EDITORIAL

Promise and Peril for Generic Drugs

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Generic drugs now make up more than 88% of all prescriptions filled in pharmacies in the United States and have provided nearly $1.7 trillion in health care savings in the past decade.[1] Yet tensions still persist between brand-name drugs and generics. Fifty years ago, pharmaceutical companies hurled the word *generic* as an insult—a reference to often unauthorized copies made by small manufacturers with questionable assurances of product utility. Yet the growth of this new industry was already under way, spurred on by waves of patent expirations, Congressional inquiries, and increasing interests of purchasers in less expensive versions of essential medications.[2(pp1-136)]

Editor's Note

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A critical inflection point in the growth curve of the generic drug industry came with the development of bioequivalence standards by the US Food and Drug Administration (FDA). These standards required not only that the generic formulation contain the active ingredient but also that this ingredient be as available to the human body as the reference drug. In 1984, the Hatch-Waxman Act included bioequivalence as part of a unified pathway for generic drug approval and set the foundation for the modern generic industry.

Since the passage of the Hatch-Waxman Act, generic medications have assumed a central role in the delivery of high-quality, low-cost health care. Laws that once prohibited generic substitution have been reversed and now permit or mandate substitution at the pharmacy for generic alternatives to brands. Millions of consumers rely on generics to be able to afford essential medical treatments. And a robust series of studies have countered lingering myths about the safety and effectiveness of generic drugs.[3,4]

Yet the path from a new law to a new industry has hardly been smooth. In the late 1980s, a generic drug scandal at the FDA involving bribery and favoritism led to years of Congressional inquiry into FDA oversight, prison terms for FDA officials, and the resignation of the FDA Commissioner. While domestic regulation of the generic industry has stabilized, the global expansion of the pharmaceutical industry has led to increased concerns about the quality of drugs manufactured overseas.[5] In recent years, the major generic manufacturer Ranbaxy has been found to have substandard quality control mechanisms for a broad range of products,[6] and the FDA's leadership has recently written about "challenges associated with the quality of generic drugs coming out of some facilities in India."[7] Nonetheless, the abundance of evidence signals that such stories are the exception and not the rule in the highly regulated generic marketplace.

Slowly but surely, the perception of generic drugs may be coming closer to reality. This issue of *JAMA Internal Medicine* includes a Research Letter by Kesselheim and colleagues[8] finding that from 2009 to 2015, the percentage of physicians who believe that generics may be less effective than brand-name drugs has decreased by half, to roughly 1 in 10. Also in this issue, Patel et al[9] found that a simple modification to an electronic health record, which required an active check to dispense as written, increased the rate of generic prescribing to more than 95%.

Yet the studies in this issue also show how the battle between generics and brand-name drugs continues in different forms. Over time, brand-name firms have developed a number of strategies for perpetuating brand-based monopolies after their initial patent-based monopolies expire. The most direct strategy is using marketing contacts to undermine confidence in generic equivalence. Kesselheim and colleagues report that those physicians whose most recent source of information about generic alternatives was a pharmaceutical representative are most likely to have doubts about their safety and effectiveness.[8] Yeh and colleagues[10] find an association between receipt of payments from pharmaceutical companies, particularly educational payments, and the largely unnecessary prescribing of brand-name statin drugs. This finding is particularly notable because several aspects of this study, including the fact that payments could not be tied to particular drugs, would tend to obscure an association.

Johansen and Richardson[11] assess the effect of a different brand-name strategy: releasing new, patent-protected "me-too" drugs as the original drug goes off patent. Many physicians prescribe these medications at great cost to the patient and health care system even when there is little to no difference from generic alternatives. Johansen and Richardson measure the net increase in health care costs of me-too drugs in hundreds of billions of dollars each year.

This new evidence of the continuing conflict between brand-name and generic drugs has several immediate policy implications. First, payers and clinical organizations interested in improving the value of health care should take additional steps to improve physician and patient understanding of generic drugs. This requires more than merely limiting opportunities for inaccurate and misleading communications on generic substitution from pharmaceutical representatives, as some academic centers have already begun to do. Rather, the articles in this issue underscore the importance of affirmatively teaching clinicians and patients about the history and structure of the generic industry, the meaning of bioequivalence standards, and the current availability of generic drugs. Physicians and other prescribers should understand,

for example, that patients are more likely to take a generic medication that they can afford compared with a me-too medication that offers no additional benefit.

Second, the FDA and the generic drug industry should recognize the continued importance of high standards of bioequivalence and good manufacturing practice. The recently passed Generic Drug User Fee Act substantially expands the resources available to the agency. The main purpose of the boost is to allow the agency to make progress on a backlog that exceeds several thousand pending applications and that has frustrated both Congress and industry. These resources should also help to accelerate review of priority drugs for generic approval, such as those linked to the threat of shortages. Over time, the FDA should invest in developing new methodologies in the fields of pharmacoepidemiology and biopharmaceutics to further address concerns of therapeutic equivalence. For its part, the generic industry should commit to keeping up with quality improvements and must see investing in modernizing facilities as an insurance policy against a loss of faith in their products.

Third, the recent visibility of sudden and dramatic price hikes for old medications may pose more of a threat to the generic industry than initially appreciated. From a policy perspective, the low price of generics is the industry's raison d'être; this enormous value basis helped move the industry from the fringes of the medical world to the center of care. Threatening this position are examples of companies colluding with brand manufacturers as part of "pay for delay" schemes[12]; opaque pricing that may undermine the value of generics for consumers[13]; and, most recently, the emergence of a business model predicated on extraordinary price increases for generic drugs that have only 1 manufacturer.[14] Such behavior by a handful of companies may play into old stereotypes of companies with substandard products seeking a quick return and has already led some to call for lowering the standards for generic drugs or a broad expansion of pharmaceutical compounding in order to bring competition back more readily. Such moves could damage the credibility of the entire industry.

The studies in this issue show great progress—but also great risks—for the generic drug industry in the United States. The industry must rise to these challenges to maintain its critical role for the health care system, for our economy, and most importantly, for our patients.

ARTICLE INFORMATION

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