# 1AC

### 1

#### Contention 1 is Drug Prices –

#### Best new studies prove that U.S. drug prices have skyrocketed in recent years because of lack of competition. That shuts off access to vital drugs and balloons household and federal debts.

Feldman 8/27 – Distinguished Professor of Law Chair & Director of the Center for Innovation, UC Hastings Law

Robin Feldman, Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation, The Price Tag of 'Pay-for-Delay', UC Hastings Research Paper Forthcoming, 27 Aug 2021, https://papers.ssrn.com/sol3/papers.cfm?abstract\_id=3846484

The skyrocketing price of prescription medication continues to plague the pharmaceutical industry. For example, an analysis of one million Medicare patients between 2010 and 2017 found that the average dosage-unit price of brand-name drugs increased by 313 percent even after accounting for rebates.2 [FN 2] 2 Robin Feldman, The Devil in the Tiers, J.L. & BIOSCI. 1, 19 (2021). The RAND Corporation found in 2021 that the price of brand-name prescription drugs in the U.S. is 256 percent of the prices in thirty-two OECD countries combined, ranging from 170 percent of prices in Mexico to 779 percent of prices in Turkey (ANDREW W. MULCAHY ET AL., RAND CORP., INTERNATIONAL PRESCRIPTION DRUG PRICE COMPARISONS: CURRENT EMPIRICAL ESTIMATES AND COMPARISONS WITH PREVIOUS STUDIES 26 (2021), <https://www.rand.org/content/dam/rand/pubs/research_reports/RR2900/RR2956/RAND_RR2956.pdf>). [End FN] Similarly, one in four Americans have difficulty affording their medications, and three in ten say costs have prohibited them from taking their medications as prescribed.3 With rising out-of-pocket costs and patients dangerously rationing medication, these prices are causing real pain for American patients. Diabetic patients, for example, paid nearly $6000 a year out of pocket for insulin in 2016, and patients with arthritis saw the price of Humira rise to $1552 a month in 2019.4 As difficult as the burdens are for any patient, the burden of paying high prices lands particularly hard on lower-income groups, threatening access to life-saving treatments and creating further gaps in equity across society.

Since the passage of legislation in the early 1980s, the nation has pinned its hopes on the disciplining effects of generic drugs. Generics are expected to enter the market rapidly when a drug’s patent protection expires, driving prices down to competitive levels.5 Something, however, is seriously amiss. Although generics continue to enter the market in record numbers, drug prices, out-of-of pocket costs, and real spending on drugs continue to soar unabated. The pharmaceutical industry is a complex and convoluted market, with significant distortions and inefficiencies.6 Among these problems, however, one cannot expect generic competitors to create a disciplining effect on prices, if brand companies are able to collude with their generic competitors.

In a landmark decision nearly a decade ago, the Supreme Court opened the door for antitrust suits against brand and generic pharmaceutical companies who engage in collusive settlements to delay the time for the generic to come to market. With these “pay-for-delay” agreements, brand-name companies offer prospective generic competitors cash in exchange for the generic’s promise not to enter the market until an agreed-upon date. Laying the groundwork for the lawsuit that would eventually lead to the Actavis decision, the Federal Trade Commission (FTC) published a study estimating that pay-for-delay agreements cost American consumers $3.5 billion annually, a figure that has been cited repeatedly by scholars and policy-makers alike.7 Similar concerns led Congress, in 2003, to require that brand and generic manufacturers file settlement agreements concerning the manufacture, marketing, or sale of generic drugs with the FTC and tasked the FTC with publishing an annual report on the state of pay-for-delay. 8

As this article will demonstrate, the $3.5 billion figure vastly understates the landscape. To understand the state of pay-for-delay agreements, this article leverages a range of methodologies to present an in-depth examination of the burden that pay-for-delay imposes, both on individual patients and society at large. Specifically, the analysis demonstrates the cost of unavailable generic options in drug markets that suffer pay-for-delay schemes. The findings are alarming, and far exceed the FTC estimate.

● Pay-for-delay settlements cost the U.S. population at least $6.4 billion annually: Calculations ranged from $6.4 billion to as high as $36.1 billion per year in total costs based on list prices, as the postponement of generic options required the continued usage of expensive brands.

● Pay-for-delay settlements saddled American patients with more than $600 million in annual out-of-pocket costs: Patients each year collectively paid between $610 million and $2.8 billion more out-of-pocket as a result of pay-for-delay.

● Pay-for-delay settlements cost the Medicare Part D program at least $2.3 billion annually: The government paid between $2.3 and $13.1 billion more each year to fund Part D because of pay-for-delay.

Moreover, although the Supreme Court’s landmark decision in Actavis opened the door for antitrust litigation, courts have failed to utilize the pathway provided. This article explores the modern legal landscape that has instead emerged since the Supreme Court’s historic pronouncement.

The article proceeds as follows. Part I describes pay-for-delay agreements, exploring the literature on the potential harm of such agreements among pharmaceutical competitors. Part II presents a new analysis demonstrating that the cost of pay-for-delay to American consumers is far greater than anyone has recognized, and well beyond the $3.5 billion figure cited by the FTC in 2010. We applied six different methodologies to provide as fair and broad a view as possible. The range of methodologies show that at a minimum, the cost of pay-for-delay settlements on the U.S. population between 2006 and 2017 is a minimum of $6.4 billion per year—almost double that of the FTC’s estimate. The methodology with the largest result suggests that the cost could be as high as $36 billion per year—10 times higher. Part III argues that courts are allowing this costly problem to flourish unchecked. This part reviews pay-for-delay decisions since Actavis, arguing that the courts have failed to properly analyze such cases from the perspective of all three notions inherent in the words “pay,” “for,” and “delay.” Finally, Part IV offers a path forward through the doctrinal haze.

#### Budgetary overstretch driven by healthcare causes global instability.

Brown, PhD, Professor of Practice and Vice Chair, Public Administration and International Affairs at Syracuse, worked as an economist at the International Monetary Fund and as Chief Economist for Eastern Europe, Africa, and the Middle East at BNP Paribas, ‘13

(Stuart S., “Global Power: Key Issues,” in *The Future of US Global Power: Delusions of Decline*, Palgrave, p. 57-58)

In the first instance, structural26 budget deficits are more likely to be symptoms of incipient overstretch then prima facie evidence of national decline. Overstretch suggests a need to realign commitments and resources, hence spending and revenues. In principle, persistently large deficits demand adjustments that need not materially impact the underlying drivers of longer-term prosperity. In contrast, if fiscal imbalances prove sufficiently chronic, they can eventually trigger growth-inhibiting alterations in microeconomic incentives. In such cases, incipient overstretch can mutate into a more primary threat to the system's underlying dynamism.

In its classical formulation, “imperial overstretch” refers to unrestrained and exorbitant foreign military campaigns. The latter can be said to redound to the detriment of great powers by crowding out more productive capital investments. Yet in contrast to widespread impression, the US fiscal challenge does not primarily reflect out-of-control defense spending and the burden of foreign entanglements. If this were the case, then the feasibility of financing an ever-expanding global power projection would be brought into question. This neither minimizes the sizable resources the US commits to military-related spending nor denies that cutbacks in such spending can help facilitate overall fiscal adjustment. Rather, the point is that an endemic failure to rein in explosive economy-wide health care costs with the latter's implications for public sector health insurance programs – the real fiscal challenge – will do more to endanger macroeconomic stability and eventually erode the material foundation of US power (see chapter 8).

By viewing (health-care driven) fiscal deficits as a necessary manifestation of overstretch is misguided for a more basic reason. The root of the US fiscal problem involves unsustainable commitments – particularly in the area of health expenditure – made by government to its citizens. It is decidedly not a question of any dearth of national resources to adequately meet the health needs of the population at large. As the richest country in the world, the US possesses more than enough resources to achieve this goal. The relevant political and social question is whether the population’s basic health requirements are best met via ever-expanding entitlements requiring increasingly higher levels of taxation.

#### Monopoly drug pricing is the primary driver of U.S. healthcare spending – AND, monopoly rent-seeking does not benefit R&D.

Ezekiel 19 – Ezekiel J. Emanuel is an oncologist, a bioethicist, and a vice provost of the University of Pennsylvania. He is the author or editor of 10 books, including Brothers Emanuel and Reinventing American Health Care.

Ezekiel J. Emanuel, 3-23-2019, "Big Pharma’s Go-To Defense of Soaring Drug Prices Doesn’t Add Up," Atlantic, https://www.theatlantic.com/health/archive/2019/03/drug-prices-high-cost-research-and-development/585253/

**How is it that pharmaceutical companies can charge patients $100,000, $200,000, or even $500,000 a year for drugs—many of which are not even curative?**

Abiraterone, for instance, is a drug used to treat metastatic prostate cancer. The Food and Drug Administration initially approved it in 2011 to treat patients who failed to respond to previous chemotherapy. It does not cure anyone. The research suggests that in previously treated patients with metastatic prostate cancer, the drug extends life on average by four months. (Last year, the FDA approved giving abiraterone to men with prostate cancer who had not received previous treatment.) At its lowest price, it costs about $10,000 a month.

Abiraterone is manufactured under the brand name Zytiga by Johnson & Johnson. To justify the price, the company pointed me to its “2017 Janssen U.S. Transparency Report,” which states: “We have an obligation to ensure that the sale of our medicines provides us with the resources necessary to invest in future research and development.” In other words, the prices are necessary to fund expensive research projects to generate new drugs.

This explanation is common among industry executives. To many Americans, it can seem plausible and compelling. It’s easy to conjure images of scientific researchers in their protective gear and goggles carefully dropping precious liquids into an array of Erlenmeyer flasks, searching for a new cure for cancer or Alzheimer’s. But invoking high research costs to justify high drug prices is deceptive.

No matter the metric, drug prices in the United States are extreme. Many drugs cost more than $120,000 a year. A few are even closing in on $1 million. The Department of Health and Human Services estimates that Americans spent more than $460 billion on drugs—16.7 percent of total health-care spending—in 2016, the last year for which there are definitive data. On average, citizens of other rich countries spend 56 percent of what

Excessive drug prices are the single biggest category of health-care overspending in the United States compared with Europe, well beyond high administrative costs or excessive use of CT and MRI scans. And unlike almost every other product, drug prices continue to rapidly rise over time. HHS estimates that over the next decade, drug prices will rise 6.3 percent each year, while other health-care costs will rise 5.5 percent. Basic economic principles suggest that drug prices should be going down, not up: For most drugs, manufacturing volumes are increasing, and little new research is being conducted on those already on the market.

Reducing these high drug prices has become a major political concern—and a rare bipartisan cause for Democrats and Republicans to rally around, albeit with disagreement about how to actually get it done. In his State of the Union address last month, President Donald Trump called the price discrepancy between the United States and other countries “unacceptable” and “unfair,” and vowed to “stop it fast.” In a Senate Finance Committee hearing on drug pricing a few weeks later, Senator Ron Wyden of Oregon compared the way the drugmaker AbbVie protects the exclusivity of one of its drugs to the way Gollum protects his ring.

Yet every time Congress debates doing something about drug prices, the industry—and the advocacy groups it funds—vociferously returns to the point that lower prices will thwart innovative research. The fear of missing a cure for Alzheimer’s or Lou Gehrig’s disease or depression contributes to stalling reform. But there are many reasons to question the widely held notion that high drug prices and innovative research are inextricably linked.

The most telling data on a disconnect between drug prices and research costs has received almost no public attention. Peter Bach, a researcher at Memorial Sloan Kettering, and his colleagues compared prices of the top 20 best-selling drugs in the United States to the prices in Europe and Canada. They found that the cumulative revenue from the price difference on just these 20 drugs more than covers all the drug research and development costs conducted by the 15 drug companies that make those drugs—and then some.

To be more precise, after accounting for the costs of all research—about $80 billion a year—drug companies had $40 billion more from the top 20 drugs alone, all of which went straight to profits, not research. More excess profit comes from the next 100 or 200 brand-name drugs.

Drug companies tend to say they are unique in needing to spend a higher proportion of their capital on research than almost any other industry. But of all the companies in the world, the one that invests the most in research and development is not a drug company. It’s Amazon. The online retailer spends about $20 billion a year on R&D, despite being renowned for both low prices and low profits. Among the 25 worldwide companies that spend the most on research and development—all more than $5 billion a year—seven are pharmaceutical manufacturers, but eight are automobile or automobile-parts companies with profit margins under 10 percent. Amazon’s operating margin is under 5 percent. Meanwhile, the top 25 pharmaceutical companies reported a “healthy average operating margin of 22 percent” at the end of 2017, according to an analysis by GlobalData.

If you watch television, you know part of the answer to where this extra money is going: sales and advertising. Of the 10 largest pharmaceutical companies, only one spends more on research than on marketing its products. But it’s hard to figure out what it actually costs drug companies to conduct the research required to get FDA approval and bring a single drug to market. The pharmaceutical industry and its advocates tend to peg the cost of creating and bringing to market just one new drug at $2.6 billion. This figure comes from a cost report published in October 2016 by the Tufts Center for the Study of Drug Development.

There are several reasons to suspect that number is unreliable. According to the Tufts Center’s website, more than a quarter of its budget comes from “unrestricted grants” from pharmaceutical companies and their partners. And no one can verify Tufts’ analyses and claims: The authors say the data come from research spending on 106 drugs produced by 10 of the top 50 multinational pharmaceutical companies, but the underlying data are deemed proprietary and confidential.

Tufts also uses a cost-accounting methodology that appears to significantly inflate its estimate. About 45 percent of Tufts’ $2.6 billion figure is attributed to the amount companies would pay to lenders and shareholders for the capital they invest in research. Tufts uses an interest rate of 10.5 percent a year, but investment bankers tend to use just 6 percent in their economic models. That one change would reduce the Tufts estimate by about a quarter of its total figure. That’s not to mention other factors the Tufts team leaves out that reduce the cost of drug development, such as tax credits the federal government offers for research and development.

