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LECTURE

PATENTS, PRODUCT EXCLUSIVITY, AND INFORMATION DISSEMINATION: HOW LAW DIRECTS BIOPHARMACEUTICAL RESEARCH AND DEVELOPMENT*

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It's a great honor for me to be invited to deliver the Levine Distinguished Lecture at Fordham, and a great opportunity to try out some new ideas before this audience. As some of you know, I've been studying the role of patents in biomedical research and product development ("R&D") for close to twenty years now, with a particular focus on how patents work in "upstream" research in universities and biotechnology companies that are working on research problems that arise prior to "downstream" product development. But, of course, the patent strategies of these institutions are designed around the profits that everyone hopes will flow from downstream products, and the most lucrative of those products are drugs. If a biotechnology company looks for a while like they are up to something other than staking out claims that will permit them to tap into drug profits, they often eventually seem to change their business model, or else they get folded into a company that is more squarely focused on profiting from drug development. So much of the impetus for private sector investment in biomedical R&D turns out to be about drug development.

Drug development is a famously patent-sensitive field of technology. But over the years I have come to suspect that looking at biopharmaceutical R&D from the perspective of the patent system alone is an incomplete and lopsided approach. Drug development is bracketed by two huge regulatory systems—the patent system and the drug regulation system, i.e., the laws administered by the Food and Drug Administration ("FDA"). The core function of the patent system is to motivate and reward the development of new inventions,

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while the core function of the drug regulation system, at least as originally conceived, is to protect consumers from products that are unsafe, ineffective, or fraudulently marketed.[1] Patent law and FDA law tend to be handled by different people, even within a firm. In the pharmaceutical industry, FDA work is typically done by regulatory departments that are separate from legal departments and are staffed mostly by scientists and doctors, not lawyers. Although there are growing legions of patent lawyers, there are still relatively few lawyers who do FDA work. Billions of dollars[2] hinge on these products, and only a tiny community of lawyers specialize in this area. Although as a formal matter patent law and drug law are independent and have different missions, they have an important functional interrelationship that bears closer examination.

I. HOW THE "REAL WORLD" WORKS

A few years ago I had a casual conversation that really brought this home to me and persuaded me that I needed to learn more about drug regulation in order to do my work as a patent scholar. I sit on a panel on Science, Technology & Law for the National Academies, a group of scientists, doctors and lawyers that meets several times a year to talk about topics in technology and law and figure out what more the Academies should be doing to study them. After one of these meetings, I was sharing a cab back to the airport with a doctor who is also a member of the same panel, and she made a casual observation that really got my attention. She told me that when a drug goes off patent, it becomes available over the counter. This is a woman of considerable intelligence and sophistication, so I was puzzled that she should fall for what seemed like a fundamental confusion between these two separate legal regimes. I patiently started to explain that patents are a system of legal rights designed to spur innovation, administered by the Patent and Trademark Office ("PTO"), while determinations of whether drugs may be sold over the counter or require a prescription are made by the FDA on the basis of considerations of health and safety, and that these decisions have nothing to do with whether a drug is still under patent. She assured me that she understood all that, but she was sharing with me her observations about how the real world works, and in practice, when a drug goes off patent, it becomes available over the counter. I wondered, could that possibly be true? Why would it be true?

Well, I realized that, in order to figure that out, I had to learn more

1. *See* Rebecca S. Eisenberg, *The Shifting Functional Balance of Patent and Drug Regulation*, Health Aff., Sept.-Oct. 2001, at 121.

2. In 2002, Merck alone had more than $51 billion in sales. Merck & Co., Inc., Annual Report Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934 for the Fiscal Year Ended December 31, 2002 (Form 10-K), File No. 001-03305, at 2, *available at* http://www.sec.gov/cgi-bin/srch-edgar.

about drug regulation. As I have set about doing that, with my patent-centric world view, I have discovered that FDA law is fundamentally about regulation of biomedical innovation and it is critical for somebody who studies Intellectual Property in biomedical innovation to understand both systems and how they relate. None of this is to understate the importance of patents. Biomedical research is a huge part of overall R&D in both public and private sectors, and it is an area in which patents really seem to matter. If you talk to people from different segments of the public and private biomedical research establishment, you get somewhat different, although ultimately complementary, stories about just why patents matter.

