AMA Journal of Ethics®

August 2019, Volume 21, Number 8: E661-667

POLICY FORUM: PEER-REVIEWED ARTICLE

Should a Law Governing the Pharmaceutical Market Be Ethically Examined Based on Its Intent or Its Practical Applications?

Jordan M. Warchol, MD, MPH

To claim one AMA PRA Category 1 Credit™ *for the CME activity associated with this article, you must do the following: (1) read this article in its entirety, (2) answer at least 80 percent of the quiz questions correctly, and (3) complete an evaluation. The quiz, evaluation, and form for claiming* AMA PRA Category 1 Credit™ *are available through the* AMA Ed Hub™.

Abstract

Prescription drug prices are a top health care concern among US consumers. Although this issue is at the forefront of current policy discussions, it is not new. In 1984, the Drug Pricing Competition and Patent Term Restoration Act (colloquially, the Hatch-Waxman Act) addressed drug pricing concerns. This article argues that Hatch-Waxman properly applies utilitarian principles to complex issues of biopharmaceutical development by balancing innovation and availability. However, the statute's efficacy has been marred by so-called pay-for-delay arrangements, which disrupted that carefully constructed equilibrium. This article also argues that the 2013 US Supreme Court holding in *Federal Trade Commission v Actavis, Inc* appropriately restored the utilitarian balance initially achieved by Hatch-Waxman.

Ethical Implications of Pharmaceutical Policy Design and Application

Prescription medication cost is a top health care priority for nearly two-thirds of Americans.[1] For example, insulin prices continue to increase,[2] making it difficult for patients to comply with medication regimens, which in turn can lead to disease complications and increased costs.[3] In response to constituents' concerns, Congressional leaders have attempted to find solutions to the problem.[4]

Thirty-five years ago, the Drug Price Competition and Patent Term Restoration Act of 1984,[5] known as the Hatch-Waxman Act, was created to increase the number of available generic medications and decrease prices through competition. Under Hatch-Waxman, brand-name manufacturers' profits are protected for a period of time when no competitors of the drug will be approved by the US Food and Drug Administration (FDA). This exclusivity period is in addition to the term of any patents on the drug but runs concurrently. Generic manufacturers also benefit from the law due to its establishment

of an alternate pathway for generics to come to market. Instead of undertaking large, expensive clinical trials to prove safety and efficacy, a generic manufacturer must show only that the generic medication achieves bioequivalence.[6] Generic manufacturers also have a process by which they can challenge the patent protections on a brand-name medication, potentially bringing their product to market earlier than would otherwise be allowed.[5]

Since Hatch Waxman's adoption, significant growth in the generic market has occurred; 89% of prescriptions written in the United States are currently filled with off-brand drugs.[7] Brand-name manufacturers have continued to develop innovative medications for a multitude of illnesses, including terminal genetic conditions[8] and refractory cancers.[9] The concurrent expansion of these competing industries underscores the balance struck by Hatch-Waxman between the need for pharmaceutical advances and the need to make those advances widely accessible.

This article will first examine the ethics of the law's design through the prism of utilitarianism. It will then turn to pay-for-delay settlements, wherein a brand-name company pays a generic company to keep the generic medication off the market, which challenge the ethical intent of Hatch-Waxman by circumventing the utilitarian principles underlying the law. An analysis of the US Supreme Court decision in *Federal Trade Commission v Actavis, Inc* will further examine such settlements.

Background of the Hatch-Waxman Act

When a brand-name manufacturer wants to bring a new drug to market, it must submit a new drug application, which is reviewed by the FDA before approval for sale.[10] It is estimated that the process of bringing a drug to market costs hundreds of millions to billions of dollars.[11,12] The capital used to fund this research and development is recouped through market exclusivity, a purposeful monopoly designed as an enticement to brand-name manufacturers to undertake the risky drug development process.[13]

