Restoring the Balance Between Innovation and Generic Manufacturing of Medicines

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Introduction

Nearly 30 years, the Reagan Administration and a Democratic Congress came together to sign The Drug Price Competition and Patent Term Restoration Act of 1984, (otherwise known as The Hatch-Waxman Act.)[1] That law incentivize companies to make low cost versions of medicines well before a drug patent expired by making it easier to challenge the intellectual property of the medicine. Since then, the generic drug industry has grown rapidly to become essential to the ability of consumers, insurers and government health programs to provide high value care for less money.

But increasingly the generic industry has lost its way. Rather than making medicines that are a life line to millions, generic companies have stopped producing drugs, particularly injectable medicines that are essentially for treating cancer, conducting surgery and staving off infections. In fact, nearly half of all generic drugs approved by the Food and Drug Administration for use are not being manufactured.

Instead of using incentives provided under The Hatch-Waxman Act to invest in new generic medicines, the industry has used a loophole in the America Invents Act of 2012 that makes it easier and cheaper to eliminate frivolous patent flings to challenge drug patents twice over. The end result has not been more generic medicines but an increase in the number of generic companies that make money generating lawsuits.

In addition, the generic industry has launched rapid-fire attacks on a patent from multiple companies and in multiple forums at a time when it is being investigated for conspiracy to raise generic drug prices. Such actions create significant uncertainty about the durability of patents

[1] Representative Henry Waxman of California and Senator Orrin Hatch of Utah sponsored the act which became effective September 24, 1984. http://www.gpo.gov/fdsys/pkg/STATUTE-98/pdf/STATUTE-98-Pg1585.pdf

for new medicines and is already discouraging companies and investors investment in medical innovation.

A recent piece of legislation entitled the Hatch-Waxman Integrity Act seeks to establish a more predictable platform for establishing patent validity that could encourage affordable and innovation. [2] This white paper describes why patent challenges outside of the Hatch-Waxman framework are undermining the mission of the generic industry as well as future innovation and why the Hatch-Waxman Integrity Action is an important first step to restoring the balance between innovation and generic manufacturing.

Generic Drugs: Lower Prices at What Cost?

The generic drug industry saves the American health system about $10 billion a year on prescription spending. Such savings are a result of the rapid introduction of generic medicines in recent years. In 1984, generic drugs were only 20 percent of the market. The generic share of prescribed medicines has climbed to 90 percent as a large number of drugs came off patent and the FDA reduced the backlog of generic drug applications.

The growth of the generic market wouldn't have been possible without the passage of the aforementioned Hatch-Waxman Act of 1984 ("Hatch-Waxman"). Hatch-Waxman permitted the Food and Drug Administration to approve applications to market generic versions of brand-name drugs without repeating costly and duplicative clinical trials to establish safety and efficacy.[3] Instead, a company could rely on the data developed by the innovator that demonstrated safety and efficacy.

The FDA established bioequivalence as the basis for approving generic copies of drug products through an abbreviated new drug application (ANDA) demonstrating bioequivalence. As the FDA notes: "Once approved, an applicant may manufacture and market the generic drug product to provide a safe, effective, lower cost alternative to the brand-name drug it references."

To encourage an increase in generic competition Hatch-Waxman also gave generic companies 180 days of market exclusivity if they successfully demonstrated that the innovation company patents were invalid. To do so, a generic company

And perhaps most important, Hatch-Waxman also created a statutory "safe harbor" that shields generic applicants from charges of patent infringement until such time as they request approval to market their products from the FDA. Additionally, innovator company patents were extended to account for the time the patented product is under review by FDA. They also gained up to five years of market exclusivity during which time a generic company could not use the innovator's safety and efficacy data.

[2] bit.ly/hatchwaxmanintegrity

[3] To be approved by FDA, the generic version must deliver the same amount of active ingredients into a patient's bloodstream in the same amount of time as the innovator drug.

The Hatch-Waxman framework was applied to biologics through the Biologics Price Competition and Innovation Act (BPCIA of 2009). BCPIA gave biologic innovators 12 years of data exclusivity and while providing makers of generic versions (called biosimilars) an accelerated Hatch-Waxman for approval.