The pharmaceutical industry has long maintained that patents are crucial to the financial viability of pharmaceutical R&D, that without patents they could not survive in the costly and risky business of drug development. Patents on drugs seem to operate the way legal scholars and economists imagine patents are supposed to work, by giving their owners monopoly power in product markets. This is not so in every industry, for a variety of reasons. In many industries patents are bargaining chips to bring about cross-licensing of complements, or patented products face significant competition from patented or unpatented substitutes.[3] But patented drugs really do command a significant price premium in the market. When patents expire and drugs face generic competition, their prices plummet. Other patented drugs in the same class (like multiple patented Angiotensin-Converting-Enzyme ("ACE") inhibitors or multiple patented antidepressants) do not seem to have the same effect on prices as generic competition from the same molecule. So while, in some contexts, it may be misleading to say patents confer monopoly power, in pharmaceuticals that statement is pretty accurate. Patents on drugs permit firms to charge monopoly prices and make high profits. And those profits motivate spending on R&D to find new patented products.

The biotechnology industry is composed of a much more diverse set of firms with different strategies for making money, but, like the pharmaceutical industry, it also tends to be a big supporter of strong patent protection. Biotech firms say that they need patents in order to raise capital from investors to conduct their research and in order to get pharmaceutical firms to partner with them to use their research platforms to develop new products.

Meanwhile, universities claim that they need patents because the private firms who are their licensees need patents, and a huge percentage of university patenting is in biomedical research. If you

3. *See* Wesley M. Cohen et al., Protecting Their Intellectual Assets: Appropriability Conditions and Why U.S. Manufacturing Firms Patent (Or Not) 22 (2000) (Nat'l Bureau of Econ. Research, Working Paper No. 7552), *available at* http://dsl.nber.org/papers/w7552.v5.pdf.

press further and ask them to explain why they need patents on inventions that others have brought to market without them, like the University of Rochester patents claiming cox-2 inhibitors,[4] they might also concede that they would like to use their patents to bring in revenue to support their own R&D.

Across the board, this is a very patent-sensitive field of research. Empirical studies indicate that this is an area where decision makers really care about patents when they think about spending money on R&D, in contrast to other fields and industries that rate other, non-patent factors as more important. Wherever patentable inventions arise in the course of biomedical R&D, the stories that one hears about why patents are important emphasize that patents drive private sector R&D, and private sector R&D is a hugely important part of biomedical research. In the past decade, despite steady increases in National Institutes of Health ("NIH") funding aimed at doubling the NIH budget, private funding has overtaken public funding.[5] From the private side, the profits that motivate investment in biomedical research for the most part have to do with drug development.

Biopharmaceutical research is often held out as a shining example of the success of the patent system in motivating private investment in R&D. But it is such an outstanding success story, and so exceptional, that one wonders whether patents are doing all the work of motivating this R&D on their own. The patent system takes much credit for motivating investment in biomedical research and product development, and the industry never gives drug regulation any credit for profits or for motivating R&D in a positive way. A standard industry view of the relationship between patents and drug regulation is that patents make drug development profitable, while drug regulation makes it costly. But the more closely I look, the more misleading this first approximation of the regulatory symbiosis between patents and drug regulation seems to me.

As a patent scholar, I can speak with greater authority to the oversimplification of the patent side of the story. It has long been clear to me that patents contribute to the costs of drug development as well as to its profits. Of course it is true that patents on *drugs* make drug development more profitable, but patents on drugs are not the only patents that accompany new drugs on the road to market. Patents on drugs make drug development profitable by providing patent owners with exclusivity in the market for new pharmaceutical products. But patents do not necessarily track product markets—they track inventions. And many inventions feed into drug development today, including genomic information and databases, newly identified

4. University of Rochester v. G.D. Searle & Co., 249 F. Supp. 2d 216 (W.D.N.Y. 2003).

5. *See* Eisenberg, *supra* note 1, at 120.

