**Testimony for the Record**
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## Making Old Drugs New Again—And Newly Unaffordable

Chairman Middleton, members of the Senate Finance Committee, thank you for the opportunity to submit testimony on this timely and important subject. The affordability of lifesaving medicines has been a subject of central concern in my own career, both as a historian of the pharmaceutical industry[1] [2] [3] and a primary care physician in a busy urban community health center in East Baltimore.[4] [5] I should add that my testimony today reflects my experience as a physician, a historian, and a health policy researcher, and does necessarily not reflect the views of Johns Hopkins University.

Until recently, most national debate over the high prices of prescription drugs has centered on the price of newer, on-patent medications, with the assumption that the prices of older, off-patent medications become negligible once they are subject to generic competition. Much of present-day American pharmaceutical policy takes it as a given that the historical relationship between on-patent brand name and off-patent generic drugs serves to balance pharmaceutical innovation and pharmaceutical access. The story goes something like this: in the first (patent-protected) phase of its life, a new drug is given a patent-monopoly to reimburse its developers for the substantial costs of pharmaceutical innovation. In the second (off-patent) phase of its life, competition brings prices down so that a supply of effective but affordable medications are widely available. So far so good. But increasingly we are finding that drugs enter a third,

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[1] Jeremy A. Greene, *Generic: The Unbranding of Modern Medicine*. Baltimore: Johns Hopkins University Press, 2014.
[2] Jeremy A. Greene, "Drug bust: For 30 years, generic medications helped make health care cheaper. Why is their cost surging?" *Slate*. Nov 20, 2014.
http://www.slate.com/articles/business/moneybox/2014/11/generic_drug_prices_why_their_prices_are_suddenly_surging.html
[3] Jeremy A. Greene, "When old drugs are made new again," *Forbes.* April 23,2015.
http://www.forbes.com/sites/matthewherper/2015/04/23/when-old-drugs-are-made-new-again/
[4] Jeremy A. Greene and Kevin Riggs, "Why is there no generic insulin? Historical origins of a modern problem," *New England Journal of Medicine* 2015; 372:1171-5
[5] Jeremy A. Greene, "Cornering the market on essential drugs" *Slate* September 23, 2015.
http://www.slate.com/articles/health_and_science/medical_examiner/2015/09/generic_drug_price_gouging_how_shkreli_and_other_monopolists_cornered_the.html

uncharted phase, where dwindling competition creates new monopolies and the accelerated series of drug shortages and price hikes now affecting millions of Americans.

**Cornering the market on essential drugs**

I'd like to begin with a case from my own urgent care clinic. Not that long ago I treated a patient for a case of pinworm, a parasitic infestation that affects roughly 400 million people worldwide, with 40 million of those cases occurring within the United States.[6] Though pinworms can be found in middle class suburbs, the parasite is no stranger in settings of urban poverty, including the low-rise public housing complexes across the street from my East Baltimore clinic, where far too many people struggle to survive on less than $2 a day.[7]

The diagnosis itself was relatively easy to make, and though my patient had no health insurance, I sent her to the pharmacy confident that the right drug for her disease, albendazole, should only cost a few dollars to fill. After all, the drug had been introduced in 1971, and by the 1980s its cost was so low and its use so broadly-validated that it was added to the Essential Drugs List of the World Health Organization. When she returned an hour later saying that she could not afford the medication, I pressed for more detail. Sometimes even a few dollars can be too much for patients scraping to make rent or buy food for their families, and our staff has a limited ability to offer hospital-sponsored vouchers to help cover drug costs in times of need. Yet I was not prepared for the figure she showed me: the 2 pills of albendazole I had prescribed would cost her an untenable $330. As I soon discovered, the U.S. market for the once-generic drug albendazole had been cornered by a small pharmaceutical company called Amedra and retrofitted into a newly exclusive brand, Albenza, at more than $150 a pill. The rights to sell the only other drug in its therapeutic class—mebendazole—had also been purchased by Amedra as Teva (the world's largest generic drug manufacturer) had ceased distributing the drug to American markets. Medicaid spending on albendazole increased from less than $100,000 per year in 2008 to more than $7.5 million in 2013.[8] But for people without insurance, like my patient, the medication simply became unavailable.

