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Essay review

Generic, yet not generic

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Generic: The Unbranding of Modern Medicine, Jeremy A. Greene. Johns Hopkins University Press, Baltimore (2014). 368 pp., Price USA$29.95 hardback, ISBN: 9781421414935

In my work on the history of antibiotics and attempts to inculcate a rational therapeutics from the 1950s–1970s, I've spent a great deal of time reading through the key sources of pharmaceutical regulatory discourse of this era—Estes Kefauver's initial hearings on the pharmaceutical industry (1959–1962), Gaylord Nelson's subsequent hearings on the industry (1967–1976), and the pharmaceutical industry's weekly "Pink Sheet" (*F-D-C Reports*) to name but a few. These were decades characterized by an outpouring of patented, branded, and heavily marketed wonder drugs from an expanding American pharmaceutical industry. Running through all of these records, though, one finds a counterpoint concerning the role of explicitly *unbranded* drugs—generics—as a means of offsetting the hazards of the market, ensuring lower drug costs, and promoting the rational standardization of drug usage.

The generic drug industry, which emerged during these crucial decades, has been glorified as the antidote to exorbitant drug prices, and vilified as the purveyor of poisonous (or at least less effective) counterfeit drugs.[1] Yet in *Generic*, Jeremy Greene has a far more nuanced, and far more interesting, tale to tell. Eschewing easy categories of heroes and villains—or even, as we'll see, Davids and Goliaths—Greene sees generic drugs and the generic drug industry simultaneously as a site of political and economic contestation over the production and distribution of pharmaceuticals, as a window into the aspirations to a rational therapeutics, and most critically, as a handle by which to examine the larger science of similarity, ultimately framing the question: "When are two objects the same … or at least similar enough in ways that we find meaningful?" Along these lines, while Greene's vitally important book focuses on the United States—the birthplace of the generic drug industry—it not only extends its analysis to the rise of the global generic, but explicitly asks us to consider how much the tensions concerning times and places examined in the book are the same as those we face today … or at least similar enough in ways that we should find relevant. The answer is, very much.

1. A private market solution to a public health concern

While unbranded drugs have been present for centuries, the origins and history of the generic drug *industry* in the United States has been tied directly to the history of the ethical drug industry itself and its branded wonder drugs, in historically situated fashion. The advent of the generic drug industry was not inevitable. And while it has often served the key public health role of affording access to efficacious drugs, it largely remains in the United States a private, market-driven solution, at times ignoring the very public health needs that many hoped it would serve.

For the most part, as Greene depicts, there was no generic drug industry in the first decades of the 20th century. There were often multiple pharmaceutical producers rendering the same, unpatented, drug, with the trademark of each firm standing in for the quality of its particular line of such drugs.[2] But the appearance of a generic drug industry and its "unbranded" drugs served as a counterpart to the rise of the branded drug itself.[3] The post-World War II wonder-drug era saw the advent of entire classes of pharmaceuticals—antibiotics, anti-psychotics, minor tranquilizers, anti-hypertensives, steroids—and parallel revolutions not only in pharmaceutical research, but in pharmaceutical marketing and branding as well. Two converging forces, however, led to the origins of a formal generic drug industry by the 1960s. First, the 17-year patents of the initial wave of wonder drugs was running out, creating a unique market opportunity. Second, by 1959, Senator Estes Kefauver (D-TN) had orchestrated his landmark investigations and hearings into the monopolistic structure and marketing

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[1] Eban (2009), Generic Pharmaceutical Association (2014).

[2] Gabriel (2014).

[3] Greene (2014a, pp. 53–89).

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practices of the pharmaceutical industry. While Kefauver's own desire that drugs be referred to by generic name alone (as a means of offsetting such marketing) would be stricken from the ultimate 1962 Kefauver–Harris amendments—most remembered for their mandate that drugs be proven efficacious via "adequate and well-controlled investigations"—the attention he focused on generic names provided the de facto public relations required for a nascent generic drug industry.

As Greene further relates, the generic drug industry received its next boost from the Drug Efficacy Study and Implementation (DESI) process, itself initiated in the late 1960s in the wake of the Kefauver–Harris amendments as a means of reviewing pre-1962 drugs and enabling the FDA to efficiently withdraw from the market seemingly inefficacious products.[4] By implication, generic equivalents of the remaining efficacious drugs—coming off patent on a regular basis—would themselves be considered effective, so long as they could be deemed equivalent to their branded counterparts. The Hatch–Waxman Act of 1984 formally abbreviated the process by which generic drug producers could demonstrate such equivalence and hence efficacy, rather than mandating entirely new studies via clinical trials, in return for permitting extended patent time for novel drugs. In other words, as Greene cleverly summarizes, new drugs (generics) could be rendered old, and thus, equivalent to their branded counterparts, while old drugs could be kept young. The Hatch–Waxman act could thus be seen as an "inflection point in [the generic drug industry's] growth curve," rather than as the genesis of the generic drug industry itself.[5]

