INTRODUCTION

Pharmaceutical Innovation: Law & the Public's Health

Kevin Outterson

At last count, global pharmaceutical spending exceeded $750 billion.[1] Unlike most medical products and services, many pharmaceuticals are sold at a price that greatly exceeds marginal cost. AIDS medicines that retail for over $10,000 per person per year in the United States can be produced generically at a marginal cost of less than $150. Patents and other related IP rights create these significant gaps between marginal cost and retail price, generating many billions of dollars in profits (patent rents) for companies.[2]

Patent rents lead to two conditions without fail. On a static basis, patent rents price some users out of the market, an economic deadweight loss. When the product is the latest Hannah Montana song, perhaps the global community can bear with the deprivation. When the product is a life-saving medicine, deadweight losses quickly translate into dead patients. Paul Hunt, the former United Nations Special Rapporteur on the right to health estimated that

> Almost 2 billion people lack access to essential medicines. Improving access to existing medicines could save 10 million lives each year, 4 million of them in Africa and South-East Asia. Access to medicines is characterised by profound global inequity. 15% of the world's population consumes over 90% of the world's pharmaceuticals.[3]

Patent rents also propel innovation, enabling drug companies to protect their investments in R&D. Innovation is the dynamic case for patent rents. While empirical research suggests that patents are an ineffective incentive for innovation generally, patents retain their paradigmatic function in the pharmaceutical and chemistry industries.[4] The drug industry estimates their global R&D expenditures to have been $65.3 billion in 2008.[5] While many suggest that this number may be inflated for public relations purposes, it does represent an upper bound estimate. More troubling has been the relatively poor output in recent years from the pharmaceutical R&D apparatus — fewer truly innovative drugs are reaching consumers, for a variety of reasons. Biomedical R&D is a global business with important impacts on global health, as well as significant inefficiencies and dramatic problems with equitable access to innovative therapies.

In this context, the *Journal of Law, Medicine & Ethics* issued a Call for Abstracts on topics related to pharmaceutical and medical device innovation. We insisted on an open Call, hoping for a wider variety of papers and viewpoints on an important topic to global public health. As such, we received submissions from a remarkably cross-disciplinary group of authors. The papers are divided into two sections.

The first collection includes five general papers from a wide range of perspectives on pharmaceutical innovation, and two review essays, with a common focus on pharmaceutical patents. Most of the authors seek to balance the competing objectives of access and innovation.

The first paper evaluates the relative efficiency of non-profit and commercial pharmaceutical R&D. Aaron Kesselheim and Jerry Avorn, both physicians at Brigham and Women's Hospital and Harvard Medical School, analyzed 25 years of patent data to assess the relative contributions of private and public funding sources in pharmaceutical innovation.[6] Dr. Kes-

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selheim is also a patent attorney. They found pharmaceutical patents from non-profit sources to enjoy a statistically significant advantage in quality, as measured by citations. Drug-related patents generated in the non-profit sector appear to be more valuable than commercial patents, which supports the importance of non-profit research institutions in the pharmaceutical sector generally. Their findings also underscore the significant overall contributions by the commercial sector to pharmaceutical patenting.

In the second article, Sean Flynn (American University, Washington College of Law), Aidan Hollis (University of Calgary, Department of Economics), and Mike Palmedo (American University, Washington College of Law) develop a complex and compelling economic case for expanding the use of compulsory licenses in developing countries to expand access without harming innovation.[7] The key to their analysis is the simple observation that each country's demand elasticity for pharmaceuticals will differ, often radically so. Richer countries will be less price-sensitive; poorer countries will necessarily suffer more convex demand curves. The implications of their work for global pharmaceutical pricing are significant, directly undermining the supposition that all countries should pay similar prices or strike similar bargains with intellectual property law. Pricing and patent rules that might be appropriate for wealthier countries will, according to their work, be inappropriate or even immoral in resource constrained settings. They analyze data from Norway and South Africa to demonstrate these points. One patent flexibility they highlight is the *compulsory license*, a mechanism that has been highly criticized by patent-based drug companies, but finds clear support in Article 31 of the TRIPS Agreement. The article by Flynn, Hollis, and Palmedo may move the debate onto firmer ground, which is welcome news indeed.