The revelation in 2015 that another small pharmaceutical company, Turing Pharmaceuticals, acquired the sole U.S. distribution rights to another antiparasitic drug on the WHO Essential Drugs List and boosted its price by 5,000 percent,[9] suggests that the price hike on albendazole was no fluke. It may interest this Committee to know that pyrimethamine had also been sold exclusively by Amedra, before the company was bought by another generic firm, Impax, which

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[6] Centers for Disease Control and Prevention, "DPDx: Laboratory identification of parasitic diseases of public health concern: Enterobiasis" http://www.cdc.gov/dpdx/enterobiasis/

[7] Gabriel Thompson, "Could you survive on $2 a day?" *Mother Jones* December 13, 2012. http://www.motherjones.com/politics/2012/12/extreme-poverty-unemployment-recession-economy-fresno

[8] Jonathan D. Alpern, William M. Stauffer, Aaron S. Kesselheim, "High-cost generic drugs: Implications for patients and policymakers" *New England Journal of Medicine* 2014; 371:1859-62.

[9] Andrew Pollack, "Drug goes from $13.50 a tablet to $750, overnight" *The New York Times* September 20, 2015. http://www.nytimes.com/2015/09/21/business/a-huge-overnight-increase-in-a-drugs-price-raises-protests.html

sold the rights to sell the drug to Turing.[10] In a report released last December the U.S. Senate Special Committee on Aging compared Turing's price to those of three other companies: Retrophin (another company founded by Turing's CEO, Martin Shkreli), Rodelis (which, dramatically hiked prices on another old essential drug for multiple drug resistant tuberculosis but then reversed itself in the face of public criticism), and Valeant, a company which has been systematically purchasing old drugs without competitors and then dramatically increasing their prices to make them competitive with on-patent drug prices. As J. Michael Pearson, then CEO of Valeant, was quoted in the *New York Times* the lower prices of older drugs can now be considered *mispricings* if there is a monopoly situation: if "products are sort of mispriced and there's an opportunity," he noted, "we will act appropriately" by raising prices to a level more commensurate with newer drugs.[11]

Valeant withered under the spotlight,[12] but Turing received far more attention in popular media, especially after its brash and unapologetic CEO, Martin Shkreli, confidently asserted in a CNBC interview that the new price of the drug should simply be born on the backs of existing patients, and calling one journalist a "moron" for contesting the ability of the new drugmaker to set whatever price he wanted to.[13] And yet there have been real consequences in the lives of people with cerebral toxoplasmosis—for decades a manageable condition with an old drug nobody stopped to think could become inaccessibly expensive. Shortly after Turing's price-hike, a team of my colleagues at Johns Hopkins admitted a patient who had been stable on pyrimethamine for years who lost the ability to speak after the dormant parasite in her brain reawoke after Turing increased prices on the drug and eliminated distribution to other outpatient pharmacies. Even once hospitalized, she suffered further adverse effects after Turing (which restricted outpatient access to the drug through a single distributor) did not adequately respond to urgent requests to restock the drug when the hospital was running low on its supply. In the four and a half days it took for Turing to respond and even allow purchase of the drug at its grossly inflated price this patient suffered a further downturn in her clinical status.

Martin Shkreli has become portrayed as a new sort of villain in the passion play of the pharmaceutical industry. He did not fit the well-rehearsed role of the CEO of a major PhRMA or BIO firm, struggling to justify high prices for blockbuster drugs on the basis of the high cost of

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[10] Impax Pharmaceuticals, "Impax announces sale of Daraprim® to Turing Pharmaceuticals AG," Press release, August 10, 2015 http://investors.impaxlabs.com/Media-Center/Press-Releases/Press-Release-Details/2015/Impax-Announces-Sale-of-Daraprim-to-Turing-Pharmaceuticals-AG/default.aspx