When asked about these issues, the report’s chief author, Joseph DiMasi, noted that one other study with public data, published in 2009, comes to similar results. He argues that even if we exclude the cost of capital, $1.4 billion per FDA-approved drug is a high price—and the cost has been growing at about 8.5 percent annually.

But in November 2017, a study published in JAMA Internal Medicine examined the costs of developing 10 cancer drugs approved by the FDA from 2006 to 2015 and provided a strong contrast to the Tufts study from a year before. Its authors, from Memorial Sloan Kettering and the Oregon Health and Science University, used annual financial disclosures from the Securities and Exchange Commission for companies that had only one cancer drug approved but had on average three or four other drugs in development. They found that companies took an average of 7.3 years to win FDA approval, at a median cost of $648 million. Only two drugs had research costs over $1 billion. Adding in the cost of capital at 7 percent increased the median research and development cost to $757 million—less than a third of the Tufts estimate.

Pharmaceutical companies often claim that the research costs of unsuccessful drugs also have to be taken into account. After all, 90 percent of all drugs that enter human testing fail. But most of these failures occur early and at relatively low costs. About 40 percent of drugs fail in preliminary Phase I studies, which assess a drug’s safety in humans and typically cost just $25 million a drug. Of the drugs that clear this first phase of testing, about 70 percent fail during Phase II studies, which assess whether a drug does what it is supposed to do. The research costs of these studies are still relatively low compared with overall R&D costs—on average, under $60 million a study.

The 2017 JAMA Internal Medicine study incorporated all research costs on drugs not yet on the market into its final calculations. The pharmaceutical companies it examined had an average drug success rate of 23 percent, which the Tufts researchers argue is too high to accurately represent the amount of money that failed drugs would usually add to a company’s research costs. But cancer drugs, specifically, do have a success rate of 20 to 25 percent—so the selection of only successful companies does not seem to be the difference.

Joaquin Duato, the vice chairman of Johnson & Johnson’s executive committee, argues that critics fail to deal with the realities of drug R&D. He told me that last year, Johnson & Johnson had $41 billion in prescription-drug sales, of which $8.4 billion went to R&D and $4.5 billion went to sales and marketing. Other costs included manufacturing, finance, IT, taxes, and more. This funds research on 100 candidate drugs, which result in one or two FDA approvals a year. “For drug companies, the return on capital is in the mid-teens, which is nowhere near tech-company returns,” Duato said.

Nevertheless, some former pharmaceutical-company executives say that research costs do not determine drug prices—and they explain how. In his book A Call to Action, Hank McKinnell, a past CEO of Pfizer, wrote under the heading “The Fallacy of Recapturing R&D Costs”:

How do we decide what to charge? It’s basically the same as pricing a car … A number of factors go into the mix. These factors consider cost of business, competition, patent status, anticipated volume, and, most important, our estimate of the income generated by sales of the product. It is the anticipated income stream, rather than repayment of sunk costs, that is the primary determinant of price.

Raymond Gilmartin, a former Merck CEO, once said to The Wall Street Journal: “The price of medicines is not determined by their research costs. Instead, it is determined by their value in preventing and treating disease.”

Exorbitant drug prices have two bad effects. First, high costs mean that lots of patients are unable to take their medications. A recent study in the Journal of Clinical Oncology assessed patients’ access to 38 different oral cancer drugs and found that 13 percent of cancer patients did not buy approved chemotherapy drugs if they had a co-payment of $10 a month, while 67 percent did not when they had to pay $2,000 or more. Another study showed that 25 percent of diabetic patient underuse their insulin because of cost.

Second, the high drug prices distort research priorities, emphasizing financial gains and not health gains. Cancer drugs are routinely priced at about $120,000 to $150,000 a year, and more than 600 cancer drugs are now being tested on humans. This can lead to great societal benefits: The United States is expected to face 1.76 million new cancer cases and more than 600,000 cancer deaths in 2019 alone. But many of the drugs that companies are pursuing have low promise, where the health gains are small—weeks of added life, not big cures. While even this short extra time can be valuable to individual families, too much investment in oncology means not enough in drugs for other illnesses whose treatments cannot be so highly priced.

Consider antibiotics. The Centers for Disease Control and Prevention ranks antibiotic-resistant infections as one of the nation’s top health threats. An estimated 2 million Americans become infected with such bacteria each year, and 23,000 die. A superbug that is resistant to all known antibiotics is an imminent threat. Yet because antibiotics are generally cheap, for most pharmaceutical and biotechnology companies they are not a primary focus. The Pew Charitable Trusts reports that only about 42 new antibiotics with the potential to treat serious bacterial infections were in clinical development for the U.S. market in December 2018. Six hundred drugs for cancer and only 42 for serious infections seems like profit maximization, not a case of sensible research priorities that reflects “value in preventing and treating disease.”

The simple explanation for excessive drug prices is monopoly pricing. Through patent protection and FDA marketing exclusivity, the U.S. government grants pharmaceutical companies a monopoly on brand-name drugs. But monopolies are a recipe for excessive prices. A company will raise prices until its profits start to drop.

To address the problem of high prices and reduced access to drugs, Johnson & Johnson advocates eliminating rebates to pharmacy benefit managers and insurers, which would increase price transparency and lower patient co-pays. But it would not necessarily lower total drug prices. The proposal avoids the standard economic response to monopoly pricing: price regulation. Every other developed country regulates drug prices, often through price negotiations pegged to cost-effectiveness analysis or some other measure of clinical benefit.

Will R&D go down if the United States follows this model? Not necessarily. Remember, the high drug prices fund R&D but also marketing, manufacturing, administrative expenses, and profits at the companies. Lower revenue from lower drug prices could reduce marketing, administration, and excessive profits before R&D costs have to be reduced.

Where cuts are made is up to drug companies. Their claims of lower R&D costs appear designed to generate fear, but as some former executives themselves have acknowledged, there is no necessary link between a decline in drug prices and a decline in R&D. Drug companies could make other choices that maximally improve the health of all Americans.

#### Specifically – Biologics account for 93% of the cost.

Roy 19 – Avik Roy is senior advisor to BPC. He is the President of the Foundation for Research on Equal Opportunity (FREOPP.org), a non-partisan, non-profit think tank that conducts original research on expanding opportunity to those who least have it.

Avik Roy, 3-8-2019, "Biologic Medicines: The Biggest Driver Of Rising Drug Prices," Forbes, https://www.forbes.com/sites/theapothecary/2019/03/08/biologic-medicines-the-biggest-driver-of-rising-drug-prices/?sh=16fb5a2618b0

The topic of high prescription drug prices is now the dominant policy issue on Capitol Hill. The new Congress has held a half-dozen hearings on the topic. But one issue that is at the heart of high prices has attracted little attention: the role of biologic drugs in rising drug costs.

In 2017, according to data from the IQVIA Institute, biologic drugs represented 2 percent of all U.S. prescriptions, but 37 percent of net drug spending. Since 2014, biologic drugs account for nearly all of the growth in net drug spending: 93 percent of it, in fact.

Why is that? And what are biologic drugs in the first place? I’ll try to explain.

The FDA regulates traditional and biologic drugs differently

In the old days, most FDA-approved drugs are what we call small molecules: traditional medicines with relatively simple chemical structures. For example, Lipitor (atorvastatin), a best-selling cholesterol-lowering drug, is comprised of 76 atoms, and is exceedingly cheap to manufacture. On the other hand, biologic drugs (or large molecules) like monoclonal antibodies are complex proteins, manufactured in living cells: a costlier process. Humira (adalimumab), the nation’s top drug by revenue, contains 20,067 atoms.

Biologic drugs are the wheelhouse of the biotechnology industry. Innovators in the 1970s and 1980s, like Genentech and Amgen, learned how to insert modified DNA sequences into harvested hamster cells, in order to make genetically engineered proteins that could treat diseases. For example, Epogen, Amgen’s first blockbuster drug, is a genetically engineered version of human erythropoietin: a protein that stimulates your bone marrow to produce more red blood cells. Because erythropoietin is normally produced in the kidney, people with kidney disease often have anemia that can be treated with Epogen.

Because biologic drugs are manufactured using different techniques than traditional, small molecule drugs, Congress and the FDA have chosen to regulate these two categories in different ways. Traditional drugs are governed by the Food, Drug, and Cosmetic Act: the law that originally created the Food and Drug Administration. Biologic medicines are governed by a different law, the Public Health Service Act.

In both cases, the FDA expects drugmakers to conduct clinical trials that demonstrate that a new drug is safe and effective. In both cases, the FDA scrutinizes manufacturing plants to ensure that medicines are consistently made from batch to batch.

Where things really change, in terms of FDA regulation, is after drugs have been on the market for a long time, with patents about to expire.

#### And – It’s a leading cause of death and suffering in the United States – Causes over 100,000 deaths per year from Medicare patients alone, and millions more suffer.

WestHealth 20 – Citing new study

New Study Predicts More Than 1.1 Million Deaths Among Medicare Recipients Due to the Inability to Afford Their Medications: Beneficiaries skipping medications is causing early death and worsening medical conditions that will cost Medicare an extra $177.4 billion over the next 10 years, Nov. 19, 2020, https://www.westhealth.org/press-release/study-predicts-1-million-deaths-due-to-high-cost-prescription-drugs/

More than 1.1 million Medicare patients could die over the next decade because they cannot afford to pay for their prescription medications, according to a new study released today by the West Health Policy Center, a nonprofit and nonpartisan policy research group.

If current drug pricing trends and associated cost-sharing continue, researchers estimate cost-related non-adherence to drug therapy will result in the premature deaths of 112,000 beneficiaries a year, making it a leading cause of death in the U.S., ahead of diabetes, influenza, pneumonia, and kidney disease. Millions more will suffer worsening health conditions and run up medical expenses that will cost Medicare an additional $177.4 billion by 2030 or $18 billion a year for the next 10 years.

### 2

#### Contention 2 is Innovation –

#### Disruptive innovation is structurally plummeting now despite skyrocketing prices. Direct govt. intervention would be a disaster, BUT a better competition regime that recalibrates patent incentives would solve both concerns.

Feldman 18 – Distinguished Professor of Law Chair & Director of the Center for Innovation, UC Hastings Law

Robin Feldman, Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation, May your drug price be evergreen, *Journal of Law and the Biosciences*, Volume 5, Issue 3, December 2018, pp. 590–647, https://doi.org/10.1093/jlb/lsy022

Out of the 106 top-selling drugs from between 2005 and 2014, more than 70% had their protection cliff extended at least once and more than 50% had their protection cliff extended more than once. The magnitude of the behavior highlights the extent to which stifling competition has become the norm in the pharmaceutical industry. When more than 70% of best-selling drugs had their protection extended, it is clearly the go-to approach for profitability.149

One can easily anticipate such maneuvering to continue going forward, particularly given the top-selling drugs going off patent. Between 2014 and 2020, an estimated $253 billion in worldwide drug sales is at risk due to expiration of patents on blockbuster drugs.150 Without societal action, the future is likely to look like more of the same.

V. SOLUTIONS

As described in the opening of this article, the intellectual property system in general and the patent system in particular are designed to provide an opportunity for innovators to garner a return. Competition may be held in abeyance for a limited time, but those who receive the benefit must pay for the privilege by disclosing sufficient information that competitors will be able to step in. This design reflects the deeply rooted notion that providing a period of exclusivity for inventors is intended to rebound to the benefit of society as a whole, not simply to the benefit of the inventors. The patent protection should end, returning the market to a competitive state.

This foundational structure of the patent system—one that delicately balances innovation and competition—is crumbling, whittled away across time as one good idea after another creates a special carve-out. Each carve-out, standing on its own, presents an appealing cause. Together, however, the result is a complete undermining of the system for pharmaceutical innovation as the repeated addition of protections, one after another, pushes competition further into the future, threatening innovation in the process. The behavior is not limited to a few bad apples. Our research reveals that it is endemic to the pharmaceutical industry.

In short, this is not an image of innovation and competitive entry. It is an image of a system that provides for repeated creation of competition-free zones, pushing a competitive market further and further out into the future. The problem is not only pervasive and persistent, but it is also growing across time.

The impact created by these repeated competition zones is not some abstract problem that our grandchildren may face. Rather, the nation's pharmaceutical system is in crisis today, with prices soaring to heights that distort both individual and government budgets.151 These dire circumstances bring calls for price controls, for government marching in to direct drug production, and for other strong measures.152 The US Government's history of directly managing pharmaceutical innovation, however, has been disappointing. In fact, prior to the Bayh-Dole Act of 1980, the federal government took responsibility for handing out licenses for innovation developed through government-funded research. Bayh-Dole shifted that responsibility from the federal government to universities, precisely because the government failed so miserably in this role. There is little reason to expect a different result this time.153

Competition is a powerful and effective tool, however, and paving the way for competition whenever it is possible remains the optimal approach. When the government itself bestows benefits that are stifling competition, society has both an obligation and an opportunity to act. One cannot, however, enter into such action lightly; it must be designed with thought and care. Pharmaceutical research and development are expensive, and companies must have sufficient incentive to travel down that risky road. Nevertheless, by incentivizing game-playing rather than innovation, society has clearly missed the mark.

#### Artificially shielding “weak patents” from scrutiny creates an incentive to avoid big breakthroughs in favor of pseudo-innovation. Real breakthroughs are hard and expensive, so companies that can profit by avoiding it will.

Elhauge and Krueger 12 – Petrie Professor of Law, Harvard Law School and Executive Director, Legal Economics

Einer Elhauge & Alex Krueger, “Solving the Patent Settlement Puzzle,” Texas Law Review, Vol. 91:283

Exceeding the optimal patent exclusion period is likewise inefficient for several reasons. First, the economic literature shows that patent profits that exceed the optimal level result in excessive investments in innovation that reduce social welfare compared to the optimal investments in innovation. Second, excessive patent protection can produce a net reduction in innovation by precluding subsequent innovations by others.