drug targets, animal models, new laboratory techniques and instruments, and new reagents. Maybe long ago in a distant era, these pre-market inventions were mostly unpatented, especially if they were made in university labs with public funding. But for the last twenty years, universities have been jumping on the patent gravy train wherever they can, with the encouragement of federal law. These early "upstream" inventions that explain disease pathways and mechanisms and identify potential drug targets are increasingly likely to be patented, and patents on these numerous discoveries impose costs on drug development. These discoveries are like so many siphons at the feeding trough of new drugs, draining away profits in many different directions. I think what we see now is just the beginning of a trend that will continue and accelerate as more institutions that are involved in biomedical R&D figure out ways to use patents to capture a share of the attractive profits that flow to the developers of successful pharmaceutical products. So patents are a source of costs as well as a source of profits for drug developers.

What about the regulatory side? Is that really all costs? Not at all. The more I learn about the drug regulation, the more I see ways that it supports the profitability of drug development even as it adds to its costs.

II. THE REGULATORY SIDE

Perhaps it goes without saying that drug regulation poses a significant entry barrier that seriously limits the firms that can compete with market incumbents. Recent estimates, which may err on the generous side, put the average costs of developing a new drug to the point of new drug approval ("NDA") at approximately $800 million, after adjusting historical costs to present value to account for the time value of money.[6] A big chunk of that money comes from the costs of conducting clinical trials to win FDA approval. Not many firms have that kind of money. FDA regulation is costly for generic competitors as well as for innovators. Generic competitors may avoid a large portion of these costs by submitting an abbreviated new drug application ("ANDA") showing bioequivalence to a previously approved product, but generics are also less profitable, so the entry barrier remains significant, although not insurmountable. This entry barrier limits competition, thereby making drug development more profitable.[7]

Beyond limiting competition indirectly by imposing costly

6. Ceci Connolly, *Price Tag for a New Drug*, Wash. Post, Dec. 1, 2001, at A10 (reporting university study estimating that the "average cost of developing a new prescription drug—including paying for the many failures—reached $802 million in the 1990s").

7. *See* Eisenberg, *supra* note 1, at 121.

regulatory burdens that limit market entry, the FDA also sometimes confers formal exclusivity in product markets. There have been a number of examples of these FDA-administered "pseudo-patents" over the past twenty years.

An early example of FDA-conferred exclusivity is the Orphan Drug Act of 1983.[8] This Act provides seven years of market exclusivity for products to treat rare diseases and conditions affecting fewer than 200,000 patients in the United States.[9] Some of these products have huge markets when you take into account off-label use.

One year later, Congress added two more provisions for FDA-administered market exclusivity in the Hatch-Waxman Act of 1984,[10] directing the FDA to award five years of market exclusivity for new chemical entities not previously approved by the FDA, and three years of exclusivity for making changes in a previously approved product that require conducting new clinical trials to win FDA approval.[11] (This latter provision sometimes applies, for example, to changes in dosage form, or approval for new indications, or switches from prescription to over-the-counter status, which may be part of the answer to the puzzle posed by my doctor friend in the taxicab.) In contrast to the Orphan Drug Act provisions, these Hatch-Waxman Act exclusivity provisions merely prevent the FDA from allowing competitors to obtain streamlined review of their applications without having to submit a full NDA. They do not prevent a competitor from obtaining approval by relying strictly on its own submitted data for proof of safety and efficacy. In effect, these provisions amount to FDA-administered proprietary rights in regulatory data, awarded to encourage particular kinds of innovation in drug development rather than to protect consumers from unsafe or ineffective drugs.

The Food and Drug Administration Modernization Act of 1997[12] added a provision for six months of exclusivity just for conducting pediatric trials. This six-month period of exclusivity is not contingent upon approval of the drug as safe and effective in children and is not limited to pediatric use of the drug. It simply extends any existing market exclusivity held by the submitter, whether under a patent, the Orphan Drug Act, or Hatch-Waxman exclusivity provisions, further deferring the time when the FDA might approve a competing generic product.[13]

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8. Pub. L. No. 97-414, 96 Stat. 2049 (1983) (codified as amended at scattered sections of 21 U.S.C.).

9. 21 U.S.C. § 360cc(a) (2000).