[11] Andrew Pollack and Sabrina Tavernise, "Valeant's drug price strategy enriches it, but infuriates lawmakers," *The New York Times* Ocober 4, 2015. http://www.nytimes.com/2015/10/05/business/valeants-drug-price-strategy-enriches-it-but-infuriates-patients-and-lawmakers.html

[12] Gretchen Morgenson, "Valeant shows the perils of fantasy numbers," *The New York Times* October 30, 2015. http://www.nytimes.com/2015/11/01/business/valeant-shows-the-perils-of-fantasy-numbers.html

[13] Ariana Eunjung Cha, "CEO of company that raised the price of old pill hundreds of dollars overnight calls journalist a moron for asking why" *The Washington Post* September 22, 2015. https://www.washingtonpost.com/news/to-your-health/wp/2015/09/21/ceo-of-company-that-raised-the-price-of-old-pill-hundreds-of-dollars-overnight-calls-journalist-a-moron-for-asking-why/

innovation,[14] [15] nor is he playing the role of the CEO of a generic drug firm arguing that the burdens of regulation and liability should not apply to a sector that promotes low prices and access. No, Shkreli comes from a new tier of smaller firms who employ retro-monopolistic strategies to corner the market on old cheap drugs that no other companies are producing and remake them as old expensive drugs. They represent a new mutation of the "little pharma" generics firms that—until very recently—were assumed to be a sort of moral underdog, producing cheap versions of old medicines and helping once innovative medicines become more widely accessible.

This increasing unaffordability of older medications is not limited to antiparasitic drugs. I have seen patients on the verge of hospitalization for diabetes because they could not afford their insulin (a drug first patented in 1923) and for asthma attacks because they could not afford their albuterol inhalers. Albuterol, an essential drug first marketed in 1968 for the treatment of this life-threatening illness affecting more than 22 million Americans (disproportionately those living in poverty), was once available in a cheap generic form but is now only available as more expensive brand-name drug. Other, equally distressing examples can be found in monopolies and oligopolies for old and essential treatments for gout, heart disease, cancer, and even the supply chain for interventions as basic as bags of intravenous saline.[16] [17] [18] In April of last year, a study revealed that the price of insulin had tripled in the course of a decade for no apparent reason; in July reported that another lifesaving drug, Naloxone, which reversed opioid overdoses, had increased in price by 1,000 percent; the next month the makers of the emergency anti-anaphylactic drug EpiPen struggled to defend a 500 percent price increase in this decades-old drug[19] These commodities represent a vital infrastructure of our health care system that is eroding from shortage to shortage and price hike to price hike, as once competitive generic markets give way to new oligopolies and monopolies of old medical interventions.

It wasn't supposed to be this way. When the essential drugs concept was formally articulated by the World Health Organization in 1977, its architects hoped to carve out a set of inexpensive interventions so central to the functioning of healthcare systems that they should be considered

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[14] Derek Lowe, "Is the blockbuster era over for Big Pharma? *The Atlantic* April 17, 2009. http://www.theatlantic.com/business/archive/2009/04/is-the-blockbuster-era-over-for-big-pharma/16287/

[15] Jason Millman, "The drug that's forcing America's most important—and uncomfortable—healthcare debate," *The Washington Post* July 24, 2014. http://www.washingtonpost.com/news/wonkblog/wp/2014/07/24/the-drug-thats-forcing-americas-most-important-and-uncomfortable-health-care-debate/

[16] Jeremy A. Greene, "When old drugs are made new again," *Forbes.* April 23,2015. http://www.forbes.com/sites/matthewherper/2015/04/23/when-old-drugs-are-made-new-again/

[17] Jeremy A. Greene, "Drug bust: For 30 years, generic medications helped make health care cheaper. Why is their cost surging?" *Slate*. Nov 20, 2014. http://www.slate.com/articles/business/moneybox/2014/11/generic_drug_prices_why_their_prices_are_suddenly_surging.html

[18] Arlene Weintraub, "How to charge $546 for six liters of saltwater" *The New York Times* August 25, 2015. http://www.nytimes.com/2013/08/27/health/exploring-salines-secret-costs.html