Third, settlements that over-reward the patent holder with a longer exclusion period than it deserves reduce the net reward for true innovation by increasing the reward more for less-deserving patents than for more deserving patents. As the proof below shows and the Second Circuit has already pointed out, settlements that exclude entry increase patent-holder profits more for weaker patents than for stronger patents. For example, the holder of a weak patent that is only 5% likely to be deemed a valid innovation could use such a settlement to secure exclusion throughout the entire patent term, even though its patent is 95% likely to be deemed a non-innovation, while the holder of an ironclad patent that is 100% likely to be deemed a true innovation could not increase its exclusion period through settlement because it would already expect 100% exclusion from litigation. Thus, settlements with an excessive exclusion period reduce the net reward for investing in a true innovation that leads to a stronger patent rather than in a pseudo-innovation that leads to a weaker patent. When a firm faces a choice between investing in true innovation or pseudo-innovation, this artificially reduced net reward for true innovation will distort its choice, and can reduce the rate of true innovation because it is generally harder, more costly, or less certain than pseudo-innovation.

For example suppose that a true innovation will produce a gross patent reward of $1 billion, but that the net reward for this true innovation is only $400 million because the firm can instead get $600 million in the same market by creating a pseudo-innovation that it can convert into a long exclusion period using a reverse payment settlement. Suppose further that the true innovation requires a $500 million investment, but the pseudo-innovation requires no investment. Then the true innovation will be deterred because the excessive reward for the pseudo-innovation reduces the net reward for true innovation below the investment required for it. Therefore, settlements that over-reward patent holders with longer exclusion periods than they deserve can actually decrease incentives to invest in true innovation. More generally, by reducing the net reward for investing in stronger patents rather than weaker patents, settlements that provide excessive exclusion periods distort investment choices away from the stronger patents that are more likely to reflect real innovation. In all three ways summarized above, settlements that exceed the optimal patent exclusion period will undermine optimal innovation incentives. For the purpose of antitrust analysis of these settlements, it is best to assume that substantive patent law is optimal. Although scholars sometimes argue that current patent law upholds too many patents, or too few, some balance must be struck. Even if one believes that current patent law does not strike the correct balance, the correct solution is to reform patent law, not to allow courts in antitrust cases to second-guess patent law doctrine and try to offset it imperfectly for the limited set of cases that produce patent settlements that raise antitrust issues. This second-guessing approach would not work both because it would require litigating the optimality of the patent system in every antitrust case that involved patent rights (not just reverse payment settlement cases), and because it would alter the innovation reward in the odd subset of cases that lead to such antitrust suits, which would distort firm incentives in choosing among possible innovations. Therefore, antitrust analysis of patent settlements should assume the optimality of patent law. Given that Congress and the courts have crafted the substantive doctrines that determine the probability that a patent would be found valid and infringed, the amount of exclusion that the patent holder deserves on the merits is equal to the probability that the patent would be found valid and infringed times the remaining patent term. To formalize this, call the probability that the patent will be found valid and infringed 0, and normalize the remaining patent term so that it spans from 0 to 1. For example, if 100 months remained on the patent term, then 100 months would be 1.0 on the normalized scale, 50 months would be 0.5, 10 months would be 0.1, and so forth. According to patent law, the patent holder deserves exclusivity for 9 of the remaining patent period because 9 percent of the time it deserves exclusivity for the entire period and 1 - 0 percent of the time it deserves no exclusivity. This means that if a settlement exclusion period T (again on the normalized 0 to 1 timeline) is greater than 0, then T exceeds the optimal patent exclusion period, and thus gives the patent holder more exclusivity and patent reward than it deserves. For example, if the remaining patent term is 100 months, and the probability of patent victory is 0.5, then the settlement exclusion period exceeds the optimal patent exclusion period only if T> 0.5; in other words, if the settlement excludes entry for more than 50 months. This measure entitles the patent holder to all the expected profits it would get if patent litigation were instant and costless, and thus enables patent holders to reap any legitimate settlement benefits that come from avoiding the delay and cost of litigation.

#### Specifically – Increasing competition is key to drive the revolution in biologics. Those are ground-breaking new treatments derived from living organisms, such as new vaccine tech and bacteriophages.

Carrier 20 – Michael A. Carrier is a leading authority in antitrust and intellectual property law with expertise in the pharmaceutical, high-technology, and music industries.

Carrier, Michael A. "Don't Die! How Biosimilar Disparagement Violates Antitrust Law." Northwestern University Law Review Online, 115, 2020-2021, p. 119-145. HeinOnline, <https://heinonline.org/HOL/P?h=hein.journals/nulro115&i=119>.

Competition is the key to low prices in the pharmaceutical industry. For decades, Americans have benefitted from affordable generic versions of brand-name drugs. But now, as biologics enter the market, we stand on the precipice of a revolution. In fact, biologics, which can cost patients hundreds of thousands of dollars per year, are predicted to be the "fastest growing segment of drug spending in the coming years."1

The hope, then, is that competition from follow-on products, known as biosimilars, will lower prices for patients. But pharmaceutical companies' campaign of biosimilar disparagement threatens to block this goal. Biologics are large, complex molecules derived from living organisms, most commonly proteins.2 According to the FDA, biologics "often represent the cutting-edge of biomedical research and, in time, may offer the most effective means to treat a variety of medical illnesses and conditions" that have "no other treatments available."3 Monoclonal antibodies, the most frequently developed type of biologic,4 include blockbuster products such as infection-reducing Neulasta, 5 as well as Humira and Remicade,7 both of which treat arthritis, colitis, and Crohn's disease. In targeting unhealthy cells without harming healthy cells, monoclonal antibodies have dramatically increased survival rates.9 Other types of biologics include vaccines, blood products, and gene therapies.10

#### Two scenarios.

#### Scenario A is Breakthroughs –

#### COVID is only the first warning shot. Continued vaccine development is key to survival

--Note: EID = Emerging Infectious Disease

Excler et al. 21 – Jean-Louis Excler, International Vaccine Institute, Seoul, Republic of Korea; Melanie Saville, Coalition for Epidemic Preparedness Innovations (CEPI), London, UK; Seth Berkley, Gavi, the Vaccine Alliance, Geneva, Switzerland; Jerome H. Kim, International Vaccine Institute, Seoul, Republic of Korea

Jean-Louis Excler, Melanie Saville, Seth Berkley, and Jerome H. Kim, "Vaccine development for emerging infectious diseases," Nat Med 27, 591–600, 4-12-2021, <https://www.nature.com/articles/s41591-021-01301-0>

Newly emerging and reemerging infectious viral diseases have threatened humanity throughout history. Several interlaced and synergistic factors including demographic trends and high-density urbanization, modernization favoring high mobility of people by all modes of transportation, large gatherings, altered human behaviors, environmental changes with modification of ecosystems and inadequate global public health mechanisms have accelerated both the emergence and spread of animal viruses as existential human threats. In 1918, at the time of the ‘Spanish flu’, the world population was estimated at 1.8 billion. It is projected to reach 9.9 billion by 2050, an increase of more than 25% from the current 2020 population of 7.8 billion (https://www.worldometers.info). The novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for the coronavirus disease 2019 (COVID-19) pandemic1,2,3 engulfed the entire world in less than 6 months, with high mortality in the elderly and those with associated comorbidities. The pandemic has severely disrupted the world economy. Short of lockdowns, the only means of control have been limited to series of mitigation measures such as self-distancing, wearing masks, travel restrictions and avoiding gatherings, all imperfect and constraining. Now with more than 100 million people infected and more than 2 million deaths, it seems that the addition of vaccine(s) to existing countermeasures holds the best hope for pandemic control. Taken together, these reasons compel researchers and policymakers to be vigilant, reexamine the approach to surveillance and management of emerging infectious disease threats, and revisit global mechanisms for the control of pandemic disease4,5.

Emerging and reemerging infectious diseases

The appearance of new infectious diseases has been recognized for millennia, well before the discovery of causative infectious agents. Despite advances in development of countermeasures (diagnostics, therapeutics and vaccines), world travel and increased global interdependence have added layers of complexity to containing these infectious diseases. Emerging infectious diseases (EIDs) are threats to human health and global stability6,7. A review of emerging pandemic diseases throughout history offers a perspective on the emergence and characteristics of coronavirus epidemics, with emphasis on the SARS-CoV-2 pandemic8,9. As human societies grow in size and complexity, an endless variety of opportunities is created for infectious agents to emerge into the unfilled ecologic niches we continue to create. To illustrate this constant vulnerability of populations to emerging and reemerging pathogens and their respective risks to rapidly evolve into devastating outbreaks and pandemics, a partial list of emerging viral infectious diseases that occurred between 1900 and 2020 is shown in Table 1.

[[Figure Omitted]]

Although nonemerging infectious diseases (not listed in Table 1), two other major mosquito-borne viral infections are yellow fever and dengue. Yellow fever, known for centuries and an Aedes mosquito-borne disease, is endemic in more than 40 countries across Africa and South America. Since 2016, several yellow fever outbreaks have occurred in Angola, Democratic Republic of Congo, Nigeria and Brazil to cite a few10, raising major concerns about the adequacy of yellow fever vaccine supply. Four live attenuated vaccines derived from the live attenuated yellow fever strain (17D)11 and prequalified by the WHO (World Health Organization) are available12.

Dengue is an increasing global public health threat with the four dengue virus types (DENV1–4) now cocirculating in most dengue endemic areas. Population growth, an expansion of areas hospitable for Aedes mosquito species and the ease of travel have all contributed to a steady rise in dengue infections and disease. Dengue is common in more than 100 countries around the world. Each year, up to 400 million people acquire dengue. Approximately 100 million people get sick from infection, and 22,000 die from severe dengue. Most seriously affected by outbreaks are the Americas, South/Southeast Asia and the Western Pacific; Asia represents ~70% of the global burden of disease (https://www.cdc.gov/dengue). Several vaccines have been developed13. A single dengue vaccine, Sanofi Pasteur’s Dengvaxia based on the yellow fever 17D backbone, has been licensed in 20 countries, but uptake has been poor. A safety signal in dengue-seronegative vaccine recipients stimulated an international review of the vaccine performance profile, new WHO recommendations for use and controversy in the Philippines involving the government, regulatory agencies, Sanofi Pasteur, clinicians responsible for testing and administering the vaccine, and the parents of vaccinated children14.

Two bacterial diseases, old scourges of humanity, are endemic and responsible for recurrent outbreaks and are increasingly antimicrobial resistant. Cholera, caused by pathogenic strains of Vibrio cholerae, is currently in its seventh global pandemic since 1817; notably, the seventh pandemic started in 196115. Global mortality due to cholera infection remains high, mainly due to delay in rehydrating patients. The global burden of cholera is estimated to be between 1.4 and 4.3 million cases with about 21,000–143,000 deaths per year, mostly in Asia and Africa. Tragic outbreaks have occurred in Yemen and Haiti. Adding to rehydration therapy, antibiotics have been used in the treatment of cholera to shorten the duration of diarrhea and to limit bacterial spread. Over the years, antimicrobial resistance developed in Asia and Africa to many useful antibiotics including chloramphenicol, furazolidone, trimethoprim-sulfamethoxazole, nalidixic acid, tetracycline and fluoroquinolones. Several vaccines have been developed and WHO prequalified; these vaccines constitute a Gavi-supported global stockpile for rapid deployment during outbreaks16.

Typhoid fever is a severe disease caused by the Gram-negative bacterium Salmonella enterica subsp. enterica serovar Typhi (S. Typhi). Antimicrobial-resistant S. Typhi strains have become increasingly common. The first large-scale emergence and spread of a novel extensively drug-resistant (XDR) S. Typhi clone was first reported in Sindh, Pakistan17,18, and has subsequently been reported in India, Bangladesh, Nepal, the Philippines, Iraq and Guatemala19,20. The world is in a critical period as XDR S. Typhi has appeared in densely populated areas. The successful development of improved typhoid vaccines (conjugation of the Vi polysaccharide with a carrier protein) with increased immunogenicity and efficacy including in children less than 2 years of age will facilitate the control of typhoid, in particular in XDR areas by decreasing the incidence of typhoid fever cases needing antibiotic treatment21,22.

A model of vaccine development for emerging infectious diseases

The understanding of emerging infectious diseases has evolved over the past two decades. A look back at the SARS-CoV outbreak in 2002 shows that—despite a small number of deaths and infections—its high mortality and transmissibility caused significant global disruption (see Table 1). The epidemic ended as work on vaccines was initiated. Since then, the disease has not reappeared—wet markets were closed and transmission to humans from civets ceased. Consequently, work on vaccines against SARS-CoV ended and its funding was cut. Only a whole inactivated vaccine23 and a DNA vaccine24 were tested in phase 1 clinical trials.

Following a traditional research and development pipeline, it takes between 5 and 10 years to develop a vaccine for an infectious agent. This approach is not well suited for the needs imposed by the emergence of a new pathogen during an epidemic. Figure 1 shows a comparison of the epidemic curves and vaccine development timelines between the 2014 West African Ebola outbreak and COVID-19. The 2014 Ebola epidemic lasted more than 24 months with 11,325 deaths and was sufficiently prolonged to enable the development and testing of vaccines for Ebola, with efficacy being shown for one vaccine (of several) toward the end of the epidemic25,26. What makes the COVID-19 pandemic remarkable is that the whole research and development pipeline, from the first SARS-CoV-2 viral sequenced to interim analyses of vaccine efficacy trials, was accomplished in just under 300 days27. Amid increasing concerns about unmitigated transmission during the 2013–2016 Western African Ebola outbreak in mid-2014, WHO urged acceleration of the development and evaluation of candidate vaccines25. To ensure that manufacturers would take the Ebola vaccine to full development and deployment, Gavi, the Vaccine Alliance, publicly announced support of up to US$300 million for vaccine purchase and followed that announcement with an advance purchase agreement. Ironically, there had been Ebola vaccines previously developed and tested for biodefense purposes in nonhuman primates, but this previous work was neither ‘ready’ for clinical trials during the epidemic nor considered commercially attractive enough to finish development28.