This last feature combined with the 180 days of market exclusivity for successful infringement substantially reduces the cost and uncertainty of challenging patents and has spurred the generic drug explosion.

Faster Access to New Medicines and Greater Use of Generic Drugs

Research has shown that over time the number of generic drugs that entered the market after successfully challenging drug patents increased, reducing the average patent life of medicines and providing people early access to generic versions of such drugs.[4] Generic medicines usually eliminate about 90 percent of a brand drug's revenue within 6 months. (Biosimilar adoption has been slower but has the same impact.) However, the safe harbor provided to innovator intellectual property has allowed companies to invest in future drug development.

The incentives provided to increase and accelerate the development of generic drugs is a unique feature of America's patent policy. It is the only law in the world that creates a safe harbor for infringing on patents. And the biopharmaceutical industry is the single target of what can only be termed a sanctioned legal assault on intellectual property.

Still, when with greater patent and market predictability, the resulting equilibrium has given America the best of both worlds. The United States has compared to any other country, faster and broader access to new medicines and uses generics at a higher level.

But recently this balance has been threatened. As Emory University patent law professor Johanna Shepherd notes: "the generic drug industry, has used a loophole in the America Invents Act to circumvent the Hatch-Waxman Act patent challenge processes. The AIA established the Patent Trial and Appeal Board (PTAB) to combat the problem of patent trolling in the tech community. It allows patent challenges immediately if a patent was granted prior to March 2013 under a process called Inter Party Review (IPR). If a patent was or is granted after March 2013, the it can be challenged only 9 months after a patent is granted through a process called Post Grant Review (PGR)."

Additionally, the IPR/PGR process requires much less evidence to initiate a challenge. PGR can be presented based on any properties that can be used to challenge the validity of a patent claim. Unlike Hatch-Waxman and BPCIA which requires substantial evidence that a patent is invalid.

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[4] Henry Grabowski, et. Al, Pharmaceutical Patent Challenges and Their Implications for Innovation AEA CONFERENCE Boston, Massachusetts January 4, 2015
https://www.aeaweb.org/conference/2015/retrieve.php?pdfid=1203

As Professor Shepherd points out: "PGR can be sought by alleging unpatentability based on evidence of public use, on-sale activity or other public disclosures, double patenting, lack of patentable subject matter. In short, PGR can be filed on any ground. Under Hatch-Waxman and BCPIA companies have to show the patent is either invalid, not infringed or unenforceable through court proceedings."

Perhaps most important, because a patent challenge can be filed with the at any time during the life of the patent, there are no constraints of the 5-year data exclusivity period or 30-month stay. While a generic company doesn't receive the same 180-day market exclusivity period, the very threat of having a patent invalidated opens it the door to all competing generic manufacturers. Finally, not only can IPR challenge can be brought in parallel with a Hatch-Waxman proceeding, they can be brought after a Hatch-Waxman proceeding fails.

Generic drug and biosimilar manufacturers are increasingly utilizing the PTAB based IPR/PRG routes to challenge drug/biologic patents to circumvent the Hatch-Waxman and BPCIA regimes or are using in tandem with the abbreviated drug/biologic approval processes. Additionally, if a company loses a Hatch-Waxman suit, it can use the PTAB to get a second bite at the apple."

Generic companies are using the PTAB route prevent to put added litigation pressure on innovators above and beyond what Hatch-Waxman already provides. The Hatch-Waxman Integrity Act would close the loophole by requiring generic companies to choose one forum for challenge patent. The Association for Accessible Medicine, the lobby organization represent the generic drug cartel that generic companies need both the Hatch-Waxman and PTAB patent challenge forums to promote competition.

Over the past five years, the generic industry has eliminated product lines, avoided producing drugs the FDA has already approved and has used litigation not to produce generic drugs but to get paid NOT to do so. Such actions give a strange new meaning to the word 'competition':

1. The generic industry is not marketing medicines even when they are able to do so. While the Food and Drug Administration approved 1,600 generic drugs since January of 2017, more than 700—or 43 percent—are not for sale in the US, according to a new analysis by Kaiser Health News. Even more noteworthy: 36 percent of generics that would be the first to compete against a branded drug because of a patent challenge aren't on the market either.