10. Drug Price Competition and Patent Term Restoration Act of 1984, Pub. L. No. 98-417, 98 Stat. 1585 (1984) (codified as amended at scattered sections of 21 U.S.C. and 35 U.S.C.).

11. 21 U.S.C. § 355 (c)(3)(D)(ii), (iii) (2000).

12. Pub. L. No. 105-115, 111 Stat. 2296 (1997) (codified as amended at scattered sections of 21 U.S.C.).

13. 21 U.S.C. § 355a; *see also* Eisenberg, *supra* note 1, at 123.

Each of these provisions confers patent-like protection under the auspices of the FDA rather than the PTO. Each may be better understood as an economic measure designed to promote costly investments in innovation than as a consumer protection measure designed to keep unsafe or ineffective products off the market. Considered together, they show a trend toward directing the FDA to use its gatekeeper role in timing approval of pharmaceutical products to serve a function traditionally relegated to the patent system: promoting and rewarding innovation by granting valuable exclusionary rights.

Other provisions of the Hatch-Waxman Act, or "Drug Price Competition-Patent Term Restoration Act," as it was once called,[14] further blur the functional distinction between drug regulation and patents, directing PTO to take regulation into account in determining patent term and directing FDA to take patents into account in approving drugs. The Hatch-Waxman Act allows the PTO to grant patent term extensions of up to five years to compensate for marketing delays during the regulatory review period prior to the first permitted commercial marketing of a new drug.[15] At the same time, it sets up a complex system for keeping track of patents that cover FDA-approved drugs and deferring regulatory approval of generic versions of those drugs during patent challenges.

Holders of approved NDAs are required to disclose all patents that they believe would be infringed by unauthorized sales of the approved drug, and the FDA publishes the list in a publication called the Orange Book.[16] Competing manufacturers who believe that their products do not infringe these patents, or that some of the patents are invalid, may file ANDAs seeking FDA approval for their products prior to patent expiration, with notice to the patent owner.[17] But if the patent owner files an infringement action against them within forty-five days, FDA approval of the ANDA is stayed for thirty months, no matter which side is correct on the legal arguments (except in the unlikely event that a court resolves the issue earlier than that).[18] This gives pharmaceutical firms an incentive to be quite expansive in listing the relevant patents, including, for example, patents covering aspects of the product formulation that are easy to design around to avoid infringement. This preserves more

14. Drug Price Competition and Patent Term Restoration Act of 1984.

15. 35 U.S.C. 156(g)(6)(B) (2000).

16. The FDA publishes the Orange Book annually, and also maintains a searchable electronic database. *See* Food & Drug Admin., Approved Drug Products with Therapeutic Equivalence Evaluations (CCH 23d ed. 2003); Ctr. for Drug Evaluation & Research, U.S. Dep't of Health & Hum. Servs., *available at* http://www.fda.gov/cder/ob/default.htm (last modified Oct. 20, 2003).

17. *See* Eisenberg, *supra* note 1, at 122.

18. 35 U.S.C. § 271(e)(2) (2000); *see also* 21 U.S.C. § 355(c)(3)(C), (j)(4)(C); Eisenberg, *supra* note 1, at 122.

opportunities to file lawsuits that will trigger the thirty month stay of FDA approval, in effect prolonging the period of profitable market exclusivity beyond what the listed patents (which may be invalid or not infringed) could do on their own.

Another controversial Hatch-Waxman provision that has the effect of prolonging exclusivity is the provision of a 180-day period of exclusivity to the first generic applicant to file a patent challenge against any approved drug.[19] This is the clearest example of unintended consequences in the Hatch-Waxman Act, and is the subject of reform proposals. Designed to spur generic competition with products covered by questionable patents, this provision has instead provided a strategic opportunity to defer generic competition in products that patent law would otherwise leave unprotected.

The first challenger and the patent owner simply reach a "settlement" that affirms the validity and infringement of the patent, knowing that subsequent challengers will be ineligible for the 180-day exclusivity and thus unlikely to bring their generic versions of the product to market in the interim.[20] The Federal Trade Commission ("FTC") has challenged this under the antitrust laws, and legislation is pending to address it.[21] Again, this is another example of how the combination of patents and drug-specific regulation provides longer exclusivity than the patent system could do on its own.