[[Figure Omitted]]

From these perceived shortcomings in vaccine development during public health emergencies arose the Coalition for Epidemic Preparedness Innovations (CEPI), a not-for-profit organization dedicated to timely vaccine development capabilities in anticipation of epidemics29,30. CEPI initially focused on diseases chosen from a list of WHO priority pathogens for EIDs—Middle East respiratory syndrome (MERS), Lassa fever, Nipah, Rift Valley fever (RVF) and chikungunya. The goal of CEPI was to advance candidate vaccines through phase 2 and to prepare stockpiles of vaccine against eventual use/testing under epidemic circumstances. CEPI had also prepared for ‘disease X’ by investing in innovative rapid response platforms that could move from sequence to clinical trials in weeks rather than months or years, such as mRNA and DNA technology, platforms that were useful when COVID-19 was declared a global health emergency in January 2020, and a pandemic in March 202031,32.

CEPI has been able to fund several vaccine development efforts, among them product development by Moderna, Inovio, Oxford–AstraZeneca and Novavax. Providing upfront funding helped these groups to advance vaccine candidates to clinical trials and develop scaled manufacturing processes in parallel, minimizing financial risk to vaccine developers. The launch of the larger US-funded Operation Warp Speed33 further provided companies with funding—reducing risks associated with rapid vaccine development and securing initial commitments in vaccine doses.

Vaccine platforms and vaccines for emerging infectious diseases

Vaccines are the cornerstone of the management of infectious disease outbreaks and are the surest means to defuse pandemic and epidemic risk. The faster a vaccine is deployed, the faster an outbreak can be controlled. As discussed in the previous section, the standard vaccine development cycle is not suited to the needs of explosive pandemics. New vaccine platform technologies however may shorten that cycle and make it possible for multiple vaccines to be more rapidly developed, tested and produced34. Table 2 provides examples of the most important technical vaccine platforms for vaccines developed or under development for emerging viral infectious diseases. Two COVID-19 vaccines were developed using mRNA technology (Pfizer–BioNTech35 and Moderna36), both showing safety and high efficacy, and now with US Food and Drug Administration (FDA) emergency use authorization (EUA)37,38 and European Medicines Agency (EMA) conditional marketing authorization39,40. While innovative and encouraging for other EIDs, it is too early to assert that mRNA vaccines represent a universal vaccine approach that could be broadly applied to other EIDs (such as bacterial or enteric pathogens). While COVID-19 mRNA vaccines are a useful proof of concept, gathering lessons from their large-scale deployment and effectiveness studies still requires more work and time.

[[Figure Omitted]]

While several DNA vaccines are licensed for veterinary applications, and DNA vaccines have shown safety and immunogenicity in human clinical trials, no DNA vaccine has reached licensure for use in humans41. Recombinant proteins vary greatly in design for the same pathogen (for example, subunit, virus-like particles) and are often formulated with adjuvants but have longer development times. Virus-like particle-based vaccines used for hepatitis B and human papillomavirus are safe, highly immunogenic, efficacious and easy to manufacture in large quantity. The technology is also easily transferable. Whole inactivated pathogens (for example, SARS-CoV-2, polio, cholera) or live attenuated vaccines (for example, SARS-CoV-2, polio, chikungunya) are unique to each pathogen. Depending on the pathogen, these vaccines also may require biosafety level 3 manufacturing (at least for COVID-19 and polio), which may limit the possibility of technology transfer for increasing the global manufacturing capacity.

Other vaccines are based on recombinant vector platforms, subdivided into nonreplicating vectors (for example, adenovirus 5 (Ad5), Ad26, chimpanzee adenovirus-derived ChAdOx, highly attenuated vectors like modified vaccinia Ankara (MVA)) and live attenuated vectors such as the measles-based vector or the vesicular stomatitis virus (VSV) vector. Either each vector is designed with specific inserts for the pathogen targeted, or the same vector can be designed with different inserts for the same disease. The development of the Merck Ebola vaccine is an example. ERVEBO is a live attenuated, recombinant VSV-based, chimeric-vector vaccine, where the VSV envelope G protein was deleted and replaced by the envelope glycoprotein of Zaire ebolavirus. ERVEBO is safe and highly efficacious, now approved by the US FDA and the EMA, and WHO prequalified, making VSV an attractive ‘platform’ for COVID-19 and perhaps for other EID vaccines26 although the −70 °C ultracold chain storage requirement still presents a challenge.

Other equally important considerations are speed of development, ease of manufacture and scale-up, ease of logistics (presentation, storage conditions and administration), technology transfer to other manufacturers to ensure worldwide supply, and cost of goods. Viral vectors such as Ad5, Ad26 and MVA have been used in HIV as well as in Ebola vaccines42. Finally, regulatory authorities do not approve platforms but vaccines. Each vaccine is different. However, with each use of a specific technology, regulatory agencies may, over time, become more comfortable with underlying technology and the overall safety and efficacy of the vaccine platform, allowing expedited review and approvals in the context of a pandemic43. With COVID-19, it meant that the regulatory authorities could permit expedited review of ‘platform’ technologies, such as RNA and DNA, that had been used (for other conditions) and had safety profiles in hundreds of people.

#### It’s a constant arms race.

**Morens and Fauci 13** – National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland, United States of America

David M. Morens and Anthony S. Fauci, "Emerging Infectious Diseases: Threats to Human Health and Global Stability," PLoS Pathog 9(7): e1003467, 7-4-2013, <https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1003467>

Will We Ever Eliminate Emerging Infectious Diseases?

While it has become possible to eradicate certain infectious diseases (smallpox and the veterinary disease rinderpest), and to significantly control many others (dracunculiasis, measles, and polio, among others), it seems unlikely that we will eliminate most emerging infectious diseases in the foreseeable future. Pathogenic microorganisms can undergo rapid genetic changes, leading to new phenotypic properties that take advantage of changing host and environmental opportunities. Influenza viruses serve as a good example of emerging and reemerging infectious agents in their ability to rapidly evolve in response to changing host and environmental circumstances via multiple genetic mechanisms. New “founder” influenza viruses [21] appear periodically, cause a pandemic, raise widespread population immunity, and then, in response to human immune pressures, evolve and persist for decades using multiple genetic evolutionary mechanisms to sustain continual immune escape. The 1918 influenza pandemic virus is one example: over the past 95 years, its descendants have evolved continually by antigenic drift, intra-subtypic reassortment, and antigenic shift, the latter producing new pandemics in 1957 and 1968 [14]. Even the genetically complex 2009 pandemic H1N1 influenza virus is a descendant of the 1918 virus [14]. Such continuous genetic hyper-evolution forces us to develop new influenza vaccines containing new antigens on an annual basis.

In the meantime, new human diseases keep emerging. As noted, in late 2012 the novel MERS coronavirus emerged in Saudi Arabia [13], and in early 2013 a new H7N9 avian influenza virus became epizootic in Eastern China, causing 132 spillover infections of humans (as of June 7, 2013), with 28 percent case fatality [10], [22]. Its pandemic potential, if any, remains to be determined. Whether or not such outbreaks become more widespread, they nonetheless attract global attention and require significant international effort to monitor and contain. Microbial advantages can be met and overcome only by aggressive vigilance, ongoing dedicated research, and rapid development and deployment of such countermeasures as surveillance tools, diagnostics, drugs, and vaccines.

We appear to be entering a new era in which several important emerging, reemerging, and stable infectious diseases are becoming better controlled (e.g., hepatitis B, rabies, Haemophilus influenzae type B, and even to some extent HIV/AIDS). However, our success in stopping the many new emerging diseases that will inevitably appear is not assured. We have many tools in our armamentarium, including preparedness plans and stockpiles of drugs and vaccines. But each new disease brings unique challenges, forcing us to continually adapt to ever-shifting threats [1]–[10], [23]. The battle against emerging infectious diseases is a continual process; winning does not mean stamping out every last disease, but rather getting out ahead of the next one.

#### The tempo and threat level is rising faster than ever, so we must update our innovation system. Evolutionary pandemics will pose a greater threat than climate change and nuclear war. Relying on post-hoc govt interventions will doom us all. (Imagine that omicron’s fatality rate was 50%...)

**Dhillon 17** – former senior govt advisor on pandemic control; MD, Instructor-Harvard Med School, Physician-Brigham and Women’s Hospital in Boston

Ranu S. Dhillon, works on building health systems in developing countries and Advisor to the president of Guinea during the Ebola epidemic; Devabhaktuni Srikrishna; and David Beier, managing director of Bay City Capital. He previously served in several leadership roles at the intersection of government, policy, and technology, including chief domestic policy advisor to then-Vice President Al Gore, vice president for government affairs and policy at Genentech, senior vice president of global government affairs at Amgen, and counsel to the U.S. House Judiciary Committee; The World Is Completely Unprepared for a Global Pandemic, MARCH 15, 2017, Harvard Business Review, https://hbr.org/2017/03/the-world-is-completely-unprepared-for-a-global-pandemic

In 2003 a doctor with SARS unknowingly infected several guests while staying at a Hong Kong hotel, and overnight the virus reached across the globe. China is currently battling a bird flu that kills nearly half of the people infected. If Ebola, which transmits through fluids, were spread by air, or if Zika, which has reached over 50 countries, were as deadly as Ebola, we would be facing an unprecedented catastrophe. An uncontrolled outbreak or bioterror attack could result in a contagion that kills over 30 million people.

We fear it is only a matter of time before we face a deadlier and more contagious pathogen, yet the threat of a deadly pandemic remains dangerously overlooked. Pandemics now occur with greater frequency, due to factors such as climate change, urbanization, and international travel. Other factors, such as a weak World Health Organization and potentially massive cuts to funding for U.S. scientific research and foreign aid, including funding for the United Nations, stand to deepen our vulnerability. We also face the specter of novel and mutated pathogens that could spread and kill faster than diseases we have seen before. With the advent of genome-editing technologies, bioterrorists could artificially engineer new plagues, a threat that Ashton Carter, the former U.S. secretary of defense, thinks could rival nuclear weapons in deadliness.

The two of us have advised the president of Guinea on stopping Ebola. In addition, we have worked on ways to contain the spread of Zika and have informally advised U.S. and international organizations on the matter. Our experiences tell us that the world is unprepared for these threats.

We urgently need to change this trajectory. We can start by learning four lessons from the gaps exposed by the Ebola and Zika pandemics.

Faster Vaccine Development

The most effective way to stop pandemics is with vaccines. However, with Ebola there was no vaccine, and only now, years later, has one proven effective. This has been the case with Zika, too. Though there has been rapid progress in developing and getting a vaccine to market, it is not fast enough, and Zika has already spread worldwide.

Many other diseases do not have vaccines, and developing them takes too long when a pandemic is already under way. We need faster pipelines, such as the one that the Coalition for Epidemic Preparedness Innovations is trying to create, to preemptively develop vaccines for diseases predicted to cause outbreaks in the near future.

Point-of-Care Diagnostics

Even with such efforts, vaccines will not be ready for many diseases and would not even be an option for novel or artificially engineered pathogens. With no vaccine for Ebola, our next best strategy was to identify who was infected as quickly as possible and isolate them before they infected others. Because Ebola’s symptoms were identical to common illnesses like malaria, diagnosis required laboratory testing that could not be easily scaled. As a result, many patients were only tested after several days of being contagious and infecting others. Some were never tested at all, and about 40% of patients in Ebola treatment centers did not actually have Ebola.

Many dangerous pathogens similarly require laboratory testing that is difficult to scale. Florida, for example, has not been able to expand testing for Zika, so pregnant women wait weeks to know if their babies might be affected. What’s needed are point-of-care diagnostics that, like pregnancy tests, can be used by frontline responders or patients themselves to detect infection right away, where they live. These tests already exist for many diseases, and the technology behind them is well-established. However, the process for their validation is slow and messy. Point-of-care diagnostics for Ebola, for example, were available but never used because of such bottlenecks.

Greater Global Coordination

We need stronger global coordination. The responsibility for controlling pandemics is fragmented, spread across too many players with no unifying authority. In Guinea we forged a response out of an amalgam of over 30 organizations, each of which had its own priorities. In Ebola’s aftermath, there have been calls for a mechanism for responding to pandemics similar to the advance planning and training that NATO has in place for its numerous members to respond to military threats in a quick, coordinated fashion.

This is the right thinking, but we are far from seeing it happen. The errors that allowed Ebola to become a crisis replayed with Zika, and the WHO, which should anchor global action, continues to suffer from a lack of credibility.

Stronger Local Health Systems

International actors are essential but cannot parachute into countries and navigate local dynamics quickly enough to contain outbreaks. In Guinea it took months to establish the ground game needed to stop the pandemic, with Ebola continuing to spread in the meantime. We need to help developing countries establish health systems that can provide routine care and, when needed, coordinate with international responders to contain new outbreaks.

Local health systems could be established for about half of the $3.6 billion ultimately spent on creating an Ebola response from scratch. Access to routine care is also essential for knowing when an outbreak is taking root and establishing trust. For months, Ebola spread before anyone knew it was happening, and then lingered because communities who had never had basic health care doubted the intentions of foreigners flooding into their villages. The turning point in the pandemic came when they began to trust what they were hearing about Ebola and understood what they needed to do to halt its spread: identify those exposed and safely bury the dead.

With Ebola and Zika, we lacked these four things — vaccines, diagnostics, global coordination, and local health systems — which are still urgently needed. However, prevailing political headwinds in the United States, which has played a key role in combatting pandemics around the world, threaten to make things worse. The Trump administration is seeking drastic budget cuts in funding for foreign aid and scientific research. The U.S. State Department and U.S. Agency for International Development may lose over one-third of their budgets, including half of the funding the U.S. usually provides to the UN. The National Institutes of Health, which has been on the vanguard of vaccines and diagnostics research, may also face cuts. The Centers for Disease Control and Prevention, which has been at the forefront of responding to outbreaks, remains without a director, and, if the Affordable Care Act is repealed, would lose $891 million, 12% of its overall budget, provided to it for immunization programs, monitoring and responding to outbreaks, and other public health initiatives.

