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Saving the Goose: Intellectual Property and Follow-On Biologics (FOB)

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EXECUTIVE SUMMARY

Congress is under pressure to cut back on intellectual property rights in drugs produced by biotechnology so as to encourage the marketing of generic versions. The underlying conventional wisdom is that this would reduce prices and thus be in the interests of consumers, and would result in cost savings to the health care system as a whole.

This paper makes a contrarian case. Consumers' dominant interest is in having new medicines created. Price reductions, while desirable, are distinctly secondary. Early introduction of generics discourages R&D and inhibits the creation of new drugs. In the long run, because introduction of new drugs is a major route to reducing costs of other parts of the system, a premature shift to generics would not only harm consumers, it would increase rather than decrease overall health care costs.

The question is, "Why has the conventional wisdom become perverse?" The paper suggests six reasons why the true nature of the interest of consumers is misunderstood.

The effect of the limited time for recovery of R & D costs;
Pharmaceutical research as a winner-take-most tournament;
Interest group and academic opposition to Intellectual Property;
Incentive structures of third-party payers and governments;
Static versus dynamic efficiency and the myth of marginal cost pricing; and
Concerns about market power.

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INTRODUCTION

Each day's newsclips repeat the accusation that an excessive level of protection of intellectual property is depriving people, especially those in the developing world, of access to life-saving drugs.[1]

The argument usually continues along the lines that some new system is needed, one with a decreased level of patent protection. In particular, we are warned that the new and exciting field of biotechnology requires Congress to cut back intellectual property rights so as hasten the introduction of generic substitutes for patented products, and thus, it is asserted, increase the public welfare.

This assertion, powered by a number of well-funded international non-governmental organizations, is attaining the status of conventional wisdom.

The purpose of this paper is to present the contrarian case, to argue that this conventional wisdom is wrong and that the full exploitation of the potential of the biotechnology revolution requires greater protection of intellectual property rights, not less. In the end:

> [Property rights and markets are not antithetical to cooperation. Quite the opposite; they are the precise mechanisms by which advanced societies achieve cooperation. Nothing else works with comparable efficiency and justice — not voluntarism, and certainly not command-and-control.[2]

This does not mean that improvements in our IP regime are unnecessary; much can be done to improve the effectiveness of the intellectual property system as a mechanism of cooperation. But to start by undermining the very institution of property rights that makes cooperative efforts possible would be a grave error.

THE BIOLOGICS REVOLUTION

Biotechnology is "a collection of technologies that capitalize on the attributes of cells, such as their manufacturing capabilities, and put biological molecules, such as DNA and proteins, to work for us."[3]

Biotechnology has important applications in many fields, including agriculture, environmental protection, energy, and manufacturing. Perhaps its most prominent current use

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[1] See, *e.g.*, *Toward a New Era of Intellectual Property: From Confrontation to Negotiation*, A Report from the International Expert Group on Biotechnology, Innovation and Intellectual Property (Sept. 2008) http://www.theinnovationpartnership.org/documents/TIP_Report_E.pdf.

[2] James V. DeLong, "Intellectual Property: A Tool for Cooperation," *Futures*, Vol. 2, Issue 1, p. 33 (2006) http://convergencelaw.com/filings_pubs/pdf/IP_Futures2.pdf.

[3] BIO, *Guide to Biotechnology* http://bio.org/speeches/pubs/er/technology_collection.asp.

is in pharmaceutical research, where "biologics" – medicines produced through biological processes, usually involving recombinant DNA technology, and usually built on improvements in natural biological processes – represent the cutting edge. The techniques "allow a company to take living cells and make them into factories to produce medicines" that "weren't possible using chemistry."[4] As explained by BIO, a leading industry association:

> All cells speak the same genetic language. The DNA information manual of one cell can be read and implemented by cells from other living things. Because a genetic instruction to make a certain protein is understood by many different types of cells, technologies based on cells and biological molecules give us great flexibility in using nature's diversity.
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> In addition, cells and biological molecules are extraordinarily specific in their interactions. As a result, biotechnology products can often solve specific problems, generate gentler or fewer side effects and have fewer unintended consequences.[5]

This is the goose that will, we hope, produce a continuing stream of life-saving golden eggs far into the future. The first biologic, human insulin, was approved by the FDA in 1982. Now, the industry comprises over 5000 companies world wide, and generates $89 billion in revenues. Twenty products produced $20 billion in sales as of 2004, and by 2007, 350 more were in late-stage clinical development.[6]

The biologics revolution is restructuring the industry as well, as new biotech firms that focus on research team up with established firms possessing hard-won expertise in clinical testing, regulation, market support, and post-market monitoring. The future is exciting, with prospects of pharmaceuticals tailored to genetic makeup of subgroups of the population, and even individuals.

A key question is: How will all of this be financed? Technological revolutions take money, and a stream of new life-enhancing and live-saving biologics will require corresponding rivers of revenue, especially because, as is true of any nascent field, many false starts and spectacular wipe-outs are inevitable. Only about 5% of existing companies specializing in biotechnology products are profitable, and the great majority are development stage companies focused on a limited range of possible products. It is an axiom of practical economics that if substantial sums are going to be lost, then a balancing possibility of substantial rewards must exist.