The next two articles are critical of compulsory licenses by developing countries, for somewhat different reasons. The article by Robert C. Bird (University of Connecticut, School of Business) acknowledges the legality of and need for compulsory licenses, but expresses strong concerns about their unwanted side effects, especially the strong negative reactions elicited from patent-based drug companies and Western governments (particularly the United States).[8] Bird earned both J.D. and M.B.A. degrees, which is evident in his analysis. Bird's concerns are with process and outcomes: he wants to maximize the public health impact of this patent strategy. In the fourth article, Dr. Kristina M. Lybecker (Colorado College, Department of Economics and Business) and Elisabeth Fowler (World Health Advocacy) make a much more fundamental criticism of compulsory licenses, especially as recently practiced by Thailand.[9] They find little to recommend from the Thai process, even if it technically complies with WTO rules (which they do not concede). Reading these three articles together gives one a clear sense of the controversy in global pharmaceutical markets concerning compulsory licensure.

The final article in the first section is by Jorn Sonderholm, a philosopher. He discusses a novel intellectual property right to promote antibiotic development, the "wild card" patent.[10] Historically, patent rewards have been inalterably linked to the value of the patented invention. The patent was valuable only to the extent that the public wanted to purchase the patented product. Sonderholm proposes to disconnect patent rewards from the underlying invention, giving drug companies a wild card as a prize if they reach a particular goal (in this particular case, a novel antibiotic). The wild card is particularly valuable because it can then be used to extend the patent of any other product, such as Lipitor. Sonderholm finds this arrangement to be valuable as an innovation incentive, while critics suggest this idea is an inefficient tax on heart disease to pay for antibiotic R&D. In a broader context, Sonderholm's article illustrates some of the "out of the box" thinking that makes this field so exciting.

As guest editor of this symposium issue, I was pleased to have this first set of articles, but hoped for a more coherent overview of the strengths and weaknesses of pharmaceutical innovation issues, including compulsory licensure. Two eminent experts agreed to write essays reviewing several of the articles on compulsory licensure and wild card patents. Jerome H. Reichman, a distinguished professor at Duke University School of Law, agreed to review the articles by Flynn, Hollis, and Palmedo; Bird; and Lybecker and Fowler.[11] The second review article is authored by Amy Kapczynski, assistant professor of law at the University of California, Berkeley. Kapczynski is a renowned expert in licensing pharmaceutical innovations for global health access. She agreed to review Sonderholm; Flynn, Hollis, and Palmedo; and Bird.[12] Reichman's review begins with an authoritative history of compulsory licensure and the TRIPS Agreement, and proceeds to offer a clear critique of the three articles on compulsory licensure. Reichman finds Flynn, Hollis, and Palmedo's views to be closest to his own. Kapczynski also discusses compulsory licensure, to similar effect, but adds her critique of Sonderholm's wild card proposal. She concludes that "now is not the time for half measures or an extension of business as usual," calling for fundamental policy changes on behalf of global health.

The second section of this symposium narrows the focus from global health to pharmaceutical innovation problems with special populations. Elizabeth Weeks

Leonard examines the terminally ill, who may demand access to experimental drugs.[13] While many have written about the ethics of the *Abigail Alliance* litigation, Professor Weeks (University of Kansas School of Law) takes it a step further by exploring the dynamic consequences of opening treatment access for the terminally ill — namely, undercutting future double-blind clinical trials. Patients may or may not have an autonomy right to threaten their own health; threatening the clinical research enterprise for all patients is another matter altogether. Weeks appropriately expands the range of concerns expressed in *Abigail Alliance* to include future patients and yet-to-be discovered innovation.

Barbara Noah focuses on children as patients and pharmaceutical research subjects.[14] As she notes, children are not "miniature adults," but people with unique clinical and ethical needs. U.S. law offers additional incentives and protections for pharmaceutical research with pediatric populations, but much remains to be done. Most pediatric prescriptions are not supported by peer-reviewed evidence, and pediatric clinical trials are more difficult to design and execute. Noah, a Professor of Law at Western New England College School of Law, gives us a concise but reliable guide to this regulatory landscape.