But such an account of the production of generic drugs, Greene continues, only tells us part of the story. The circulation and use of such drugs was shaped by an evolving cast of characters and professions—the brand-name pharmaceutical industry, the pharmacy and medical professions, congress, and academicians mobilized to both sides of the debate.[6] Unsurprisingly, the brand-name pharmaceutical industry fiercely contested the advent of generic drugs at first. Claiming that brands were not marketing fluff, but rather, markers of quality, they formed the National Pharmaceutical Council (NPC) and through this body led to the passage of formal "non-substitution" laws—due to which, pharmacists could not fill generic drugs or other brands in place of drugs prescribed by name—across the U.S. by the early 1970s. But by this time, in the wake of the passage of Medicaid and Medicare and rising drug costs, proponents of generic drugs had brought in new allies, such as the American Association of Retired Persons (AARP), which led to the repeal of non-substitution laws across the country, effectively completing the process by 1984. Nevertheless, the specifics of such permitted substitution—e.g., whether framed around positive formularies (enumerating which drugs *could* be substituted) or negative formularies (enumerating which ones *could not* be substituted)—varied from state to state, leading to a decentralized "patchwork" of practices across the country.[7]

In tandem, generic drugs became a contested site over the power relations between prescribing physicians and centralized oversight from the one end, and between physicians and patients from the other.[8] Regarding centralized oversight, as Dominique Tobbell has elsewhere described,[9] the years following the passage of Medicare and the onset of DESI saw resistance from private practitioners to "ivory tower" suggestions and efforts to delimit therapeutic autonomy. Accusations of "irrational" antibiotic prescribing and attempts to impose guidelines or mandated in-hospital antibiotic consultation services became one rallying point in this resistance.[10] But generic drugs serving as a rallying point as well, with the defense of physician autonomy mobilized against the seeming encroachment of clinical pharmacists or those mandating generic substitution.

The role of generic drugs in the evolving patient–doctor relationship throughout the 1960s and 1970s requires the nuanced depiction provided by Greene of the rise of consumerism itself in medicine during this era. Complementing the work of Nancy Tomes,[11] Greene argues that the advent of generic drugs played a key role in the very transformation of the patient into a "consumer," as patients found available to them guidebooks on generic drugs that they could tote alongside guides to low-cost groceries or appliances. At the same time, while generic drugs could erode the physician's autonomy—whether having generic drugs forced upon them from above, or suggested to them by patients—they could likewise seemingly create a space for the physician to play the role of über-consumer, choosing particular brands or unbranded drugs for his or her patient. However, this last role would be countered in two key respects. First, while the physician may have feared centralized delimitations of therapeutic autonomy through mandated generics, it was demonstrated that his own therapeutic decision-making was often at the mercy of pharmaceutical marketing.[12] Second, as Paul Starr has related with respect to health insurance more generally, while physicians feared imposition on their prescribing autonomy from the government, decision-making regarding which drugs—generic, or even in-class substitution of me-too drugs—would be permitted increasingly came under the control of health maintenance organizations, or, in recent years, Pharmacy Benefit Managers (PBM's), beholden to the logic of the market rather than solely to the health needs of the public itself.[13]

This focus on the market brings us to a key point with respect to the role of generic drugs in the United States, rendered all the more salient by findings unearthed since the publication of Greene's book, though addressed by him elsewhere. The prescribing of generic drugs in the United States has increased from less than 20% of all prescriptions filled in 1984 to more than 80% today.[14] It has led globally, in key instances (for example, antiretrovirals for HIV), to dramatic reductions in drug prices and hence access to effective care. Yet as Greene reveals, initial notions of a legion of generic drug Davids versus brand name Goliaths has been entirely subverted, if not inverted. Brand-name pharmaceutical companies have created both "branded" and unbranded generic drug divisions, while such global generic producers as Ranbaxy and Teva have grown into some of the largest pharmaceutical corporations in the world. The issue, then, is that the logic of the market continues to dictate the accessibility and affordability of generic drugs, especially in the United States.[15] For example, if there is only a single provider of a particular generic drug, then there is little to prevent dramatic price escalations. Aaron Kesselheim and his colleagues have recently traced the increases in pricing for particular generic drugs (fifty-fold, in the case of doxycycline) in response to such market logics.[16] What was conceived as a "rational" approach to ensuring drug access has

[4] Greene (2014a, pp. 64–67, 83–89); see also Carpenter & Tobbell (2011).
[5] Greene (2014a, p. 88).
[6] Greene (2014a, pp. 131–170).
[7] Greene (2014a, pp. 147–150).
[8] Greene (2014a, pp. 173–208).
[9] Tobbell (2012, 2013).
[10] Podolsky (2012, 2015, pp. 112–139).
[11] Tomes (2001).
[12] Greene (2014a, pp. 184–186).
[13] Greene (2014a, pp. 231–242).
[14] Aitken & Kleinrock (2013), Berndt & Aitken (2011).
[15] Greene (2014a, pp. 253–260).
[16] Alpern, Stauffer, & Kesselheim (2014).