Another increasingly important role played by the FDA in supporting the profitability of drug development beyond what patents do has to do with parallel imports. Drug markets are most lucrative in the United States; somewhat less so in Canada, Western Europe, and Japan; and much less so in sub-Saharan Africa, especially with pressure to provide drugs cheaply to meet public health needs.[22] Overall profitability depends on the ability to keep cheap drugs from moving to higher-margin markets through arbitrage. Although U.S. patent law in this area is quite murky, drug regulation offers reasonably effective protection against parallel imports without regard to patent law.

The "first sale" doctrine,[23] which permits me to sell my car without

19. 21 U.S.C. § 355(j)(5)(B)(iv); *see also* Eisenberg, *supra* note 1, at 122.

20. Eisenberg, *supra* note 1, at 122-23.

21. Greater Access to Affordable Pharmaceuticals Act of 2003, S. 54, 108th Cong. § 5(a)(2) (2003); *see also* Janet A. Gongola, Note, *Prescriptions for Change: The Hatch-Waxman Act and New Legislation to Increase the Availability of Generic Drugs to Consumers*, 36 Ind. L. Rev. 787, 802-16 (2003) (summarizing past litigation and pending legislation); Thomas F. Cotter, *Refining the "Presumptive Illegality" Approach to Settlements of Patent Disputes Involving Reverse Payments: A Commentary on Hovenkamp, Janis & Lemley*, 87 Minn. L. Rev. 1789, 1798 n.43 (2003) (discussing past litigation and listing consent decrees entered into by the FRC and drug companies).

22. *See* Eisenberg, *supra* note 1, at 129.

23. *See, e.g.*, Donald S. Chisum et al., Principles of Patent Law 1118-41 (2d ed. 2001); Tait R. Swanson, *Combating Gray Market Goods in a Global Market:*

permission from whoever owns all the patents on its various components, arguably limits the power of patent owners to exclude imports of patented products that they previously agreed to sell abroad. The national laws of different countries disagree on this point. Some hold that the first sale doctrine only permits resales within the same country, while others follow a rule of "international exhaustion" and hold that once the patent holder has authorized sale of an item anywhere in the world, the purchaser is free to resell anywhere in the world without needing further permission of the patent owner.[24] There has been a big debate about this issue in trade negotiations, but so far no agreement, leaving each nation free to choose its own exhaustion rule. The United States' bargaining position, supported by the pharmaceutical industry, has been that every nation should follow a rule of national exhaustion. But it is not at all clear that this is the law in the United States.

If patented drugs sold abroad could be imported into the United States and resold over the objections of the patent holder, it would be very difficult to maintain the higher prices for patented drugs that now prevail in the U.S. market. Importers would simply buy the drugs in a low-price market and resell them in the United States. But whether U.S. patent law permits this arbitrage really does not matter, because drug regulation fills this potentially important gap in patent protection.

For one thing, differences in drug regulation make it hard to get imports into U.S. and other lucrative markets. The Food, Drug, and Cosmetic Act prohibits the introduction into interstate commerce (including by importation) of new drugs except pursuant to approved NDAs, and these approvals are limited to products made in specified manufacturing facilities and sold under an approved label.[25] This protection from imports is fortified by Prescription Drug Marketing Act of 1987, which specifically prohibits re-importation of previously exported U.S.-manufactured drugs except by the manufacturer, unless required for emergency medical care.[26] There is a genuine health and safety issue lurking behind these provisions, but they also have an economic side effect that may be even more important. This economic side effect has brought renewed political attention to the prohibition against re-importation, as some legislators have sought to give U.S. consumers the benefit of cheaper drug prices in Canada.

We can see in this brief overview that FDA regulation, in addition

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Comparative Analysis of Intellectual Property Laws and Recommended Strategies, 22 Hous. J. Int'l L. 327, 342-44 (2000).

24. Chisum, *supra* note 23, at 1121-28.

25. 21 U.S.C. § 355(a) (2000).