Following a pioneer drug's period of exclusivity, generic drug makers can file an abbreviated new drug application (ANDA), which has less stringent thresholds for drug approval.[5] In filing the ANDA, generic companies can attempt to enter the market before the expiration of the brand-name company's patent term(s) by certifying that their product does not infringe upon any patents held by the brand-name manufacturer or that any patent infringed upon is invalid; this is known as a Paragraph IV certification.[5] Although the generic is certifying that it has not violated any of the brand-name company's patents, the statutory language of Hatch-Waxman deems a Paragraph IV certification an act of patent infringement in itself, allowing the brand-name company to bring legal action against the generic company. Historically, Paragraph IV disputes that have proceeded to judicial decision have generally been found in the generic manufacturer's favor.[14]

Utilitarian Principles Underlying Hatch-Waxman

Utilitarianism, according to J. S. Mill, follows the "Greatest Happiness Principle, [which] holds that actions are right in proportion as they tend to promote happiness, wrong as they tend to produce the reverse of happiness."[15] On contemplating the utility of a choice, it is not merely the happiness of the decider that must be considered but the happiness of all who will be affected by the decision; the ethical choice is that which maximizes this happiness. Some modern utilitarian thinkers have argued that it is not only happiness but also well-being that must be maximized.[15] In any case, utilitarianism relies wholly on the ethical tenet of utility to decide the morality of a choice.[16]

Hatch-Waxman exemplifies the application of utilitarianism by a government that is representative of the myriad entities it serves because it seeks to optimize positive outcomes for all involved stakeholders. This goal is accomplished through consideration of the many complexities of the biopharmaceutical industry and its impact: the for-profit nature of pharmaceutical companies that contribute to economic growth; society's desire for continued advances in the field of medicine; the cost of medications and the societal consequences of those costs, including medication nonadherence and its own costs; and the societal and economic contributions of patients whose conditions are improved by such medications. The ripple effects of the pharmaceutical industry are wide and various. Accordingly, Hatch-Waxman aims to balance stakeholders' various interests.

Some might contend that the application of utilitarian principles by government is inappropriate. One charge is that utilitarianism is based on subjective preferences, allowing otherwise immoral ideas to be considered as benefits based on an individual's satisfaction.[16] Others critical of the legislation could point to the apparent injustice of utilitarian theory, which can promote the majority's interests over those of the minority.[15] According to Beauchamp and Childress, "injustice involves a wrongful act or omission that denies people resources or protections to which they have a right."[16] Under utilitarianism, any act would be classified as "wrongful" that does not promote the highest utility, and utility must be considered relative to all entities to which the policy applies. Under Hatch-Waxman, utility is maximized through careful balancing of the competing interests of multiple stakeholders without depriving others of their rights. The questions of injustice and what is "wrongful" become more complex in examining the current environment of Hatch-Waxman.

Emerging Legal Challenges

Since it was enacted, Hatch-Waxman has been tarnished by legal maneuvers that comply with the letter of the law but undermine its intent. One such tactic, known as pay for delay, occurs when a reverse settlement is reached between brand-name and generic manufacturers regarding Paragraph IV litigation. This arrangement is unique because of the terms of the settlement agreement. Whereas a typical patent dispute settlement results in the infringer paying the infringed, in a pay-for-delay settlement,

the infringed brand-name company pays the infringing generic company. In exchange, the generic company agrees not to bring to market its product until a later time. These agreements typically occur during Paragraph IV litigations, after the generic manufacturer has been sued for patent infringement by the brand-name manufacturer as a way for the brand-name manufacturer to avoid judicial opinions. The Federal Trade Commission (FTC) has declared such pay-for-delay arrangements violations of antitrust laws.[17]

The antitrust infringement question posed by pay-for-delay arrangements was addressed by the US Supreme Court in *Federal Trade Commission v Actavis, Inc*, in which a pay-for-delay settlement between Actavis and Solvay Pharmaceuticals was at issue.[18] The agreement stipulated that Actavis would delay its generic's entry into the market for 9 years and serve as a marketing arm for the brand-name drug. In return, Solvay would pay Actavis a substantial sum of money,[18] presumably much larger than the value of the marketing provided by Actavis. This agreement was upheld by the Eleventh Circuit Court of Appeals, which ruled that the anticompetitive effects of the pay-for-delay settlement were within the exclusionary potential of the patent that was under Paragraph IV challenge and that therefore the settlement did not violate antitrust laws.[18]