2. As FDA commissioner Scott Gottlieb observes, generic drug makers wait until they've stockpiled a number of newly approved generics and have landed a contract with a purchaser before bringing their medicines to market: : "It's a real problem, because we're not getting all the expected competition. "Nearly half the time, patients and taxpayers aren't seeing the fruits of the FDA's efforts to clear the Abbreviated New Drug Approval (ANDA) backlog, because generics often file applications for drugs they don't intend to swiftly bring to market."

3. Generic companies are not only halting the introduce of additional products, they are pulling existing medicines from the market. As the Drug Channels blog has observed: "some generic

manufacturers have signaled their intention to exit highly competitive generic drug categories in which prices have dropped."

4. Indeed, the push towards consoliation and product retrenchment has been ongoing. A National Bureaur of Economic research paper found that "between 2004 and 2016, the market exodus has resulted in a few generic drug producers making the vast majority of products." The same study found that "more than 50 percent of generic drugs have at most two competitors; for 40 percent of drugs, there is only one".

5. The decline in generic drug product is an important reason there is a critical shortage of life saving sterile injectable medicines for cancer and delivering babies. The number of drug companies making products widely used in hospitals and other healthcare settings is declining, particularly companies that produce generic sterile injectable products. It turns out that for many medicines one company produces 90 percent of the total supply. In fall of 2017, interruption of manufacturing by a single firm led to shortages of multiple critical drugs including injectable pain medicines used in surgery.[5]

6. Finally, on the heels of parking patents and pulling drugs from the market, the generic industry is also being investigated for price fixing. An ongoing investigation launched by 47 state attorneys general alleges that 16 generic drug companies – which coincidentally are members of the aggrieved AAM -- have colluded to fix prices on 300 individual drugs. In one example, generic asthma drug albuterol saw a price increase of over 3,400 percent as a result of price-fixing.

There is no evidence that PTAB challenges have been used to increase generic production, particularly for medicines in short supply. Nor is there any evidence that the PTAB has resulted in any more successful challenges that in turn would lead to competition. Rather, as the next section discussion, PTAB has just made just the act of challenge patents more lucrative and less expensive that making generic drugs.

Efficient Infringement: The Impact of PTAB on Patent Strength and Investment in Medical Innovation

AAM also claims that the PTAB process does not hurt investment in medical innovation because very few of the patent challenges are upheld. In making this argument it points to a recent USPTO report, 83% of all petitions challenging small molecule drug patents between September 2012 and September 2017 were rejected by PTAB.

But that ignores the legislative history of the AIA regarding the purpose of the law: "Congress intended for IPRs and PGRs to provide an alternative to expensive and time-consuming district court litigation. So far, however, it appears that petitioners for IPR and PGR generally prefer to use those proceedings as parallel tools to infringement proceedings."

[5] Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions, Duke University Margolis Center for Health Policy, November 27, 2019

In fact, there is substantial increase in the number of patent challenges since the PTAB loophole began being used. A recent study found that 10 petitions on patents were filed in 2013 and surged to a record high of 127 petitions in 2016. Similarly, biologic patent challenges jump from 1 in 2013 to 53 biologic challenges in 2017. Meanwhile the vast majority (more than 90%) of drug patents challenged in IPRs are also involved in district court l(Hatch-Waxman) litigation." As a result, drug "patent owners must typically defend their patents in both proceedings simultaneously".

Finally, as research conducted by patent attorneys Stephen Maebus and Wenhua Hu shows: "when multiple related patents are under attack by the same petitioner, which may be more common for pharmaceutical IPRs, patent owners tend to defend or settle them en masse. Particularly, twenty-eight (28) out of the forty four (44) total settlements in the current data pool are between parties litigating multiple related patents before the PTAB."

All told, it is apparent the generic industry is pursuing a strategy of what is called "efficient infringement". In essence, since PTAB has made it cheaper and faster to challenge patents it makes economic sense to simply attack patents even if they are not invalidated. Efficient infringement also explains the number of patents being challenged by multiple companies. The target of the attack has to pay for legal fees to fight off every challenge, but each individual generic firm will pay less in either legal fees or in court-ordered damages than it would have paid in seeking to negotiate a license.