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[4] Susan Desmond-Hellman (President of Product Development for Genentech), Innovators' Dilemmas, *The American* (Sept./Oct. 2008) http://www.american.com/archive/2008/september-october-magazine/innovators2019-dilemmas.

[5] BIO, *Guide to Biotechnology*.

[6] Italian Biotechnology Directory, *Facts & Trends Analysis 2007*, pp. 12-15 http://www.biodirectory.it//files/F&T2007_biopolo.pdf [hereafter *Facts & Trends*].

FINANCING PHARMACEUTICAL INNOVATION

Pharmaceutical research is financed by our system of using patents to protect intellectual property, and no other industry is as completely dependent on that system. The reasons are simple. Pharmaceuticals require large upfront investment in research and testing. They are also the product of a "tournament" system – many candidates start the process, but few survive to become approved drugs. "On average, only five of every 10,000 compounds investigated are tested in clinical trials. Of those five, only one is every approved for patient use," and of those approved, "only three of every 10 . . . generate revenues that meet or exceed average R&D costs."[7]

Once a winner emerges, imitating it is relatively cheap. So the industry is vulnerable to free riders who wait until the outcome is determined, then introduce an imitation that can be priced lower because the imitator need not recapture the investment in R&D and clinical testing, and need not make large capital investments that earn no return while the innovation awaits regulatory approval. An imitator is like a past-poster at a race track who finds a way to bet on the winning horse after the race is over.

Medical economist Henry Grabowski notes the particular importance of patents in the pharmaceutical industry, which differs from some other industries, "such as computers and semiconductors, [which] placed greater stress on factors like lead-time and learning-by-doing efficiencies in production accruing to first movers." He cites research on the economic value of patents that concluded that the absence of patent protection would reduce R&D by about 8% across all industries – but for pharmaceuticals, such absence would reduce R&D by 64%.[8]

A company files an application for a patent on a possible pharmaceutical product, usually long before it is approved for clinical use by the Food and Drug Administration. Once the patent is granted, the company has an exclusive right to use the substance for 20 years from the date of the application. Given the length of time it takes to process a patent application and to receive approval from the FDA, the realistic period of exclusivity created by a patent averages 12 years. After expiration, the substance enters the public domain, and anyone can copy it without paying anything to the discoverer.

This basic patent system of a term of exclusivity after which the invention falls into the public domain is applicable to patents in all fields. The theory is that the inventor can earn enough during his period of exclusivity to make his investment in creation worthwhile. The term chosen, 20 years, has no particular theoretical basis. The term of a patent was 17 years until 1994, when Congress extended it to conform with international practice. The 17 year

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[7] Phrma, *What goes into the cost of prescription drugs?* (June 2005), p. 2 http://www.phrma.org/files/Cost_of_Prescription_Drugs.pdf.

[8] Henry Grabowski, *Patents, Innovation and Access to New Pharmaceuticals* (July 2002), p. 3 http://levine.sscnet.ucla.edu/archive/grabow-patents_innov.pdf.

term was also a-theoretical. It just seemed about right when first selected, and people have found it workable enough.

Pharmaceuticals present a special situation because, unlike most other inventions, they are subject to elaborate regulation by the FDA to ensure both safety and efficacy. On average, 8.5 years elapse from preliminary tests to final approval,[9] so the regulatory process reduces the effective life of the patent. It also imposes huge costs not borne by other types of inventions. In 2003, the consulting firm Bain & Co. estimated the costs of bringing a new drug to market at $1.7 billion.[10] The "Discovery" stage – the basic R &D – cost about $500 million while the Stage III clinical trials in human beings soaked up about $870 million.[11] The most recent estimate by the DiMasi and Grabowski, who are the premier authorities on the question, is that development costs for ordinary (non-biologic) drugs averaged $1.318 billion as of 2005, as compared with $1.241 billion for biologics.[12] (The major difference seems to be due to Bain's inclusion of launch costs, which is not contemplated in the DiMasi/Grabowski work.)

GENERIC DRUGS

Patented drugs are always marketed under a special brand name, such as "Prozac." But a drug also has a generic name that describes the basic chemical substance, such as "fluoxetine," which is the generic name for Prozac. "Aspirin" is the trade name that Bayer gave to the generic substance "acetylsalicylic acid.**"**

The system of relying on the patent system to finance pharmaceutical innovation creates problems upon the expiration of a patent. Imitators assert that they should then be legally free to market the generic compound, and to rely on the innovator's original research as proof that the generic substance is safe and effective.

The innovators object to giving the makers of generics a free ride not only on the innovators' R&D but on its expensive testing program. The innovators' view is that imitators should also be required to prove that their drugs are safe and efficacious, a requirement that would of course delay the introduction and add to the costs of generics, which would make them less competitive.