Investing in our ability to prevent and contain pandemics through revitalized national and international institutions should be our shared goal. However, if U.S. agencies become less able to respond to pandemics, leading institutions from other nations, such as Institut Pasteur and the National Institute of Health and Medical Research in France, the Wellcome Trust and London School of Hygiene and Tropical Medicine in the UK, and nongovernmental organizations (NGOs have done instrumental research and response work in previous pandemics), would need to step in to fill the void.

There is no border wall against disease. Pandemics are an existential threat on par with climate change and nuclear conflict. We are at a critical crossroads, where we must either take the steps needed to prepare for this threat or become even more vulnerable. It is only a matter of time before we are hit by a deadlier, more contagious pandemic. Will we be ready?

**Independently – Antibiotic resistance will cause extinction now – New studies prove that boosting the innovation pipeline is necessary**

**Talkington 20** – oversees teams of policy experts, scientists, and advocates for Pew’s work on public health issues, including the rise of antibiotic-resistant bacteria,

Kathy Talkington, "The U.S. Is Not Prepared to Combat 'Existential Threat' of Antibiotic-Resistant Superbugs," The Pew Charitable Trusts, 7-27-2020, <https://www.pewtrusts.org/en/research-and-analysis/articles/2020/07/27/the-us-is-not-prepared-to-combat-existential-threat-of-antibiotic-resistant-superbugs>

At the July launch of the AMR Action Fund, Admiral Brett P. Giroir, U.S. assistant secretary for health, said the following:

"Antimicrobial resistance, I do believe, is the existential threat of this century."

Giroir’s warning is dire—but it’s not new. For years, leading public health and national security experts around the world have sounded the alarm about the growing threat posed by antibiotic-resistant bacteria. Commissions led by world-renowned economists, declarations from the United Nations General Assembly, urgent threat reports from the Centers for Disease Control and Prevention, and more have all come to the same conclusion: Antimicrobial resistance is a known and certain danger—and the global level of preparedness does not match the magnitude of the threat.

In June, The Pew Charitable Trusts sent a letter to the leaders of the Senate Committee on Health, Education, Labor, and Pensions, providing recommendations for how the U.S. can better prepare for future pandemics. The letter highlighted the urgent need for government incentives to help fix the broken antibiotic market. Pew recently reiterated this call to action in partnership with the World Health Organization.

There is widespread and longstanding consensus that such incentives are needed to revitalize and sustain the woefully inadequate antibiotic pipeline. Without them, antibiotic developers will continue to go bankrupt, and innovation will continue to stagnate. Now is the time for action. Policymakers must ensure that the U.S. is not caught flat-footed when the inevitable superbug outbreak hits. Some threats we cannot begin to anticipate, but when it comes to antibiotic-resistant bacteria, there’s no excuse for being unprepared.

**Specifically – Only new bacteriophage breakthroughs at-scale will solve ABR**

**Principi et al. 19** – Nicola Principi, Professor Emeritus of Pediatrics, Università degli Studi di Milano, Milan, Italy, Ettore Silvestri and Susanna Esposito, Department of Surgical and Biomedical Sciences, Pediatric Clinic, Università degli Studi di Perugia, Perugia, Italy

Nicola Principi, Ettore Silvestri, and Susanna Esposito, "Advantages and Limitations of Bacteriophages for the Treatment of Bacterial Infections," Front. Pharmacol. 10:513, 5-8-2019, <https://www.frontiersin.org/articles/10.3389/fphar.2019.00513/full#h4>

Potential Advantage of Bacteriophage (BP) Use to Treat Bacterial Infections

Theoretically, there are no bacteria that cannot be lysed by at least one BP. In this regard, BPs are significantly more effective than antibiotics, as, although some antimicrobial drugs have a very large spectrum of activity, an antibiotic able to kill all the bacterial species does not exist. However, the most attractive characteristic of BPs is their specificity of action, i.e., their ability to kill only the pathogen that they can recognize.

They have a very narrow spectrum of activity, which avoids the most important problem strictly related to the antibiotic administration, i.e., the influence on the entire microbiome with elimination of potentially beneficial bacteria, the overgrowth of secondary pathogens and the emergence of resistant bacteria (Domingo-Calap and Delgado-Martínez, 2018). Use of BPs without modification of the microbiota has been reported by several studies in both animals and humans. In mice, oral administration of four T4-like BPs effective against diarrhea-associated E. coli did not lead to any collateral damage of non-pathogenic bacteria of the same species (Chibani-Chennoufi et al., 2004). In humans, data confirming the specificity of BP action were shown in the study conducted by Sarker et al. (2012). These authors administered for 2 days an oral cocktail of nine T4-like E. coli BPs to 15 healthy adults. After a wash-out of 5 days, even though the given BPs could be detected in the feces of almost all treated subjects, no modification of gut microbiota composition was evidenced.

In comparison to antibiotics, BPs are supposed to have several other advantages. It is thought that BPs are significantly safer and better tolerated, as they replicate only in the target bacterium but cannot infect mammalian cells. This conclusion seems supported by all the experiences gathered in the past in Eastern Europe and all the studies carried out more recently in experimental animals and humans, which have not reported significant adverse events following BP administration (Kakasis and Panitsa, 2018). Moreover, administration is easier, as BPs do not need repeated administrations shortly after one another over several days, as is commonly required for antibiotics because they can remain in the human body for relatively prolonged periods of time, i.e., up to several days (Bogovazova et al., 1991, 1992). In general, very few doses are needed because of the increase in BP concentration in the site of infection after the initial administration. Contrarily to antibiotics, their effect is limited to the site of infection that can be reached, even when bacteria are situated in a body organ or system in which antimicrobials can hardly penetrate. A lytic phage, EC200(PP), active against S242, a fatal neonatal meningitis E. coli strain, was evaluated in models of meningitis with 100% fatality. Though low titres of the BP were detected in the central nervous system, treatment 1 and 7 h post-infection rescued 100% of pups (Pouillot et al., 2012).

Using the new cost-effective, large-scale DNA sequencing and DNA synthesis technologies, BPs can be engineered to be able to overcome some limitations of antibiotic treatment. A good example of this is given by the evidence that BPs can disperse biofilm, a structure that makes infections difficult to eradicate with standard antibiotic therapy even if bacteria are sensitive to the administered drug. In an in vitro study, Lu and Collins engineered a BP affective against an E. coli producing biofilm to express a biofilm-degrading enzyme (Lu and Collins, 2007). A simultaneous attack to the bacterial cells and the biofilm matrix was possible. The results were very encouraging, as the engineered BP reduced bacterial biofilm cell count by approximately 99.9%. Moreover, BP genetic modifications can help to fight bacterial resistance to antibiotics. Edgar et al. (2012) introduced in lysogenic phages the genes rpsL and gyrA, which confer sensitivity in a dominant fashion to two antibiotics, streptomycin and nalidixic acid, respectively. They found that, after engineering, the minimal inhibitory concentrations of bacterial strains previously defined resistant to these drugs were significantly reduced to levels usually found in sensitive pathogens.

Finally, the use of BPs might be less expensive than that of antibiotics whose targets are multidrug-resistant pathogens. In a small group of patients suffering from methicillin-resistant Staphylococcus aureus infection, Miedzybrodzki et al. (2007) found that use of BPs significantly reduced healthcare costs.

#### Scenario B is Leadership –

#### Biotech lead will be the key determinant

Carlson et al 9/14 – Engineering Prof @ UWA; inaugural deputy assistant secretary of defense for China; and IR Prof focused on biosecurity @ GU with a PhD in molecular biology from JHU

Rob Carlson, also managing director at Bioeconomy Capital, an early-stage venture capital firm; and Chad Sbragia, also former director of the China Research Group for the U.S. Marine Corps and now a research staff member at the Institute for Defense Analyses; and Kate Sixt, also assistant director of the Strategy, Forces and Resources Division at the Institute for Defense Analyses, where she leads the Chemical, Biological, Radiological, and Nuclear Analysis group; BEYOND BIOLOGICAL DEFENSE: MAINTAINING THE U.S. BIOTECHNOLOGY ADVANTAGE, 14 September 2021, https://warontherocks.com/2021/09/beyond-biological-defense-maintaining-the-u-s-biotechnology-advantage/

From 2007 to 2008, tainted supplies of Chinese-manufactured heparin, a common blood thinner, led to 81 deaths across the United States. This should have been a wake-up call to the Department of Defense. Over the last two decades, biotechnology has become a key component of American supply chains, perhaps accounting for 20 percent of the chemicals the U.S. military uses. Those supply chains now span the globe and contain a significant amount of material produced in China. Remarkably, the full extent of the military’s dependence on Chinese biotechnology is unknown because the U.S. government is not assessing it. These dependencies extend beyond pharmaceuticals to fundamentals such as solvents and polymers. Just try and paint an aircraft without xylenes. If you’ve never thought about how difficult it would be, well that’s exactly the problem.

The Department of Defense has historically viewed biotechnology narrowly in relation to military medicine and biodefense. As a result, the vital role of biotechnology in military readiness and national security remains poorly understood. Biowarfare and bioterrorism are real risks, but approaching the nation’s biotechnology security needs only in these terms will leave the country ever more vulnerable.

China, by contrast, has been integrating biotechnology into its strategic development and elevating biotechnology to a key component of national security. China’s military-civil fusion development strategy makes biotechnology a core priority for the People’s Liberation Army. This strategy has one goal: to bring together China’s civilian and military industrial bases in order to better project power. To that end, China has cornered supply chains in multiple sectors, including pharmaceuticals ingredients and other important chemicals.

Stephanie Rogers, the Defense Department’s acting principal director for biotechnology, recently declared that “the nation that leads the world in biotechnology will accrue enduring economic, societal, and defense gains.” Unfortunately, this awareness has yet to be reflected in government policy. Biotechnology security is national security — for the United States and for China. The Department of Defense should recognize biotechnology’s role as a foundational technology and make biotechnology development and supply chain security a priority.

Maintaining America’s Biotechnology Advantage

Biotechnology in the United States is a significant contributor to the economy. By one estimate, in 2017, U.S. biotechnology revenues exceeded $400 billion, or 2 percent of gross domestic product, substantially surpassing better-measured sectors such as mining. Bioeconomy revenues have grown at an average rate of 10 percent annually for two decades. Notably, U.S. biotechnology revenues alone were approximately equal to worldwide semiconductor revenues for 2017. Biotechnology now supplies critical medicines, and, as more than 90 percent of the corn and soy grown in the United States is genetically modified, biotechnology feeds the armed forces. Industrial biotechnology is responsible for upward of 20 percent of chemicals produced in the United States, suggesting a similar proportion of chemicals used in the military are also biologically derived. And these impressive figures may still be significant underestimates: Using a different methodology, the U.S. National Academy of Sciences recently concluded that the biotechnology industry contributes 5 to 7 percent of U.S. gross domestic product. Biotechnology, therefore, may already constitute an even larger share of the military supply chain.

As biotechnology continues to mature, its contribution to physical and economic security will become even more significant. Tools are now being deployed that enable the engineering and biomanufacturing of materials that will eventually not only displace petrochemicals but also surpass them in production scale and performance. Over the next ten to twenty years, biological production could soon supply up to 60 percent of physical inputs across the global economy, and biotechnology could have a “direct economic impact of up to $4 trillion a year.”

While the United States is arguably still leading in biotechnology, it risks losing this lead to China. In China, biotechnology is a national development and a security matter. China’s Innovation Driven Development Strategy emphasizes biotechnology’s essential role in the country’s economic development, while the Military-Civil Fusion Development Strategy seeks to ensure that biotechnology research is also oriented toward the country’s military and broader security goals. Chinese biotechnology revenues are reported to be of a similar size to those in the United States, although they are subject to even lesser clarity in reporting.

While China continues its licit and illicit acquisition efforts targeting the U.S. biotechnology sector, it is also shifting its attention to domestic innovation. In time, this will provide the People’s Liberation Army with new capabilities and increase both America’s and the Pentagon’s reliance on Chinese biotechnology products.