[19] Arlene Weintraub, "Mylan CEO Bresch admits 'full responsibility' for EpiPen price hikes." *Forbes* December 1, 2016; Senate Special Committee on Aging, United States Senate, *Sudden Price Spikes in Off-Patent Prescription Drugs: The Monopoly Business Model That Harms Patients, Taxpayers, and the U.S. Health Care System.* December, 2016.

collective public goods instead of a set of private commodities. These agents were agreed to be "of the utmost importance, and are basic, indispensible, and necessary for the health needs of the population"[20] Ideally, their wide availability would be supported by strong government policies. Advocates of the essential drug program saw the generic industry as an ally: a "little pharma" that provided old drugs on the cheap.

And yet the history of the generic drug industry over the past five decades has demonstrated materially that manufacturers of off-patent drugs are no more *moral* or *immoral* than members of PhRMA or BIO: Rather, they are *amoral* actors who will move to maximize their revenues as much as any other private firm. That means, ironically, that a new sector of the off-patent drug market is now making old essential medicines newly unaffordable to patients living in poverty.

**Revisiting the generic solution**

In the fall of 2014, a gathering at the Food Drug Law Institute here in Washington celebrated the 30th birthday of the Price Competition and Patent Extension Act of 1984, also known as the Hatch–Waxman Act.[21] When the bill was signed into law more than three decades ago, it streamlined the approval process for bioequivalent generic drugs as soon as the patent expired on the original medication. The subsequent expansion of the generic drug market, from less than 3 out of 10 prescriptions in 1984 to more than 8 out of 10 by 2014, is one of the few success stories among the United States' long struggle to provide high-quality health care at a lower price. Total U.S. pharmaceutical expenditures actually *dropped* in 2012,[22] and the Generic Pharmaceutical Association estimates that generic drugs saved the American health system nearly $1.7 trillion dollars from 2005–2014.[23] These savings have been crucial to individual consumers and to our health system as a whole.

[20] *The Selection of Essential Drugs: Second Report of the WHO Expert Committee*. Geneva: World Health Organization, 1979. https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=3&ved=0CC8QFjACahUKEwjZ-aH8qYzIAhUFrD4KHaDdDPs&url=http%3A%2F%2Fwww.who.int%2Firis%2Fbitstream%2F10665%2F41361%2F1%2FWHO_TRS_641.pdf&usg=AFQjCNGqERsJfBevbCnk-rDBZ5BR3bWMUw&sig2=0fbLEVBgN4AKf1zqe8hh8Q

[21] Food and Drug Law Institute, "Celebrating the 30th anniversary of the Hatch-Waxman amendments: The past, present, and future of generics" September 18, 2014" http://www.fdli.org/conferences/conference-pages/generic-drugs/agenda-slides

[22] Katie Thomas, "U.S. drug costs dropped in 2012, but rises loom" *The New York Times,* March 18, 2013 http://www.nytimes.com/2013/03/19/business/use-of-generics-produces-an-unusual-drop-in-drug-spending.html?pagewanted=all

[23] "Generic drugs deliver a record $254 billion in savings to U.S. health care system in 2014, new report shows" Generic Pharmaceutical Association (GPhA) Press Release, November 3, 2015. http://www.gphaonline.org/gpha-media/press/generic-drugs-deliver-a-record-254-billion-in-savings-to-u-s-health-care-system-in-2014-new-report-shows

Yet we are having a very different conversation about off-patent drugs today. Drugs previously available at pennies per pill now cost hundreds of dollars per bottle.[24] And not just esoteric, small-market drugs, either: the antibiotic doxycycline, a workhorse drug for common infections from Lyme disease to pneumonia, cost $20 per 500-count bottle in October 2013, by October 2014 the average price for the same supply was $1,849.[25] For a drug initially approved by the FDA in 1967, the price hike seems mystifying—and I say that as both a clinician and a historian. Nor is this limited to a just a handful of drugs or a handful of patients.