26. Pub. L. No. 100-293, 102 Stat. 95 (1987) (codified as amended at scattered sections of 21 U.S.C.). The specific provision banning unauthorized re-importation is located at section 381(d)(1).

to imposing costs in the form of tests to ensure health and safety, also limits competition in drug markets in ways that enhance the profitability of drug development. As the population ages and becomes more concerned about health care, and as public and private payors struggle to control rising health care costs, the laws that set the ground rules for biomedical innovation are receiving closer and more skeptical scrutiny, making it all the more important to understand just what work is done by different parts of this complex regulatory web.

III. RE-EXAMINING THE FDA'S ROLE

Does the current functional allocation make sense? In particular, does it make sense to locate legal protection for exclusivity as an economic incentive for R&D in FDA administered rules rather than patent law? There are reasons to worry about it. Questions about appropriate economic incentives for R&D seem to be peculiarly the province of the patent system, and arguably outside the competence of FDA. But there are also advantages to using FDA regulation as a mechanism for providing exclusivity.

Our patent laws are one-size-fits-all, applying essentially the same rules to biopharmaceutical research that apply to automotive engineering, information technology, semiconductors, and rocket science. But the needs of these fields for patent protection differ. FDA regulation, by contrast, is industry-specific. It is hard to fine-tune the patent laws to meet the needs of the pharmaceutical industry when the needs of other industries are different. We have some industry-specific provisions, including the Hatch-Waxman patent term extension provisions discussed earlier, biotechnology process patents provisions, and prior user rights for business method patents. But these provisions are awkward and cumbersome, and often ill-considered. It is also at least arguable that they violate our treaty obligations. The Agreement on Trade-Related Aspects of Intellectual Property Rights (the "TRIPS Agreement")[27] prohibits discrimination in the terms of patent protection depending on the field of technology. Paradoxically, this provision was included at the behest of the pharmaceutical industry to eliminate discrimination *against* drugs, but the treaty language is written in broader terms that also prohibit discrimination in favor of drug patents. It is arguable that we are already in violation of these provisions. To the extent that the exclusivity needs of the pharmaceutical industry differ from those of other industries, it might be less problematic to fine-tune the drug regulation rules than it is to fine-tune the patent system. Even if the

27. Agreement on Trade-Related Aspects of Intellectual Property Rights, Dec. 15, 1993, Marrakesh Agreement Establishing the World Trade Organization, Annex 1C, Legal Instruments–Results of the Uruguay Round vol. 31 (1994), 33 I.L.M. 81 (1994).

World Trade Organization were to decide that so-called FDA exclusivity is really a patent by another name, and that industry-specific pseudo-patents still violate our treaty obligations, the issue might be easier to finesse if it were framed initially as drug regulation.

There are also reasons why it might be attractive from the perspective of industry to get exclusivity from the FDA rather than from the patent system. This is because the FDA provides product exclusivity, while the patent system provides invention exclusivity. When new product development uses many prior patented inventions, strengthening patents adds to the costs of drug development as well as the profits from selling new drugs.

On the other hand, in a political environment that is more concerned with controlling the rising costs of drugs than with fortifying incentives for new drug development, it may be harder to sustain the complex regulatory web that currently supports high drug prices. It is politically difficult to change the patent system, particularly in the post-TRIPS era,[28] but there are lots of other levers to push in the drug regulation system to chip away at the market exclusivity that supports current drug prices, and FDA regulation might make a better political target than patents. Eliminating FDA-imposed restrictions on access to product markets fits with a pro-business, anti-regulation narrative, while cutting back on patent rights sounds anti-business.

It is particularly important to understand the role of FDA regulation in supporting biopharmaceutical innovation in the current political environment, which is characterized by some hostility toward the core functions of the FDA in protecting health and safety by historical standards. For much of the FDA's history, Congress and the courts have been broadly supportive of the agency's conservative stance toward protecting the public from products that might be hazardous or useless or both.[29] In the past two decades that attitude has turned around dramatically, as consumer sovereignty has come to dominate consumer protection in the political discourse of product regulation. Today, rather than being praised for keeping bad products off the market, the FDA is more likely to be criticized as a paternalistic bureaucracy imposing costly regulatory barriers between patients who demand new products and an industry eager to deliver those products.