Recommendations As early as 1958, the Department of Commerce was tracking the economic contribution of semiconductors, even though they made up less than 0.1 percent of the gross domestic product. Yet, today, the U.S. government has made no equivalent effort to track the much more significant role of biotechnology. This illiteracy is a national security issue. American and Chinese bioeconomies are in competition, and Beijing asserts that it is investing with the intent to take, and to then maintain, the lead. To sustain America’s advantage, the U.S. Department of Defense should better understand its reliance on biotechnology and increase investment in it accordingly. The Pentagon’s recent investment in the BioIndustrial Manufacturing and Design Ecosystem is a notable step in the right direction. However, the seven-year budget for this project is approximately the cost of a single F-35A. For an investment that could impact the entire defense supply chain, this is inadequate. We recommend the following plan of action for the Department of Defense to take its place alongside the Departments of Commerce and State in the broader interagency effort to secure America’s biotechnology advantage. First, in close coordination with the Department of Commerce, the Department of Defense should make a systematic effort to better understand the role of biotechnology in the economy, supply chains, and manufacturing. This, in turn, should inform additional oversight and regulatory controls. The responsibility to understand, prepare for, and respond to biotechnology threats is balkanized, spread across at least nine departments and agencies. Vulnerabilities in the bioeconomy will affect the Department of Defense in terms of readiness, soldier health, and the ability to fulfill missions. Addressing those vulnerabilities begins with a sustained, comprehensive effort to understand the role of biotechnology in industry today, as well as how that industry contributes to defense supply chains, and how military acquisition policy shapes biotechnology. To that end, the Pentagon should work with the Department of Commerce to create domestic reporting codes for biotechnology revenues and employment for the quarterly and annual economic census, and further incorporate those codes into the North American Industrial Classification System. Institutionalizing the gathering of these data is the first step toward sustainable policymaking and rational spending. The Department of Commerce should then consider adding import/export controls on biotechnology, while avoiding overly broad restrictions that suffocate innovation. Protecting foundational technologies using the Foreign Investment Risk Review Modernization Act and Export Control Reform Act will be critical for securing biotechnology. However, biotechnology competition is not exclusive to commercial activities. The Pentagon should assess critical vulnerabilities and dependencies to assist the other agencies in bringing China’s foreign biotechnology access in line with standards in other major markets. The Department of Defense has been asked to document and secure supply chains critical to defense applications and to the overall U.S. economy. This should also apply to biotechnology. Current Pentagon efforts to expand domestic biological manufacturing capabilities are an important start, but a broader effort is needed. An empowered deputy national security adviser could help oversee the relationship between the Pentagon and the National Economic Council to promote and secure the military’s broader technology needs. Second, the Department of Defense should better study the accomplishments and intent of China, especially the Chinese military, in developing biotechnology as a strategic technology. Once the Department of Defense better understands critical U.S. biotechnology dependencies on China, it can begin the work of reducing them. This requires an interagency examination to identify cross-cutting resources, develop mitigation strategies, formulate best practices to bolster innovation, and expand outreach to allies and partners to reduce systemic gaps China could exploit. Partnership with industry and allies will allow the U.S. government to understand and counter Beijing’s efforts to distort commercial activity in its favor. To this end, the Department of Defense should mirror the National Security Council’s effort by creating an emerging technology portfolio within Office of the Under Secretary of Defense-Policy. While other technology offices in the Department of Defense are internally focused, an entity in this office that concentrates externally on foundational technology competition is required. Such an office may be able to address uncertainties in assessments of Chinese biotechnology revenues and capabilities. Finally, in coordination with the Department of State, the Department of Defense should identify opportunities for dialogue with the People’s Liberation Army about biotechnology-related security issues. It is time to include biotechnology in the dialogue mechanisms that compose bilateral U.S. defense relations with the People’s Liberation Army. This dialogue should prioritize the ethics of biotechnology in the context of future conflicts, the escalatory risks this technology creates, and the possibility of cooperation where the interests of the two nations intersect. Both sides should work toward a common understanding related to ethics, policies, and standards when operationalizing biotechnology. This will help avoid miscalculation and promote strategic stability. Unlike the U.S. government, Chinese leadership has a carefully considered position on the importance of biosafety and “biological problems” in national security. While these problems are understood to encompass traditional weapons concerns, they also extend to the health of the entire natural world in the context of ever-expanding applications of biotechnology. This position might provide an opportunity for constructive engagement at a time when tensions are rising. Conclusion The Pentagon needs to expand its approach to biotechnology beyond biodefense. If China maintains biological warfare aspirations, by all means address those. But defense planners should also address China’s broader approach to biotechnology and its integrated approach to civil-military fusion.

Securing biotechnology secures the nation. Maintaining the U.S. lead in biotechnology is critical to the nation’s economic and military resilience in war, peace, and the gray zone short of conflict. This requires better biotechnology collaboration — within the U.S. government, with allies and partners, and even, where possible, with competitors.

#### Retrenchment causes extinction

Rapp-Hooper 20 – Senior Fellow for Asia Studies at CFR & Senior Fellow in the China Center at Yale Law

Mira Rapp-Hooper, Stephen A. Schwarzman Fellow at the Council on Foreign Relations, 2020, Saving America’s Alliances: The United States Still Needs the System That Put It on Top, Foreign Affairs

The stakes of failing to reform the alliance system could scarcely be higher. If Washington does not act, it will miss the opportunity to protect its dearest interests on relatively favorable terms, before China’s growing power and Russia’s revanchism undermine the system’s proven guarantees. The reform agenda recommended here is vast, but it is far less burdensome than a U.S. foreign policy that cannot rely on allies. The United States can no more go it alone now than it could in the immediate postwar years. Whether the United States has alliances or not, American security and prosperity will still require an open and independent Asia and Europe. Even if Washington pulled back from both theaters, the United States would still face cyberattacks, financial and infrastructural disruptions, and assaults on its democratic institutions. And by retrenching, Washington would lose whatever readiness for conflict it currently has. If the country later joined a war abroad, it would have to do so only after significant time delays and without the allied cooperation that might have allowed it to prevail. Put simply, the United States might fall into a conflict that it could have instead deterred—one now waged with hypersonic speed and destruction.

#### Strong commercial innovation will be the key

Saeed 21 – former senior American diplomat with expertise on North Asia and the Middle East, she served as deputy U.S. coordinator for information and communications technology policy at the State Department, worked on the negotiating team for China’s accession to the World Trade Organization, and advised the under secretary of state for economic and business affairs on U.S. economic policy towards Asia; now CEO, Telegraph Strategies LLC, a risk management firm focusing on the analysis of political and economic trends

THE SINO-AMERICAN RACE FOR TECHNOLOGY LEADERSHIP, 2021, <https://warontherocks.com/2021/04/the-sino-american-race-for-technology-leadership/>

Setting the right foundation is crucial. Sound analytical judgments about China’s policies, plans, and prospects, along with a new framework for the relationship, are the starting point. Neither wholesale confrontation nor wholesale engagement are adequate to address U.S. concerns, but the relationship should be stable for this approach to have any chance of success. The view that economic competitiveness, innovation, and democratic norms are core components of national security should drive the development of a comprehensive strategy into which discrete policies of pressure, negotiation, multilateralism, high-level dialogue, and domestic measures fit. Industry should work closely with the government to ensure this perspective underpins U.S. policy, and the government should recognize that industry is central to the United States winning the technology race and therefore should get a vote on how to run it.

Out-competing and out-innovating China requires that America remain the world’s most attractive innovation hub, enticing the best talent, drawing in the most venture capital, and generating the largest revenues to support U.S. leadership of technology’s newest frontiers. It means continuing to “move fast and break things.” The ethos that made America a technology superpower can keep it so. It also means injecting some strategic realism into U.S. policy. As former Secretary of Defense William Cohen put it, China’s actions have caused the United States to say, “we can’t do business the way we’ve been doing business,” but, “we still have to do business.”

#### And, that will hinge on whether big pharma anticipates predictable and large net-revenues from pursuing innovative products

Robinson 11/15 – Ph.D., Professor of Health Economics & Director of the Berkeley Center for Health Technology, UC-Berkeley

James C. Robinson, the Leonard D. Schaeffer Professor, whose research and teaching focus on biotechnology and the healthcare delivery sectors, Competing With, And Learning From, China In The Global Pharmaceutical Innovation Race, 15 November 2021, https://www.healthaffairs.org/do/10.1377/forefront.20211110.463732/full/

The scale-up of pharmaceutical innovations generated by US biotechnology startups currently depends on product licensing by large pharmaceutical corporations. It works best for drugs eligible for the generous regulatory, tax, and subsidy provisions of the Orphan Drug Act of 1983, proving again the importance of public investment in ensuring commercial viability. Approximately half of the new drugs launched on the US market now are for orphan conditions. The ability of government to pick winners has been evident during the COVID-19 pandemic, as Operation Warp Speed financed vaccine product development, expansion of manufacturing capacity, and product distribution at a scale and speed exceeding the capacity of private investors. President Biden has proposed the creation of an Advanced Research Projects Agency for Health (ARPA-H) to fund cross-sectoral, high-risk research and R&D using the model of the Defense Advanced Research Projects Agency, the technology promoter responsible for the most fundamental innovations in defense in the past three decades, with $6.5 billion in dedicated funding. Yet, these proposals face adverse political headwinds.

For its part, the Chinese government provides direct subsidies for the scale-up of domestic firms that show the potential to become global leaders. Public funds account for 25 percent of total industry investment, and state development banks supplement these grants with low interest loans. Tax credits for business investment in applied product R&D, an effective policy instrument originally developed in the US, now are several times more generous in China.

Pricing And Product Demand

Innovation requires large-scale and predictable revenues to reward successful product launch. US pharmaceutical firms traditionally have enjoyed prices and revenues far in excess to those available in other nations. Congressional Democrats and the Biden administration have put forth proposals that would moderate drug prices, in turn, necessitating the expansion of other mechanisms for rewarding innovation. Some support would derive from initiatives to expand insurance coverage. High patent-protected drug prices would generate few revenues if manufacturers were to depend on patients for payment, as distinct from health insurers. Here again, the government already plays the decisive role. More than a third of the US population is covered by tax-financed public health insurance, and half has its private insurance subsidized through tax exclusions and premium subsidies. The Biden administration is committed to filling the remaining gaps in insurance coverage, which would support innovation by reducing the need for manufacturers to supply free drugs to the uninsured and finance copayment support programs for the underinsured. But further insurance expansion faces fierce opposition.

China favors domestic over foreign products in the design of its national drug formulary, with the intention of enabling its champions to achieve the economies of scale necessary to compete in global markets. For example, Chinese pharmaceutical firms have invested heavily in PD-1 oncology monoclonal antibodies. In 2020, the national formulary accepted four domestic PD-1 products and delisted foreign products in the therapeutic class. Access to the national formulary requires price discounts averaging 50 percent in the first year and further discounts in subsequent years. The low prices paid for foreign drugs in the domestic Chinese market will be accompanied by high prices charged for Chinese products launched in the US market. China interprets direct subsidies for product commercialization as an alternative to high prices as a reward for innovation, with the obvious advantage that governmental grants and loans are available only to Chinese firms. In contrast, the profits earned in the US market also accrue to foreign firms, which repatriate them to further develop their domestic innovation ecosystems.

China As Challenge And Opportunity

The challenge from China impacts each of the four pillars of pharmaceutical innovation, including the foundation in university research, the startup ecosystem, the scale-up of startups into global champions, and the assurance of predictable market demand. Unlike the imperative for rapid development of COVID-19 vaccines, the challenge from China cannot be dismissed as a once-in-a-century event. It is not going away.

Although the rise of China threatens the US life sciences industry, it also may indirectly support it. Fear of and competition with China may enable the US to overcome political gridlock and refurbish its science, revive its industry, and restore its erstwhile prominence.

### 3

#### Contention 3 is Solvency.

#### Most recent evidence proves that pharma companies are rampantly preventing drug competition by compensating one another not to challenge their weak patents, creating *de facto* monopolies. That is because antitrust law DOES forbid SOME direct payments, but currently ALLOWS more complex anticompetitive deals of this kind. Creates a huge perverse incentive to hide the ball.

Feldman 8/27 – Distinguished Professor of Law Chair & Director of the Center for Innovation, UC Hastings Law

Robin Feldman, Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation, The Price Tag of 'Pay-for-Delay', UC Hastings Research Paper Forthcoming, 27 Aug 2021, https://papers.ssrn.com/sol3/papers.cfm?abstract\_id=3846484

Our empirical results highlight the fact that pay-for-delay is a far more costly problem than previously recognized. The Supreme Court opened the door to deal with these settlements in Actavis, but in applying the decision, lower courts, competition agencies, and relevant parties have struggled with each of the three aspects of the phrase: “pay,” “for,” and “delay.” Despite the opinion’s expectation that lower courts would be able to provide structure to the rule of reason in a pay-for-delay inquiry, 125 that structure has not materialized in a meaningful manner. The problem arises in part from the nature of the rule of reason inquiry and in part from the forms of deals that have emerged. Although it is possible that the Justices never intended to allow pay-for-delay cases to move forward, the tone of the opinion belies such a cynical interpretation.

A. What Constitutes “Pay”

One might imagine that the notion of “pay” would be simple. Nevertheless, some courts have struggled with the question of what might constitute an exchange of value and whether the notion of payment can extend beyond cash. Beyond the notion of what types of value might be included in the notion of pay, the way in which the inquiry unfolds has created obstacles for parties and competition authorities to actually measure value in a way that would be satisfactory under a rule of reason analysis.

In particular, some parties have asserted that cash is king. From this perspective, the only exchange of value that might matter would be dollars changing hands. In the immediate wake of Actavis, some courts initially failed to recognize non-cash forms of compensation—such as no-authorized-generic clauses—as unexplained payments from brands to generics.126 Although higher courts eventually rectified decisions in Lamictal and Loestrin, for example, expanding the Actavis precedent to include methods of payments other than cash,127 damage was done. Effectively permitting certain forms of pay-for-delay—even temporarily—serves to incentivize similarly designed anticompetitive deals, at great cost to patients and society. 128 Protracted court battles also present a significant drain on regulatory bandwidth, particularly when every instance of anticompetitive conduct must be demonstrated to the courts.

In the sophisticated world of modern commerce, however, there are many ways to provide value beyond simply handing over bags stuffed with bills. For example, one of the most valuable assets for an entering generic is the 180-day period in which the first filing generic can enter the market free of competition from other generics. Generic companies may earn a substantial portion of their profit during this period of time.129 Brand-name companies, however, found a way to make that period of time into an asset that can substitute for a cash payment.

[FN]

126 See, e.g., In re Loestrin 24 Fe Antitrust Litig., 45 F. Supp. 3d 180 (D.R.I. 2014), vacated and remanded, 814 F.3d 538 (1st Cir. 2016); In re Lamictal Direct Purchaser Antitrust Litig., 18 F. Supp. 3d 560 (D.N.J. 2014), vacated and remanded sub nom. King Drug Co. of Florence v. Smithkline Beecham Corp., 791 F.3d 388 (3d Cir. 2015). The payment in the settlement litigated in Actavis was a cash transfer from the brand to the generic; subsequent pay-for-delay settlements have featured payment forms that are less easily enumerated, such as no-authorized generic agreements. In this case, the brand company—in lieu of a cash payment—agrees to not launch an authorized generic during the first-filing generic company’s 180-day exclusivity period, thereby boosting the generic company’s revenues.

