase the safe use of the drug product; (4) To delete false, misleading, or unsupported indications for use or claims for effectiveness; or (5) Any labeling change normally requiring a supplement submission and approval prior to distribution of the drug product that the FDA specifically requests be submitted under this provision.

7. US Food and Drug Administration, "Supplemental Applications Proposing Labeling Changes" (analyses).

8. Pliva is now a part of Teva Pharmaceuticals.

9. Scott Gottlieb, "Obama White House Sides with Trial Bar at Costly Expense of Generic Drugmakers," Forbes.com, December 19, 2013, www.forbes.com/sites/scottgottlieb/2013/12/19/obama-white-house-sides-with-trial-bar-at-costly-expense-of-generic-drug-makers/.

10. US Food and Drug Administration, "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products: A Proposed Rule by the Food and Drug Administration," November 13, 2013, section III, www.federalregister.gov/articles/2013/11/13/2013-26799/supplemental-applications-proposing-labeling-changes-for-approved-drugs-and-biological-products#p-112.

11. Alexander Gaffney, "As Legislators Join with Industry in Opposition, Is FDA's Generic Drug Labeling Rule Dead on Arrival?" *Regulatory Focus*, January 23, 2014, www.raps.org/focus-online/news/news-article-view/article/4532/as-legislators-join-with-industry-in-opposition-is-fdas-generic-drug-labeling-r.aspx

12. Senator Lamar Alexander et al., Letter to Margaret A. Hamburg, US Food and Drug Administration, January 22, 2014, http://energycommerce.house.gov/sites/republicans.energycommerce.house.gov/files/letters/20140122FDA.pdf.

13. US Food and Drug Administration, "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, A Proposed Rule."

14. Ibid.

15. US Government Accountability Office, *Medical Liability: Impact on Hospital and Physician Costs Extends Beyond Insurance*, Report to the Chairman, Committee on Ways and Means, House of Representatives, September 1995, 16, www.gao.gov/assets/230/221826.pdf.

16. Alex Brill, "FDA's Proposed Generic Drug Labeling Rule: An Economic Assessment," Matrix Global Advisors, February 5, 2014, www.matrixglobaladvisors.com/GenericLabelingRule.pdf.

17. US Food and Drug Administration, "Generic Competition and Drug Prices," March 1, 2010, www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm129385.htm.

18. There are exceptions—for example, products sold as branded generics. But even in these cases, if one generic drug maker had a label that contained more warnings than the same drug manufactured by a different generic firm, it would not confer any competitive disadvantage.

19. See, for example, 44 Fed. Reg. 37434, 37436 (FDA, June 26, 1979); 73 Fed. Reg. at 2848, 2851 (FDA, January 16, 2008); 71 Fed. Reg. 3922, 3935, 3927 (FDA, January 24, 2006); and US Food and Drug Administration, "Draft Guidance for Industry: Brief Summary: Disclosing Risk Information in Consumer-Directed Print Advertisements," January 2004, 2.

20. Randall Lutter (US Food and Drug Administration), "The Safety of Medical Products Regulated by FDA," statement before the House Committee on Oversight and Government Reform, May 14, 2008, www.fda.gov/NewsEvents/Testimony/ucm101513.htm.

21. See 40 Fed. Reg. 28582, 28583 (FDA, July 7, 1975). The FDA cautioned that unsubstantiated risk information in labeling "would result in such uncertainty and confusion that the usefulness of [existing] warnings in protecting the public against possible harm would be severely undermined, if not destroyed."

22. US Food and Drug Administration, Center for Devices and Radiological Health, *Guidance on Medical Device Patient Labeling; Final Guidance for Industry and FDA Reviewers*, April 2001, 42.

23. James English, "Supreme Court Blocks Generic Drug Liability Suits," *Nutrition Review*, July 10, 2013, http://nutritionreview.org/2013/07/supreme-court-blocks-generic-drug-liability-suits/.

24. US Food and Drug Administration, "Supplemental Applications Proposing Labeling Changes for Approved Drugs and Biological Products, A Proposed Rule."

25. US Food and Drug Administration, "Supplemental Applications Proposing Labeling Changes" (analyses).