What explains the sudden spike in the prices of so many off-patent drugs? To answer that question, it is not enough to just point the finger at companies like Turing, Valeant, Retrophin, and Rodelis (or even Amedra) as a handful of bad actors who are spoiling an otherwise healthy system for access to essential medications. Rather, it is crucial to understand the specific historical process by which generic drugs emerged as a private sector solution to the public health problem of pharmaceutical access, and why our assumptions about the competitive nature of the generic drug sector may now be unfounded. It turns out we may have put too much faith in the competitive nature of the generic drug sector, which works for the vast majority of drug classes but leaves some corners of the therapeutic marketplace in oligopolistic or monopolistic conditions.

The Hatch–Waxman Act did more than provide a pathway for generic drug approval. It also naturalized the two-phase model of the pharmaceutical life cycle that balanced the necessities of pharmaceutical innovation and pharmaceutical access. In the first, patent-protected phase, a new drug would be available at higher prices exclusively from the company that created it, so that it could recoup its R&D investment. In the second, post-patent phase, a drug would be open to free-market competition, which would bring down prices and make medications affordable for the general public. Thirty years later we have come to accept this model as common sense without recognizing that it rests on two debatable assumptions: that free-market principles work flawlessly to match supply and demand, and that the generic drug industry is a virtuous agent of public policy rather than simply another sector of the pharmaceutical industry, no more and no less virtuous than the larger firms that comprises PhRMA.

As the rolling waves of generic drug shortages and recent escalations in generic drug prices should remind us, both of these assumptions now need to be questioned. The market's invisible hand works until it doesn't, and then we are often left with conditions of market failure when supply doesn't meet demand. In the generic drug industry, market failure occurs when a crowd of different companies that once competed to sell a drug like doxycycline ditch it to pursue more profitable drugs—or consolidate through mergers and acquisitions—leaving just one or a handful of generic suppliers that are now able to raise prices just like brand-name manufacturers. This happens in part because generic companies are drawn toward the market exclusivity of newer

[24] Jonathan D. Alpern, William M. Stauffer, Aaron S. Kesselheim, "High-cost generic drugs: Implications for patients and policymakers" *New England Journal of Medicine* 2014; 371:1859-62. http://www.nejm.org/doi/full/10.1056/NEJMp1408376

[25] Ed Silverman, "Lawmakers probe "staggering" price hikes for generic drugs," *The Wall Street Journal* October 2, 2014. http://blogs.wsj.com/pharmalot/2014/10/02/lawmakers-probe-staggering-price-hikes-for-generic-drugs/

drugs when they come off patent, in part because of bottlenecks in the supply of precursor chemicals, and in part because of shrinking margins in the production of older generic drugs. The stampede leaves the supply of many older but essential medicines in the hands of just a few suppliers, whose production lines are unprepared to deal with surges in demand, leading to shortages of key pharmaceutical agents needed for the treatment of cancer, pneumonia, and heart disease, as well as for basic anesthesia. Prices eventually recede—but by then, usually, other drugs are seeing similar cost surges.

The root cause of both shortages and price-hikes is noncompetitive markets, especially oligopolistic and monopolistic situations where the actions of individual firms now have the ability to distort the balancing of supply and demand. [26] Although competition among generic drug firms is the key means by which we provide access to affordable off-patent pharmaceuticals, we have done little to monitor the competitiveness of these markets. Data from the FDA suggests that 17% of all drugs approved since the passage of Hatch-Waxman that are now eligible for generic competition are still only available from a single source under monopoly situation, while more than one-third are only available in monopolistic or oligopolistic terms. The wave of mergers that has consolidated the generic drug industry further reduces the competitiveness of off-patent drug markets.[27]

**The case for state action**

Over the past two years, the federal government has brought sustained attention to this issue in a series of hearings before the U.S. House of Representatives and Senate. CEOs from manufacturers accused of price-gouging off-patent prescription drugs have been brought before the hearings, sharply questioned, and chastised. Yet in spite of sustained advocacy from multiple stakeholders—including Attorney General Frosh[28]--and bills proposed with bipartisan support,[29] we have seen no federal solution to the problem of noncompetitive off-patent drug markets, and none is forthcoming in the immediate time horizon. There is to date no legal means to prevent the next Martin Shkreli from cornering the market on another off-patent drug and hiking prices.