Hence, it is hard to find evidence that consumers are benefiting from efficient infringement. An article from the Center for the Protection of Intellectual Property points out that in theory the (infringing) company benefits privately because it pays less via a patent infringement lawsuit in either legal fees (invalidating the patent) or in a compulsory license (court-awarded damages). Society is supposedly better off, too, because the company engaging in efficient infringement has more resources to put to productive endeavors, as opposed to paying for use of an invalid patent (a monopoly) or in making a larger wealth transfer payment on the basis of a negotiated license.

However, efficient infringement has long term negative consequences:

> In the real world, though, efficient infringement creates more costs than merely the lost licensing profits for the patent owner, or the lost patent itself. The more fundamental problem with efficient infringement is that it undermines the proper functioning of the patent system. It frustrates the promise of the reward to the innovator for one's inventive labors. Once inventors know that the deck of (legal) cards is stacked against them and that they will suffer efficient infringement, they will create less patentable innovation. Without legal security in stable and effective property rights, venture capitalists will not invest in inventors or startups and the innovation economy will suffer.

As noted, Hatch-Waxman has, independent of PTAB, has reduced investment in new drug development. Research on the impact of Hatch-Waxman patent challenges shows how the wave of patent challenges since the late 1990s has shortened patent life and is influencing innovation

outcomes and generic accessibility" and found that " pervasive patent challenges also can increase uncertainty about expected returns to R&D and result in reduced investment in R&D for new drug therapies."

Another recent study found that "while the overall level of innovation has increased, a 10 percent increase in generic penetration in a given market is associated with a 7.9 percent decline in the number of early-stage innovations, and a 4.6 percent decline in the number of "first-in-class" pharmaceutical innovations in that market."

Such research suggests that innovation is sustained under Hatch-Waxman even when a patent is successfully challenge and leads a rapid loss in revenue because the patents protecting future investment are secure. Hence, the increase in the number of challenges, including multiple challenges, undermine the value of biopharma IP. Hatch-Waxman gave innovators companies a safe harbor from immediate and ceaseless infringement to create patent certainty and has allowed innovation to continue, albeit at a slower pace.

Under the current Hatch-Waxman system, patent protection mitigates market uncertainty because patents allow companies to raise money for R&D investment even if revenues decline. By comparison, as we have seen with the generic industry, if you are just a copycat, patenting firms should be less responsive to revenue volatility than non-patenting firms..

These attacks are creating uncertainty about the validity or sustainability of a patent which in turn reduces the value of the patent itself even if there is no successful challenge. Ashley Keller, writing for the IP WatchDog blog states:

"The value of a patent is the expected value it will produce in litigation, discounted to the present based on the time it will take to extract a judgment (or judgments). By definition, when the expected value of litigation goes down and the time to final judgment goes up, the asset is less valuable. Moreover, the PTAB has placed a heavy enough thumb on the scales that accused infringers almost always will pursue PTAB proceedings before considering settlement options. As a result, patent litigation today is more of a binary bet, as opposed to one where parties can reach reasonable settlements at various points during the life cycle of a case."

For example:

1. When Acorda Therapeutics' patents for Amprya (a drug that improves multiple sclerosis patients' mobility) were attacked and invalidated by PTAB, the company lost more than $150 million in value. Moreover, Acorda was forced to lay off employees and reduce spending on other new products.

2. In 2016, the share price of Teva fell by 6 percent after two patents for Copaxone (a biologic for multiple sclerosis) was overturned by PTAB

3. Similarly, after patent claims for drugs generating $6.5 billion for drug company Sanofi were invalidated in an PTAB proceeding it led to a 1.5 percent decline in share price.

To be sure, large pharmaceutical companies may be better able to adjust to such decisions but the same does not hold for smaller firms, especially those that are not generating money but raising capital. Uncertain patent rights will lead to less innovation because drug companies will not spend the billions of dollars it typically costs to bring a new drug to market when they cannot be certain if the patents for that drug can withstand IPR proceedings that are clearly stacked against them.

Investors regard patent strength a critical factor in whether to put money into an early stage company. A recent survey of investors found that elimination of patents would either somewhat decrease or strongly decrease their firms' investments in biotech (77%), medical device (79%) and pharmaceuticals (73%). [6]

At a CPIP conference, Paul Stone—a partner at venture capital firm 5AM Ventures—discussed his backing over 60 life science startups in the last 15 years, all of which specialized in therapeutics aimed at developing life-saving drugs and drug delivery technologies noted that more companies are producing more new medicines overseas because the patent environment in places like Europe or China are more predictable. And at a time when companies are developing personalized medicines for smaller market, a weaker patent system is threatening the ability to realize a return on investments in this area.