The Supreme Court reversed the lower court's ruling against the FTC, holding that reverse payment settlements could sometimes violate antitrust laws, depending on the conditions of the settlement. Consequently, any pay-for-delay settlement must be evaluated according to 5 conditions: the effects on competition; the justified or unjustified nature of the consequences of the agreement; the strength of the brand-name company's incentive to keep a generic out of the market; the perceived strength of the original patent that the generic company was contesting; and the rationale of the settlement.[18]

Actavis underscores the role of utilitarianism in government. In *Actavis*, the Supreme Court held that the collective ratio of benefit to harm was not maximized by the settlement.[18] Specifically, in *Actavis*, the court applied *act utilitarian* principles, wherein utility must be examined independently for each case under the specific set of circumstances that define it.[17]

One of the major criticisms of act utilitarianism is that case-by-case determinations of utility can result in the waiving of rules that would otherwise uphold the moral standard,[17] which could result in scenarios wherein an otherwise immoral act would be seen to result in the most utility. However, in the evaluation of pay-for-delay settlements under Hatch-Waxman, the application of act utilitarian standards to an antitrust question is arguably the best answer. US antitrust statutes are intended to protect citizens from competitive monopolies and collective harm.[19] If the particulars of a settlement agreement are not examined, it cannot be determined if it would result in harm. A blanket application of antitrust law, such as would be applied under *rule*

utilitarian principles, could have grave consequences. Take, for example, a case similar to that of *Actavis*: a brand-name manufacturer pays a generic manufacturer a sum of money, and, in exchange, the generic manufacturer takes over the marketing of the brand-name drug and agrees to delay the generic's entry into the market. Further imagine that, unlike in *Actavis*, the brand-name company no longer has the resources to adequately market the drug, which is why the marketing is being outsourced. Without the agreement, the brand-name company would no longer market the drug, which could decrease its use and decrease societal benefit. While not typical of pay-for-delay arrangements, this agreement—if it was not evaluated independently and was determined to be in breach of antitrust law simply because it was a reverse payment—could result in greater harm from inadequate marketing than from keeping the generic out of the market.

Furthermore, application of act utilitarian principles to pay-for-delay settlements entails acceptance of flexibility as societal norms change. Generally, if a court rules on a matter, that ruling must be applied to a similar legal question under that court's jurisdiction unless another case with the same question is brought forward.[20,21] Through its opinion in *Actavis*, which required that a set of conditions be applied to a pay-for-delay settlement, the Supreme Court built in a mechanism for future rulings on similar cases to take into consideration the natural changing of cultural perceptions of benefits and harms. The calculation of utility must be responsive to the ebb and flow of social norms.

Conclusion

When writing or interpreting policy, agents of government must maximize utility for all stakeholders both at the current moment and into the future. Legislation such as Hatch-Waxman, which balances the various needs of involved parties, is necessary to achieve this mission. Equally important is the role of the judiciary branch in preserving the equilibrium between innovation and competition as new, potentially destabilizing legal challenges emerge. While concerns over drug pricing continue to swirl, policymakers must consider the delicate balance between innovation and competition. Whatever solutions might be proposed, the greatest good for the greatest number must be paramount.

References

1. Kirzinger A, Munaña C, Wu B, Brodie M. Data note: Americans' challenges with health care costs. Henry J. Kaiser Family Foundation. https://www.kff.org/health-costs/poll-finding/data-note-americans-challenges-with-health-care-costs/. Published June 11, 2019. Accessed December 14, 2017.
2. Johnson CY. Why treating diabetes keeps getting more expensive. *Washington Post*. October 31, 2016. https://www.washingtonpost.com/news/wonk/wp/2016/10/31/why-insulin-prices-have-kept-rising-for-95-years/?utm_term=.4b69308bec18. Accessed December 15, 2017.