In the interim, the state of Maryland continues to pay increasingly high prices through its Medicaid programs, through its prison health care system, and through pensions and health insurance benefits on state employees. The proposed legislation would be a powerful step for ensuring access to affordable off-patent medicines for citizens of Maryland, and would have the potential to serve as a model legislation for uptake among other states as well.

I would remind the Committee that this is how generic drugs became widely available in American pharmacies in the first place. Generic substitution laws—the crucial legal mechanism

[26] Jeremy A. Greene, Gerard Anderson, Joshua M. Sharfstein, 'Role of the FDA in affordability of off-patent pharmaceuticals. *JAMA* 2016; 315(5):461-2
[27] William McConnell, "FTC detail concerns on generic drug company mergers." *The Street* Aug 26, 2016.
[28] Brian Frosh, "A cure for the $750 pill" *Baltimore Sun*, October 30, 2015
[29] https://www.congress.gov/bill/114th-congress/senate-bill/2615/text

for achieving cost-savings in off-patent pharmaceuticals—were not developed initially on the federal level but rather were pioneered in state legislatures and then spread throughout the country. Kentucky passed the first law in favor of generic substitution in 1972, two more states followed in 1973, and between 1975 and 1979 another thirty-five states developed similar laws to ensure that their citizens could access affordable off-patent therapeutics. In a similar vein, with this measure to ensure access to affordable medicines for Maryland citizens, this legislature has the opportunity to similarly take the lead on a crucial issue affecting the public health of our nation.

I congratulate the attorney general for taking on the issue of off-patent pharmaceutical price-gouging, and for calling for clear and measured action to deter and remove bad actors from this arena. To be clear: SB 415 is not a bill to regulate the innovative pharmaceutical or biotechnology industry, and should not affect the research, development, manufacturing or sales of innovative drugs from member firms of PhRMA or BIO. Nor is it a bill to regulate the generic drug industry, as it does not affect the actions of those core members of the Generic Pharmaceutical Association whose products participate in building competitive markets as the spirit of the Hatch-Waxman Act intended. Rather, it only applies to the growing group of marginal firms *with no interest in participating in competitive markets*, and whose business strategies follow the plan outlined in the Senate Special Committee on Aging's report to acquire monopoly pricing power for sole-source off-patent drugs and raise prices without any justification.[30]

The bipartisan committee that produced this report, led by Senator Claire McCaskill of Missouri and Senator Susan Collins of Maine, was able to clearly and accurately describe the business model used by a series of firms to inflate prices of off-patent pharmaceuticals. Yet no existing law prohibits the next Martin Shkreli from cornering the market on any of a number of off-patent medicines that have fallen into monopolistic situation. Attempts by other state attorney generals to take action on the basis of antitrust law have found no purchase, because this form of price-gouging, though unconscionable and endangering of the public health, is nonetheless still considered to be legal.[31] This law will take a bold step to correct that omission, so that the laws and regulation we have created to ensure that our generic drug supply is safe and effective cannot be used as a shield to extort unsustainable price increases.

Three decades ago, the Hatch-Waxman Act helped to make generic drugs the cornerstone in guaranteeing access to off-patent medications. As the rising costs of this sector now threaten the ability of citizens of Maryland to afford older their prescriptions, we should remember not just the means but the original ends of generic drug policy: wider and fairer access to high-quality essential medicines for all.

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[30] Senate Special Committee on Aging, United States Senate, *Sudden Price Spikes in Off-Patent Prescription Drugs: The Monopoly Business Model That Harms Patients, Taxpayers, and the U.S. Health Care System.* December, 2016.

[31] Andrew Pollack, "New York Attorney General examining whether Turing restricted drug access." *New York Times,* October 12, 2015.