The Return of Pay for Delay

Finally, efficient infringement is an efficient way to make money by not making a generic drug. A recent study investigates whether generic companies have been "using the PTAB — which has not previously received antitrust attention — as a platform for striking settlements that delay the rivals' entry. Such settlements are common in pharmaceutical markets and are typically antitrust violations in cases where the patentee pays the challenger ("pay for delay").

A study of PTAB pharma patent challenges between 2012-2015 found that in 75 percent of PTAB cases that were settled, a generic firm received a payment but did not bring a drug to market thereafter. And nearly half of these PTAB settlements occurred PTAB ruled that it was "reasonably likely" that one or more patent claims are invalid.

The study concludes by noting, "badly-designed statutory inducements lead to excessively-delayed competition even in lieu of such payments. Our empirical findings suggest that delayed entry settlements are now commonly executed in the PTAB, and that they comprise a large majority of all PTAB settlements reached between pharmaceutical rivals."

Future Considerations: Hatch Waxman Integrity Act and Beyond

[6] Taylor, David O., Patent Eligibility and Investment (February 24, 2019). Cardozo Law Review, Forthcoming; SMU Dedman School of Law Legal Studies Research Paper No. 414. Available at SSRN: https://ssrn.com/abstract=3340937 or http://dx.doi.org/10.2139/ssrn.3340937

To sustain medical innovation while ensuring long term affordability, patent law reform must focus on encourage harnessing these trends to improve health and promote prosperity rather than protecting or favoring one industry over another.

The Hatch-Waxman Integrity Act of 2018 was introduced and is being considered in this Congress to "restore the careful balance" of in turns advances this broader goal. The Act does not eliminate PTAB use, rather it provides companies a choice of using the Hatch-Waxman and the BPCIA approach or an IPR/GPR, but not both:

> "Generic or biosimilar makers wishing to challenge a brand drug or biologics patent, and related entities ("any party in privity with the applicant"), will be required to (i) choose between the specific Hatch-Waxman or BPCIA patent procedures and the PTAB proceedings under the AIA, rather than taking advantage of both; and (ii) not rely "in whole or in part on any decision issued by" the PTAB as the evidence that the brand patent is invalid in the Hatch-Waxman or BPCIA procedures. Further, the Securities Exchange Act will be clarified to specify that filing PTAB patent challenges to profit from short sale of the patent owner stock, as practiced by certain hedge funds, is a form of the prohibited "manipulative or deceptive device."[7]

Conclusion

Closing the patent challenge loophole is essential to restoring the balance between innovation and imitation. As it stands, PTAB proceedings also undermine other laws that provide additional market exclusivity to medicines that addresses issues or needs that Congress deems important. Market exclusivity has been given to medicines that help children with rare disease, to companies that establish the safety of new drugs for pediatric patients, and to firms that develop new antibiotics. All of these important needs are threatened by efficient infringement.

The goal of US patent policy and the establishment of the US Patent Office was to promote aggressive licensing of patents in order to democratize invention. It was based on two principles. First, that individual effort and innovation would be stimulated by the possibility of economic returns. Second, the genius of invention was viewed as the province of many, not the inherited gift of the few. Allowing inventors to benefit from investment was and is an instrument of dynamic democratic capitalism.

The focus on the patent disputes obscures the fact that until two decades ago, licensing was the principle way in which inventions were financed and commercialized.

The difference between now and then is that today the vast majority of patents go unexplored and undeveloped. Licensing was established as a low-cost way of settling disputes and steering resources into commercialization as opposed to legal battles. And the process of diffusing knowledge about patents was envisioned as a way to allow all Americans with an idea to test

[7] The Hobson's Choice Of The Hatch-Waxman Integrity Act

them in the marketplace. We need to encourage licensing of medical technologies rather than litigation.

But to get to that place, the safe harbors for innovators and generic firms must be repaired. The Hatch-Waxman Integrity Act is part of that innovation sustaining solution.