128 Evidence since Actavis suggests that pharmaceutical companies hew closely to guidelines implied by court decisions. According to the FTC 2017 report, only 3 of 20 agreements with explicit compensation exceeded the $7M allowed by Actavis for litigation fees; moreover, following a spate of court cases finding that a no-AG promise amounted to anticompetitive payment, 2017 saw no settlement agreements that included a no-AG clause. See Betsy Lordan, FTC Staf Issues FY 2017 Report on Branded Drug Firms' Patent Settlements with Generic Competitors, FTC (Dec. 3, 2020), <https://www.ftc.gov/news-events/press-releases/2020/12/ftc-staff-issues-fy-2017-report-branded-drug-firms-patent>

[End FN]

The scheme springs from the fact that although a generic must obtain FDA approval to enter the market, the brand-name company already has such an approval in its pocket. Thus, the brand-name company may market its own generic version of a drug—called an authorized generic or a branded generic—without the need for a lengthy approval process.130 Although the Hatch-Waxman system does not explicitly provide for authorized generics in its legislation, court rulings have affirmed that nothing prevents the innovator company from marketing an authorized generic version of their branded drug.131

The launch of an authorized generic has significant consequences for a first-filing generic. According to the FTC, competing with an authorized generic can cost a generic first-filer up to 45% of its revenue during the exclusivity period.132 The ability to remove that threat becomes an asset that the brand-name company can hand to the generic, in exchange for an agreement to stay off the market. A brand-name company can promise not to introduce an authorized generic, particularly during the valuable 180-day period. The deal is a little like old movies portraying protectionist rackets, in which the neighborhood shakedown artist says, “Nice front window you have there. Be a real shame if it got smashed in.” Here, a brand-name company can say the equivalent of, “Nice 180-day exclusivity period. Be a real shame if you lost half of it. Tell you what, just stay off the market for a while, and it is all yours.”

As courts and competition authorities have become suspicious of these “no-authorized-generic” agreements, companies have developed ever-more-complex variations on the theme. Rather than explicitly promise to not compete by producing an authorized generic, a brand-name company can promise not to license any third parties to make authorized generics, while reserving the right to make an authorized generic itself. If the brand manufacturer has a limited track record of launching authorized generics, this agreement can have the same effect as the no-authorized generic clause.133 In yet another variation, the brand and generic can enter into an agreement in which the generic is obligated to pay a royalty amount, but that royalty will decline if the brand-name company launches a competing authorized generic.134

In other complicated variants, brand-name companies may give the generic who agrees to stay off the market a license to make an authorized generic version of their brand drug, with the generic paying a royalty to the brand.135 Particularly if the royalty payment that the generic must pay is less than the market value of the benefit, that excess value may be camouflaging a “reverse” flow of payments in exchange for the generic’s agreement to stay off the market.136

Courts and competition authorities now generally recognize that no-authorized-generic agreements can constitute a form of payment for the purposes of pay-for-delay, although it took some time to reach that point.137 Nevertheless, the law has not fully absorbed the anticompetitive potential of the complex variations. These convoluted variants are difficult to tease out, let alone establish sufficient proof through the rule of reason standards, making obfuscation a successful strategy. For example, the most-recent FTC reports showed 226 agreements between brand and generic companies that year, 138 a significant increase from the 170 settlements just two years prior.

139 Ninety percent of those agreements included a transfer of patent rights that were not at issue in the lawsuit. Many of these could easily constitute a transfer of value.140 Challenging even a simple no-authorized-generic agreement is no easy task. For example, although the judicial definition of payment now includes “no-authorized-generic” agreements,141 private plaintiffs or the government bears the burden of evaluating and presenting the terms of a no-authorized-generic agreement in terms of cash value.142 The requirement follows the logic that in order to demonstrate the unreasonably large nature of a payment, as the Actavis decision specified, plaintiffs generally are required to translate that agreement into a specific, quantifiable value to the court’s satisfaction. Thus, a plaintiff who wishes to challenge even a simple no-authorized-generic agreement as anticompetitive must be prepared to engage in an expensive and lengthy court battle, with no consistent approach to valuation.143 Consider the Effexor case.

The district court in Effexor rejected the plaintiffs’ valuation of a no-authorized-generic agreement, which was based on an estimation of what an authorized generic cost the generic manufacturer of a different drug with nearly identical sales.144 Plaintiffs were able to obtain a reversal on appeal,145 but obtaining the appellate decision, however, took three years beyond the time that had already passed for the trial court ruling. The more a deal reaches behind the back and around the ears, the harder it is tease out the value transfer and pin down a specific dollar equivalent.

[FN 141]

141 See, e.g., United Food & Com. Workers Loc. 1776 & Participating Emps. Health & Welfare Fund v. Teikoku Pharma USA, Inc., 74 F. Supp. 3d 1052, 1070 (N.D. Cal. 2014) (“I agree with the bulk of the recent decisions holding that courts need not restrict the definition of “payments” under Actavis to cash. See, e.g., In re Nexium (Esomeprazole) Antitrust Litig., 968 F.Supp.2d 367, 382 (D.Mass.2013) (rejecting a motion to dismiss because a no-authorized-generic term could be a payment for the delay because a broader definition of payment “serves the purpose of aligning the law with modern-day realities.”)”); see also Time Ins. Co. v. Astrazeneca AB, 52 F. Supp. 3d 705, 710 (E.D. Pa. 2014) (“reverse payments deemed anti-competitive pursuant to Actavis may take forms other than cash payments” when considering a no-authorized-generic agreement); King Drug, 791 F.3d at 403 (“We do not believe Actavis 's holding can be limited to reverse payments of cash. For the following reasons, we think that a no-AG agreement, when it represents an unexplained large transfer of value from the patent holder to the alleged infringer, may be subject to antitrust scrutiny under the rule of reason.”).

142 See Feldman & Misra, Fatal Attraction, supra note 8, at 259-260 (explaining how the often-onerous burden of proving anticompetitive harm under rule of reason rests on the plaintiffs); see also Feldman, Defensive Leveraging, supra note 51 (describing the difficulty of successfully pleading a rule of reason case).

[End FN]

The 2003 Medicare Modernization Act requires generic-brand agreements to be submitted to the FTC for review, 146 and the reports the FTC publishes from these insights can point other investigators to possible anticompetitive conduct.147 However, the FTC is limited in its resources to investigate individual cases; reports are frequently beset by publishing delays, offer only annualized statistics, and may fail to adequately appreciate the nuanced, rapidly evolving techniques used by drug companies.148

For example, in December 2020 the FTC finally released its annual report covering the year 2017. The report lists as examples of “possible compensation” arrangements including: declining royalty structures,149 AG licensing to subsequent filers, and agreements to not license AGs to third parties.150 The FTC declines to assess the anticompetitive quality of these arrangements as “beyond the scope of this report.”151 The report also finds zero cases of the no-authorized-generic agreements so prevalent a decade earlier. 152

It would be naïve, however, to assume that the end of simple no-authorized-generic clauses marks the end of authorized generics in pay-for-delay. Rather, anecdotal evidence suggests that the character of brand-generic patent settlements is simply changing in response to the spate of court rulings finding that no-authorized-generic clauses constitute payment under Actavis. 153

B. What Constitutes “For”

Similar to the notion of what constitutes “pay,” courts and agencies have struggled over whether a transfer of value in an agreement constitutes a payment for staying off the market or simply a payment for legitimate value provided by the generic.

Side deals come in many shapes and sizes including: 1) arrangements to promote other drugs in the firms’ portfolios; 154 2) licensing deals that allow the brand or generic to manufacture the other party’s drug;155 3) agreements authorizing the generic to manufacture and/or sell a brand’s “authorized generic” without filing for generic approval; 4) research and development collaboration on future projects; and 5) deals to supply the brand company with raw materials for manufacturing.156 Such side deals are rarely found outside the settlement context. According to one prominent academic in the field, “many—such as an arrangement by which a brand relies on a generic for its marketing expertise—belie common sense.”157

The valuation of agreements featuring noncash provisions is further complicated by the fact that the details of these settlements are kept secret.158 This shroud of secrecy makes it difficult to identify and quantify the value of noncash settlements. Even if the presence of side deals is suspected, plaintiffs will rarely, if ever, have access to the terms of those agreements. Several district courts have already dismissed pay-for-delay litigation for failing to plausibly allege a large and unjustified payment.159 For example, the district court in Actos dismissed the indirect purchasers’ claims that Takeda engaged in anticompetitive conduct by entering into settlement agreements with generic manufacturers.160 While the court shared the majority view that Actavis was not limited to settlements dealing with pure cash, it also held that to find an unlawful reverse payment involving non-cash settlement terms, the court “must be able to estimate the value of the term, at least to the extent of determining whether it is “large” and “unjustified.””161 Because the plaintiffs could not explain the basis for their assertions nor offer any method of calculating the value of the licensing side deal, there was no factual basis for the court to reasonably estimate the value of the settlement terms and evaluate the settlements’ alleged anticompetitive effect.

The legality of settlements featuring side deals continues to be challenged. While the majority view is that side deals are not immune to antitrust scrutiny, plaintiffs still bear the burden of pleading information sufficient to estimate the value of these agreements. To describe the task of determining whether these terms are “large” and “unjustified” as difficult is an understatement.

It is interesting to note that although the FTC’s reports on pay-for-delay settlements for fiscal years 2015162 and 2016163 reported no side deals, the most recent report for fiscal year 2017 listed three settlements with side deals.164 These side deals included an agreement in which the brand manufacturer assigned the generic manufacturer five patents unrelated to the litigated product at no cost, another in which the generic sold intellectual property related to the litigated product to the brand manufacturer, and a third in which the brand manufacturer acquired the generic manufacturer's potentially competing 505(b)(2) product that was the subject of the patent litigation.165 These indicators suggest there is reason for concern that side deals can be used to hide payments for delay and that courts and agencies would be unable to ferret out any anticompetitive conduct.

C. What Constitutes “Delay”

Creating a full sweep, courts have also struggled with the question of what constitutes delay. The uncertainty centers on whether an agreement in which the generic enters before the patents expire should be considered delay. Supporters of pay-for-delay settlements routinely argue that such settlements can be procompetitive because they facilitate early entry of a generic before a branded drug’s patents have expired.166

In such instances, consumers would benefit from lower prices sooner than if the Paragraph IV challenge had never taken place. In Actavis, the Supreme Court recognized this procompetitive potential, commenting that early entry settlements, or settlements permitting the patent challenger to enter the market before the patent expires, could “bring about competition . . . to the consumer’s benefit.”167

That argument, however, assumes the patent is valid and infringed.168 Various studies suggest that assumption is unwarranted. For example, a 2002 Federal Trade Commission report found that considering all the patent infringement cases between generic and brand manufacturers between 1992 and 2000, generic applicants prevailed in a staggering 73 percent of cases.169 Similarly, an academic analysis of Federal Circuit decisions between 2002 and 2004 in which the court made a final ruling on the merits of a pharmaceutical patent claim found that generic challengers had a 70 percent success rate.170

In a more recent analysis, a study of patent lawsuits filed in a federal district court between 2008 and 2009 found that accused infringers won 74 percent of the definitive merits rulings while patentees won only 26 percent of the time.171

In fact, the FDA has gone so far as to provide a registry of disputed patent information in order to address inaccurate or extraneous patent listings on new drugs.172 As the author has previously written, “one can never assume that just because a company holds a patent that the patent is either valid or validly applied to the drug at issue.”173

A patent that is invalid or not infringed would have no power to stop entry. Thus, if the generic had pursued the litigation to conclusion, the result could easily have moved the patent barrier out of the way, allowing the generic to enter right away. As a result, it would be nonsensical to say that there is no delay if the parties agreed to stay out of the market until the expiration date of a noninfringed patent. Nevertheless, some courts have failed to contemplate that possibility in analyzing agreements.

Consider In re Humira. 174 Plaintiffs alleged that AbbVie’s settlement agreements with biosimilar manufacturers, in which the biologic company granted licenses for biosimilars to market the Humira biosimilar in Europe in 2018 while delaying entry into the U.S. market until 2023, constituted an unlawful pay-for-delay scheme.175

In dismissing the lawsuit, the district court found that the settlements were permissible because they allowed AbbVie’s rivals to enter the U.S. market before the patents on Humira (the latest of which expires in 2039) expired.176 The court failed to recognize, however, that the settlements eliminated the possibility that the biosimilars might have entered the U.S. market earlier than the stipulated date if they had pursued the litigation to conclusion and prevailed. As with many cases, the patents might not have been valid or validly applied.

#### And – So-called “pay for delay” deals in the biologics context specifically do not yet fall within the legal scope of antitrust – But logically, they ought to

Carrier 18 – Michael A. Carrier is a Distinguished Professor at Rutgers Law and a leading authority in antitrust and intellectual property law with expertise in the pharmaceutical, high-technology, and music industries. Carl J. Minniti III, Rutgers Law School, J.D. 2017.

January 12, 2018, “BIOLOGICS: THE NEW ANTITRUST FRONTIER,” https://www.illinoislawreview.org/wp-content/uploads/2018/01/Carrier.pdf

In determining the appropriate antitrust analysis of settlements, an initial question centers on the application of FTC v. Actavis. We believe that, in a broad holding of general applicability, Actavis confirmed antitrust law’s vital role in evaluating the legality of settlements involving payment and delayed entry. The Court relied on **an array of previous cases to confirm that its precedents “make clear** that patent-related settlements can sometimes violate the antitrust laws.”

To be sure, the Court was not offering an antitrust assessment of biologic settlements. Nor could it have given that no court—even now, several years later—has considered settlements under the BPCIA. But we believe the **setting** of **complex pharmaceutical regulation under the BPCIA easily offers sufficient similarities to the Hatch-Waxman Act** to allow application of Actavis’s broad principles. In addition, payment to avoid the risk of biosimilar competition presents the same concerns highlighted in Actavis.