3. Iuga AO, McGuire MJ. Adherence and health care costs. *Risk Manag Healthc Policy*. 2014;7:35-44.
4. Edney A. A bipartisan approach on drug prices is emerging. *Bloomberg*. December 14, 2017. https://www.bloomberg.com/news/articles/2017-12-14/bipartisan-approach-on-drug-prices-emerging-after-health-fights. Accessed December 15, 2017.
5. Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of 1984, Pub L No. 98-417, 98 Stat 1585.
6. Kesselheim AS, Darrow JJ. Hatch-Waxman turns 30: do we need a re-designed approach for the modern era? *Yale J Health Policy Law Ethics*. 2015;15(2):293-347.
7. Association for Accessible Medicines. Generic drug access & savings in the US. Washington, DC: Association for Accessible Medications; 2017. https://accessiblemeds.org/sites/default/files/2017-07/2017-AAM-Access-Savings-Report-2017-web2.pdf. Accessed November 30, 2018.
8. Finkel RS, Mercuri E, Darras BT, et al; ENDEAR Study Group. Nusinersen versus sham control in infantile-onset spinal muscular atrophy. *N Engl J Med*. 2017;377(18):1723-1732.
9. FDA approval brings first gene therapy to the United States [press release]. Washington, DC: US Food and Drug Administration; August 30, 2017. https://www.fda.gov/news-events/press-announcements/fda-approval-brings-first-gene-therapy-united-states. Accessed July 17, 2017.
10. US Food and Drug Administration. New drug application (NDA). https://www.fda.gov/drugs/types-applications/new-drug-application-nda. Published March 29, 2016. Accessed May 17, 2019.
11. Prasad V, Mailankody S. Research and development spending to bring a single cancer drug to market and revenues after approval. *JAMA Intern Med*. 2017;177(11):1569-1575.
12. Mullin R. Cost to develop new pharmaceutical drug now exceeds $2.5B. *Scientific American*. November 24, 2014. https://www.scientificamerican.com/article/cost-to-develop-new-pharmaceutical-drug-now-exceeds-2-5b/. Accessed December 15, 2017.
13. Winegarden W. The economics of pharmaceutical pricing. San Francisco, CA: Pacific Research Institute; June 2014.
14. Pensabene LB, Butler L. Supreme Court to decide legality of reverse-payment settlements in Paragraph IV disputes. *Financier*. March 2013. https://www.financierworldwide.com/supreme-court-to-decide-legality-of-reverse-payment-settlements-in-paragraph-iv-disputes#.XQFe-xZKgdU. Accessed June 12, 2019.
15. Mill JS. *Utilitarianism*. Kitchener, ON: Batoche Books; 2001.
16. Beauchamp TL, Childress JF. *Principles of Biomedical Ethics*. 7th ed. New York, NY: Oxford University Press; 2012.
17. Federal Trade Commission. Pay-for-delay: how drug company pay-offs cost consumers billions.

https://www.ftc.gov/sites/default/files/documents/reports/pay-delay-how-drug-company-pay-offs-cost-consumers-billions-federal-trade-commission-staff-study/100112payfordelayrpt.pdf. Published January 2010. Accessed November 30, 2018.
18. *FTC v Actavis, Inc*, 570 US ___; 133 SCt 2223 (2013).
19. Hemphill SC. Paying for delay: pharmaceutical patent settlement as a regulatory design problem. *N Y Univ Law Rev*. 2006;(81):1553-1623.
20. *Plessy v Ferguson*, 163 US 537 (1896).
21. *Brown v Board of Education of Topeka*, 347 US 483 (1954).

Jordan M. Warchol, MD, MPH is an assistant professor in the Department of Emergency Medicine at the University of Nebraska Medical Center in Omaha. She attained a BS in biochemistry from Creighton University and an MD from the University of Nebraska Medical Center, after which she earned an MPH in health policy from George Washington University. Her academic interests include federal drug policy and physician understanding of and involvement in health policy.

Citation
AMA J Ethics. 2019;21(8):E661-667.

DOI
10.1001/amajethics.2019.661.

Acknowledgements
The author would like to thank Melissa M. Goldstein, JD for her encouragement and editorial prowess.

Conflict of Interest Disclosure
Dr Warchol previously worked as a health policy fellow in the office of Sen Orrin Hatch.

The viewpoints expressed in this article are those of the author(s) and do not necessarily reflect the views and policies of the AMA.

Copyright 2019 American Medical Association. All rights reserved.
ISSN 2376-6980