It became strikingly apparent in the early days of the AIDS epidemic that many patients were willing to take risks that the FDA did not approve of rather than allow their illnesses to progress pending definitive clinical trials of new products. Disease advocacy groups and pharmaceutical firms forged a powerful political alliance

28. *See* Eisenberg, *supra* note 1, at 128-29.
29. *See* Eisenberg, *supra* note 1, at 123.

to cut back on regulatory obstacles and bring new products to market on a fast track. At the same time, the FDA's efforts to control marketing claims by manufacturers for off-label uses have also come under assault as violating the First Amendment, with the opponents of regulatory controls scoring some significant victories in the courts.[30] In this changed political environment, the roles of the FDA as a market gatekeeper (and censor of marketing claims) are likely to be reappraised, making it especially important to understand just what work the FDA does.

I suggest that any such reappraisal should consider the role of the FDA in promoting biomedical innovation. Indeed, many of the powers and authorities of the FDA make more sense from this perspective than they do from the perspective of the agency's traditional function of protecting consumers from purveyors of snake oil.

Consider, for example, what may be the most powerful authority exercised by the FDA: the power to approve or disapprove new drug applications based on evaluation of data concerning safety and efficacy. This market gatekeeper function was first granted to the agency by Congress in 1938[31] to exclude unsafe products from the market, and later expanded in 1962[32] to exclude ineffective products. It imposes significant costs and risks on drug development, and seems quaintly paternalistic when patients enjoy relatively unfettered access to products like Ephedra. From a consumer protection perspective, it is difficult to make sense of the present two-tiered market that subjects ethical pharmaceutical products to rigorous regulatory standards for scientifically sound proof of safety and efficacy, while leaving the shelves of Whole Foods market full of substantially untested and unregulated "dietary supplements" that purport to have similar effects.

One might argue that we should eliminate the exemptions that currently allow these dietary supplements and nutriceuticals to remain on the market, but some consumers (including some members of Congress) want these products and do not want the FDA to regulate them, and they have succeeded so far in persuading Congress to keep the FDA off their backs. Yet the existence of a relatively unregulated dietary supplement market alongside a highly regulated

30. *See, e.g.*, Thompson v. W. States Med. Ctr., 535 U.S. 357 (2002) (holding prohibitions against prescription solicitations and advertising violated First Amendment); Pearson v. Shalala, 164 F.3d 650, 651 (D.C. Cir. 1999) (invalidating regulations requiring sellers of dietary supplements to obtain FDA approval before labeling supplements with health claims).

31. Federal Food, Drug, and Cosmetic Act of 1938, Pub. L. No. 75-717, 52 Stat. 1040 (codified as amended at 21 U.S.C. §§ 301-95 (2000)).

32. Drug Amendments of 1962, Pub. L. No. 87-781, 76 Stat. 780 (codified as amended at scattered sections of 21 U.S.C.).

pharmaceuticals market poses a challenge to a justification for regulation that rests on safety and consumer protection.

The FDA's approach to off-label use of products that have been approved only for a narrower set of indications is also puzzling in terms of consumer protection. On one hand, the FDA has no authority over the practice of medicine,[33] and leaves doctors free to prescribe approved drugs for any purpose,[34] notwithstanding the absence of clinical trials to establish the safety and efficacy of the drug for off-label uses. On the other hand, the FDA sharply curtails (insofar as the courts will permit[35]) manufacturers' efforts to disseminate information about off-label uses of drugs to physicians. Do prescriptions for off-label uses threaten health and safety or not? If so, then why permit them? If not, then why not permit—indeed promote—dissemination of whatever information is available about these uses to physicians to help them make the best choices possible for their patients?

These boundaries of FDA regulation, although puzzling from a consumer protection perspective, make considerably more sense from the perspective of promoting innovation. The FDA uses its powers as market gatekeeper and censor of marketing claims to promote investments in scientifically sound clinical trials to generate valuable information about drugs. This information is socially valuable—valuable to consumers, insurers, and health policy makers—but manufacturers are not always in a position to capture that value, and so we can't trust them to generate it in an unregulated market.