The linchpin in the antitrust analysis of settlements is whether a generic is excluded from the market based on a patent or payment. Exclusion based on a patent generally does not present antitrust concern because it is commonly understood that patent-term split agreements, by which brands and generics divide the remaining patent term by selecting a time for generic entry, do not violate the antitrust laws. The reason is that the parties’ compromise on the entry date reflects the odds of success in patent litigation. The greater the likelihood the patent is valid and infringed, the later in the period generic entry would be expected. The lower the likelihood, the earlier entry would be expected. A brand, however, is likely to gain additional exclusivity not explained by a patent by supplementing the parties’ entry-date agreement with a payment to the generic.

The same distinction between patent and payment should apply in the setting of biologics. The biologic manufacturer is entitled to rely on its patent to exclude a generic. But **it should not be able to pay a biosimilar to gain additional delay.** In determining whether there is payment, the court should consider, as one of us has explained before, whether the biologic manufacturer conveys “a type of consideration not available as a direct consequence of winning the lawsuit.” If the biosimilar manufacturer is able to obtain such consideration, “its exclusion from the market cannot be traced to the strength of the [biologic] patent.” In such a case, “the [biologic maker] is providing compensation beyond what even a valid and infringed patent would justify.”224 And, presenting antitrust concern, the biosimilar delays entering the market because of this payment.

One example of a form of payment that could arise in this setting involves a biosimilar’s access to a biologic’s distribution or reimbursement networks. In contrast to distribution through wholesalers and specialty distributors (each of which obtains a portion of revenues, reducing a biosimilar’s profitability), biologics could offer access to a “manufacturer direct” channel which, in selling directly to purchasers (e.g., specialty pharmacies and large hospitals), removes the “middleman.” Setting up an efficient supply chain is difficult and expensive, and not all biologics will be able to implement such a scheme. As a result, if a biologic has already set up direct distribution, one form of payment to a biosimilar could be access to, and integration into, the valuable network, which it would not be able to obtain through patent litigation.

Another type of payment could involve Group Purchasing Organizations (“GPOs”) or Pharmacy Benefit Managers (“PBMs”). GPOs are collections of providers that pool resources to maximize economies of scale in drug purchasing and sometimes function as distributors, gaining control over products offered to downstream purchasers.228 PBMs also manage prescription drug pro

[FOOTNOTES BEGIN]

221. HERBERT HOVENKAMP, MARK D. JANIS, MARK A. LEMLEY, CHRISTOPHER R. LESLIE, & MICHAEL A. CARRIER, IP AND ANTITRUST: AN ANALYSIS OF ANTITRUST PRINCIPLES APPLIED TO INTELLECTUAL PROPERTY LAW § 16.01[f] (3d ed. 2016). 222. Carrier, Payment After Actavis, supra note 219, at 9. 223. Id. 224. Id. 225. Id. 226. NIAZI, supra note 21, at 354–56; see also Jack McCain, Connecting Patients with Specialty Products, BIOTECHNOLOGY HEALTHCARE, Summer 2012, at 8, https://www.ncbi.nlm.nih.gov/pmc/articles/ PMC3411231/. 227. NIAZI, supra note 21, at 354–56. 228. Id. at 352, 353.

[FOOTNOTES END]

grams for downstream buyers and, in some cases, after negotiating rebates with manufacturers, limit the drugs sold under their plans. This latter role ensures that they “are very important” to a biosimilar manufacturer in controlling access to a biosimilar product.

We envision a scenario by which a settlement could include payment in the form of a biologic bringing a biosimilar under its umbrella, granting access to certain GPO and PBM agreements to which it would otherwise not have access.

Where there is payment, the court should consider its size. The Actavis Court compared the payment’s size to litigation costs. It stated that payments that “amount to no more than a rough approximation of the litigation expenses saved through the settlement” could be justified. Litigation costs in the biologics setting will generally be higher than in the small-molecule setting. In contrast to litigation in the Hatch-Waxman setting, with a generic in the initial stage only needing to review the Orange Book, law firms must conduct substantial pre-application investigations to identify patents that could be raised in the patent dance.

Finally, where there is at-risk entry, a settlement could include a “payment” from the biologic to the biosimilar, but that payment could constitute a legitimate forgiveness of damages. This presents **a nuanced case** that could be explained by the results of patent litigation. In other words, if the biologic wins, it is entitled to recover damages from the biosimilar. But if the biosimilar wins, it will not be required to pay anything. As a result, a biologic firm’s partial waiver of damages that the biosimilar could have owed falls within the range of what the latter could have obtained through successful litigation. In short, just like it has done in the Hatch-Waxman setting, the distinction between patent and payment can provide an appropriate framework for the antitrust analysis of settlements between biologics and biosimilars.

#### Plan: The United States federal government should increase prohibitions on anticompetitive reverse settlements of biologics.

#### That solves.

#### First – The plan prohibits all anticompetitive pay-for-delay deals. It establishes a presumption of illegality, which can be rebutted by a defendant if and only if they can conclusively prove that the deal bolstered competition. That flips their incentive structure.

Feldman 8/27 – Distinguished Professor of Law Chair & Director of the Center for Innovation, UC Hastings Law

Robin Feldman, Arthur J. Goldberg Distinguished Professor of Law, Albert Abramson ’54 Distinguished Professor of Law Chair, and Director of the Center for Innovation, The Price Tag of 'Pay-for-Delay', UC Hastings Research Paper Forthcoming, 27 Aug 2021, https://papers.ssrn.com/sol3/papers.cfm?abstract\_id=3846484

There is an old saying in the field of psychology that insanity is doing the same thing over and over again while expecting to get a different result. After watching plaintiffs and competition authorities struggle to satisfy the rule of reason in order to establish a pay-for-delay case, it is clear that continuing down the same path is unlikely to be fruitful.

The rule of reason, untethered, is a meandering test that cannot even be described in a simple sentence. The formulation rises from the 1918 Board of Trade case:

“The true test of legality is whether the restraint imposed is such as merely regulates and perhaps thereby promotes competition or whether it is such as may suppress or even destroy competition. To determine that question the court must ordinarily consider the facts peculiar to the business to which the restraint is applied; its conditions before and after the restraint was imposed; the nature of the restraint and its effect, actual or probable. The history of the restraint, the evil believed to exist, the reason for adopting the particular remedy, the purpose or end sought to be attained, are all relevant facts. This is not because a good intention will save an otherwise objectionable regulation or the reverse; but because knowledge of intent may help the court to interpret facts and to predict consequences.”177

Application of the rule in practice is no less nebulous than its formulation, despite the fact that courts add numbers to each of the various steps. The Supreme Court itself has called the rule of reason complex and burdensome. The intricate requirements of the rule, not to mention the burden it places both on parties and the courts,178 make the rule of reason particularly ill-suited for examining the ever-increasing number of agreements between brand and generic competitors. Although some scholars have argued that the rule of reason should be shelved entirely, such a broad-scale change is unnecessary for these purposes.

Pinning pay-for-delay reform squarely on an outright ban may not prove tenable, and other commentators have proposed intriguing alternatives. By one policy, for instance, if companies are unable to prove that their patent infringement settlement value was less than the cost of litigation and other services, then all that the generic company can receive is what it would be entitled to by a court ruling that a brand patent is invalid or not infringed.179

In other words, all the brand company can promise is what the court would give the generic company if the parties proceeded with the patent infringement litigation, and the generic won. No-authorized-generic clauses, among other creative anticompetitive ploys, would be presumed illegal by this framework. At the same time, it would permit patent settlements to remain where they are potentially procompetitive, eliminating unnecessary litigation between drug companies. Other prospective solutions seek to improve upon the fines used currently to disincentivize pay-for-delay conduct. As our analysis demonstrates, even companies fined by the FTC for pay-for-delay may profit handsomely from the practice.180 Considering the failure of fines to sufficiently discourage pay-for-delay, some scholars have advanced alternative punishments for cited drug companies. For instance, a first-filing generic company that agreed to postpone production in exchange for a no-authorized-generic clause could be stripped of its 180-day exclusivity period.181 Additional legislation might stipulate that brand companies forfeit the chance to earn additional non-patent regulatory exclusivities for a drug whose monopoly period they paid off competitors to extend. This way, instead of simply reducing the profits of offending drug-makers, the repercussions of pay-for-delay redound as social benefit.

Despite potential remedy-related reforms, however, the most important change needed pertains to evaluating the anticompetitive nature of the agreement itself. The landmark decision in Actavis expressed optimism that courts would be able to manage the analysis in a more structured manner. That reality has not materialized. To resolve the problem, one should return to the basic notion that agreements between competitors are strongly disfavored under antitrust law.

Given that agreements between competitors are disfavored, the test for agreements between brands and generics in the context of Hatch-Waxman litigation should begin with a presumption that the agreement is anticompetitive. This approach respects the essential design of the Hatch-Waxman system to ensure rapid entry of generic drugs, in part, by providing an incentive for generic drug companies to challenge patents that are invalid or invalidly applied.182 Only when the public interest is clearly served should the presumption fall.

#### Second – Settlements which either delay entry or are based on weak patents would be found anticompetitive. That uniquely solves circumvention, and restores the patent system to its intended calibration, lowering prices and spurring real innovation.

Anderson 20 – Professor of Public Health & Professor of Medicine, Johns Hopkins; Director, JHU Center for Hospital Mgmt.

Gerard F. Anderson, PhD; Laura Karas, MD, MPH, Dept. of Health Policy & Mgmt. in the JHU Bloomberg School of Public Health; and Robin Feldman, Arthur J. Goldberg Distinguished Professor of Law and Director of the Center for Innovation at UC Hastings Law, Visiting Professor at UCLA Law, Pharmaceutical “Pay-for-Delay” Reexamined: A Dwindling Practice or a Persistent Problem?, 71 Hastings L. J. 959 (May 2020), <https://hastingslawjournal.org/wp-content/uploads/Karas-et-al.-71.4.pdf>

We propose several substantive changes to the antitrust approach to pay-for-delay settlements.

First, the key criterion in determining an unlawful agreement should be the existence of a restriction on generic entry—not the size or presence of a value transfer—considered in light of the strength of the category of patent in question. Arguably, the legitimacy of a pay-for-delay settlement is predicated on the strength of the underlying patent; in other words, pay-for-delay is only a problem insofar as the patent to which the deal relates is invalid or aimed at the wrong product, since the generic could enter the market immediately upon that determination. Much is at stake in these deals; several years of lost patent protection could translate into several billions of dollars of lost savings for the brand company. 57 Pay-for-delay agreements tend to settle litigation over a “secondary patent,” which is a patent on some feature of a drug other than the active pharmaceutical ingredient, such as a production process, a method of treatment, a salt or crystalline form, a new delivery mechanism, a new formulation, or even an ancillary aspect of a drug, such as the pill’s coating.58 Evidence shows that secondary patents form part of a deliberate strategy to prolong a drug’s effective period of patent protection.59 Though few patent cases reach a final decision on validity,60 secondary drug patents are frequently found invalid when challenged.61 Thus, secondary patents may over-reward a pharmaceutical drug’s actual innovative contribution with unwarranted extensions of effective patent protection, and both the brand and generic companies may have a good sense of the likelihood that a disputed secondary patent will survive a court challenge. For this reason, the category of the patent in question in a pay-for-delay agreement is highly germane to a meaningful examination of the potential illegality of the deal.

Next, the United States should move closer to a presumptive standard in evaluating pay-for-delay settlements in order to achieve more efficient and effective antitrust enforcement. The pay-for-delay bills introduced in Congress will help achieve that goal, as would adopting a standard similar to that of the European Union that places emphasis on an agreement’s aim to restrict competition rather than downstream effects on the marketplace.62 Although intent can be difficult to establish under U.S. law—particularly if plaintiffs must find smoking-gun evidence of subjective intent—those difficulties can be overcome by designing standards that use objective criteria as a means of inferring a company’s likely intent. The category of patent and the failure to sue on the core chemical or biological patent could be part of those objective criteria. The reluctance to call pay-for-delay presumptively illegal in the United States reflects a desire to preserve the freedom to settle and to avoid clogging the courts with costly and protracted patent litigation. However, the current approach to pay-for-delay favors industry over patients, and unless the approach is changed, drug prices will remain supra-competitive for periods longer than the HatchWaxman regulatory regime intended. In addition, deterring the litigation in the first place would reduce the burden on the courts, as well as the burden on society.

Finally, regulatory disincentives may be a more effective deterrent of payfor-delay deals than monetary penalties. For example, the FTC and FDA could jointly prohibit a generic company that is found to have participated in pay-fordelay from eligibility for the 180-day exclusivity period for any Abbreviated New Drug Application (ANDA) that it files in the ensuing five years. Without exclusive marketing rights as the first generic to file an ANDA, the generic company stands to lose the bulk of its profits on any generic drug launched in that five-year period. By enticing generic companies with profitable settlements, brand companies have co-opted the paragraph IV challenge, initially intended to enable generic companies to challenge weak or invalid patents.63 As a penalty for participation in pay-for-delay deals, the generic company could be prohibited from filing a paragraph IV certification on any ANDA for a certain number of years, effectively making the company ineligible for the 180-day exclusivity period and shutting them out of pay-for-delay settlements—at least those arising from patent litigation. Regulatory disincentives can counterbalance the “carrots” in the Hatch-Waxman Act, thereby rewarding innovation and hastening competition when the time is ripe.

CONCLUSION

Settlement agreements to end patent disputes are common and not in and of themselves indicative or suggestive of antitrust infringement. Often, settlements are a favored alternative to continuing costly litigation. However, pay-for-delay settlements come at a steep cost to patients by delaying the entry of less expensive generic alternatives to brand drugs. The ability to wield competition laws effectively against these settlements is of major importance to regulators, policymakers, and patients. Shifting the focus of antitrust scrutiny to restrictions on generic entry vis-à-vis the strength of the category of underlying patent, and creating disincentives for generic companies to acquiesce to pay-for-delay deals, will help grease the wheels of the Hatch-Waxman Act and accelerate the path to affordable drug prices for U.S. patients.