One very special population is those afflicted with Chagas, a parasitic disease endemic to South and Central America. Diseases like Chagas are often neglected by global commercial enterprises due to the poverty of the afflicted. In WHO parlance, Chagas is a Type III very neglected disease, and for-profit companies cannot be expected be responsive. Sara Crager and Matt Price approach the problem with clinical intensity, and break free from existing R&D paradigms to fashion a novel solution for this neglected disease.[15] The solution they articulate is a prize fund for a Chagas vaccine, with remarkable sophistication and detail in their analysis.

In the Call for Abstracts, the *Journal of Law, Medicine & Ethics* specifically requested papers on medical device topics, understanding that this important area was grossly underexplored by scholars. Bruce Patsner (University of Houston Law Center) gives us an account of R&D in medical devices, post-*Riegel v. Medtronic, Inc.*[16] In that case, the U.S. Supreme Court upheld federal pre-emption of state tort law for certain categories of medical devices. Today, drug and device law have moved further apart due to the different regulatory schemes, tort rules, and their effects on incentives to innovate. Dr. Patsner (a physician and a lawyer) explores the relationships between the regulatory structure, tort claims, and future innovation in the field. Many times we assume that drug and device incentives are similar, often without specific analysis of the device market. Dr. Patsner illustrates the need to dig into the details of medical devices, rather than just make broad assumptions.

Indeed, this lesson applies across the entire field of biomedical innovation, as this symposium issue aptly demonstrates.

References

1. *IMS Health Lowers 2009 Global Pharmaceutical Market Forecast to 2.5 – 3.5 Percent Growth*, Press Release, April 22, 2009, *available at* <http://www.imshealth.com/portal/site/imshealth/menuitem.a46c6d4df3db4b3d88f611019418c22a/?vgnextoid=1e61fa8adbec0210VgnVCM100000ed152ca2RCRD&vgnextchannel=b5e57900b55a5110VgnVCM10000071812ca2RCRD&vgnextfmt=default> (last visited May 6, 2009).
2. See generally K. Outterson, "Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets," *Yale Journal of Health Policy, Law & Ethics* 5, no. 1 (2005): 193-291.
3. P. Hunt, "Human Rights Guidelines for Pharmaceutical Companies in Relation to Access to Medicines," draft for consultation, September 19, 2007.
4. J. Bessen and M. J. Meurer, *Patent Failure: How Judges, Bureaucrats, and Lawyers Put Innovators at Risk* (Princeton: Princeton University Press, 2008).
5. PhRMA, *Pharmaceutical Industry Profile* (2009).
6. A. S. Kesselheim and J. Avorn, "Using Patent Data to Assess the Value of Pharmaceutical Innovation," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 176-183.
7. S. Flynn, A. Hollis, and M. Palmedo, "An Economic Justification for Open Access to Essential Medicine Patents in Developing Countries," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 184-208.
8. R. C. Bird, "Developing Nations and the Compulsory License: Maximizing Access to Essential Medicines While Minimizing Investment Side Effects," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 209-221.
9. K. M. Lybecker and E. Fowler, "Compulsory Licensing in Canada and Thailand: Comparing Regimes to Ensure Legitimate Use of the WTO Rules," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 222-239.
10. J. Sonderholm, "Wild-Card Patent Extensions as a Means to Incentivize Research and Development of Antibiotics," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 240-246.
11. J. H. Reichman, "Comment: A Trilogy of Views about Compulsory Licensing of Patented Pharmaceutical Inventions," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 247-263.
12. A. Kapczynski, "Commentary: Innovation Policy for a New Era," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 264-668.
13. E. W. Leonard, "Right to Experimental Treatment: FDA New Drug Approval, Constitutional Rights, and the Public's Health," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 269-279.
14. B. A. Noah, "Just a Spoonful of Sugar: Drug Safety for Pediatric Populations," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 280-291.
15. S. E. Crager and M. Price, "Prizes and Parasites: Incentive Models for Addressing Chagas Disease," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 292-304.
16. B. Patsner, "*Riegel v. Medtronic, Inc.*: Revisiting Pre-emption for Medical Devices," *Journal of Law, Medicine & Ethics* 37, no. 2 (2009): 305-317.