Indeed, in an important sense FDA-approved drugs are information products. One could argue that information gathered in clinical trials is what distinguishes the products we call "drugs" from chemicals sold for other purposes, like industrial solvents, laundry detergents, and herbal remedies. If this information were so valuable, one might expect it to be generated without the intervention of the FDA, and of course some of it is. But FDA-approved trials have more credibility—with patients, doctors, and health payors—than studies done without regulatory oversight, for an obvious reason. Manufacturers have an interest in selling more of their products, and rigorous clinical trials might generate information that has just the opposite effect.

A conspicuous example of this risk is the recent disclosure of surprising results of an NIH-sponsored, double-blind, placebo-

33. *See, e.g.*, Chaney v. Heckler, 718 F.2d 1174, 1179 (D.C. Cir. 1983) (noting legislative history of the Food, Drug, and Cosmetic Act "expresses a specific intent to prohibit FDA from regulating physicians' practice of medicine"), *rev'd on other grounds*, 470 U.S. 821 (1985).

34. *See, e.g.*, United States v. Evers, 643 F.2d 1043, 1044 (5th Cir. 1981) (holding physician could not be found liable for violating FDA regulations against misbranding when administering drug to his own patients).

35. *See supra* note 30 and accompanying text.

controlled study of the effects of hormone replacement therapy ("HRT") on risk of heart disease in post-menopausal women.[36] Less rigorous observational studies had previously suggested that women who take HRT reduce their risk of heart disease, and this was enough to lead to widespread off-label use of HRT for that purpose, although the FDA had only approved it for relief of menopause symptoms. When the NIH finally conducted a more rigorous study, the results indicated a slightly increased risk of heart disease in women receiving HRT,[37] and sales of the product have dropped off significantly. In this case, government funding provided valuable information that the product's manufacturer had little incentive to uncover on its own.

We can think of FDA-mandated clinical trials as a way of internalizing the cost of this sort of research to the manufacturers who stand to profit from product sales, but that certainly is not the only way to go. Alternatives include: publicly-funded clinical trials of drugs, like the HRT study; regulatory "carrots" from the FDA, like the market exclusivity offered as an inducement to conduct pediatric clinical trials, rather than regulatory "sticks" such as restrictions on marketing; tort liability for harms resulting from risks that should have been discovered in the course of clinical trials and revealed to patients or doctors; or perhaps payor/HMO-funded clinical trials to determine which drugs are worth paying for (although payors thus far have shown little interest in sponsoring such trials). Each of these approaches has its pros and cons.

CONCLUSION

I have no strong bottom line about whether or how far the functions of the FDA should be curtailed, augmented or reallocated. Currently the National Institute for Alternative Medicine is conducting clinical trials on some popular herbal remedies and nutriceuticals, such as chondroitin and glucosamine sulfate for arthritis. These trials are worth watching closely to see what we might expect from leaving clinical trials of minimally regulated products to the government. Another interesting innovation that makes sense if one considers the role of the FDA from the perspective of innovation policy rather than strictly consumer protection is greater reliance on post-marketing studies, conducted under FDA supervision after a product is brought to market, rather than requiring definitive clinical test results before a product may be sold. The FDA pioneered this approach without clear

36. *See* Writing Group for the Women's Health Initiative Investigators, *Risks and Benefits of Estrogen Plus Progestin in Healthy Postmenopausal Women: Principal Results from the Women's Health Initiative Randomized Controlled Trial*, JAMA, July 17, 2002, at 321-33.

37. *Id.*

statutory authority as a part of its fast-track procedures, and Congress later endorsed it in the Food and Drug Modernization Act of 1997.[38]

What alternatives we imagine depends on how we understand the functions that the agency currently performs. If the function of the FDA is understood solely in terms of protecting consumers from dangerous or fraudulently marketed products, then some of its current regulatory authorities might appear to be unduly costly and paternalistic, and thus good candidates for reform. On the other hand, if we recognize that the FDA has come to play an important role in structuring incentives for biopharmaceutical innovation, some otherwise puzzling features of its authorities make a bit more sense, and we might be more reluctant to tamper with them without considering the adequacy of other measures to achieve similar policy goals.

38. Pub. L. No. 105-115, 111 Stat. 2296 (1997) (codified as amended at scattered sections of 21 U.S.C.).