The manufacturers of generics counter that requiring a replication of the original testing would be a waste of money and time. They argue that the active ingredient in a

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[9] U.S. Dept. of HHS, Centers for Medicare and Medicaid Services (CMS), *Health Care Industry Market Update: Pharmaceuticals* (Jan. 10, 2003), p. 14 http://www.cms.hhs.gov/CapMarketUpdates/Downloads/hcimu11003.pdf [hereafter CMS, *Pharmaceuticals*].
[10] Bain & Co., *Has the Pharmaceutical Blockbuster Model Gone Bust?,* Dec. 08, 2003 http://www.bain.com/bainweb/About/press_release_detail.asp?id=14243&menu_url=for_the_media.asp.
[11] *Facts & Trends*, p. 14, Fig. 3.
[12] J.A. DiMasi & Henry Grabowski, The Cost of Biopharmaceutical R&D: Is Biotech Different? *Managerial and Decision Economics*, 28:469-79 (2007).

pharmaceutical is the key factor, and that once this has been tested for safety and efficacy by the original patentee, it makes no sense to require a repetition that would, by the laws of science, reach the same result.

This issue was debated for years, and in 1984 a compromise was reached, the Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman), which U.S. government researchers call "the single most important piece of legislation to affect the modern pharmaceutical industry."[13] A generic drug is allowed to piggyback on the clinical testing performed by the original patentee, once the manufacturer shows that its product is indeed the bioequivalent. In exchange, the pharmaceutical companies were given data exclusivity for five years, meaning that the piggybacking is not allowed for that period. They also got patent extensions when the slowness of the FDA process eats up too much of the patent term.[14]

Most public commentary praises Hatch-Waxman as a big success, and so it is, viewed from the single-value perspective of increasing the use of generics and reducing the dollars that consumers spend on prescription drugs in the short term. (As discussed later in this paper, there is room for considerable ambivalence when Hatch Waxman is appraised from a broader perspective.) By 2003, it took only 6-8 weeks for a generic to take a 50% market share once it became available,[15] and generics now represent at least 65% of all prescriptions and 20.5% of all money spent on them.[16]

Because Hatch-Waxman is regarded as a policy-making triumph, demand has arisen to extend its basic provisions from conventional drugs to biologics, to let Follow-On Biologics (FOBs), or "Biosimilars," as they are called in Europe, or "Follow-On Proteins" (the FDA's preferred term) free ride on the testing performed to establish the safety and efficacy of the original drugs.

All the relevant players, including the pharma and biotech innovators as well as the imitative generic manufacturers, endorse in principle then need for a regulatory pathway to the creation of FOBs. Of course, there are disagreements about how smooth this pathway should be.

A serious problem is that both the safety and bio-equivalence of FOBs are much more difficult to determine than is true for conventional pharmaceuticals. Broad agreement on the

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[13] CMS, *Pharmaceuticals*, p. 16.
[14] The law also addressed the problem of "orphan drugs," those with a potential market insufficient to justify an investment in development. A readable primer on the regulatory process is contained in Donna M Gitter, "Innovators and Imitators: An Analysis of Proposed Legislation Implementing an Abbreviated Approval Pathway for Follow-On Biologics in the United States," *Florida State University Law Review*, Vol. 35, No. 3, 2008. Available at SSRN: http://ssrn.com/abstract=1012859 [hereafter cited as Gitter].
[15] CMS, *Pharmaceuticals*, p. 3.
[16] Generic Pharmaceutical Association, *Statistics* http://www.gphaonline.org/Content/NavigationMenu/AboutGenerics/Statistics/default.htm (visited July 24, 2008).

nature of the problems exists, and the reasons are well covered in the literature. Typical is a description provided by Representative Anna Eshoo (D-CA), who cannot be accused of being overly solicitous of the pharmaceutical companies:

> As a primary matter, it's important to recognize that traditional "small-molecule" pharmaceuticals and biologics are fundamentally different in their development, their manufacture and their chemical makeup. A traditional small-molecule drug is manufactured through synthesis of chemical ingredients in an ordered process, and the resulting product can be easily identified through laboratory analysis. A biologic is a large, complex molecule, which is "grown" in living systems such as a microorganism, a plant or animal cell. The resulting protein is unique to the cell lines and specific process used to produce it, and even slight differences in the manufacturing of a biologic can alter its nature. As a result, biologics are difficult, sometimes impossible to characterize, and laboratory analysis of the finished product is insufficient to ensure its safety and efficacy.
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> The pharmaceutical drug production process is easily replicated and a "generic" drug product is virtually identical to the original innovative product, so generic drug manufacturers are permitted to reference the original testing data submitted by the innovator companies when the original drug is submitted to the FDA for approval. With biologics, the manufacturing process is unique to each biologic and is not generally disclosed as part of the published patent. A biosimilar manufacturer would have to have intimate knowledge of these proprietary processes in order to "duplicate" the biologic product, and even then it is extremely difficult – no two living cell lines are identical, so no two biologics manufacturing processes have identical starting materials or proceed in the same way.
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> It's also important to note that because biologics are produced with cells from living organisms, many of them can cause an immune reaction which is normally benign and does not affect safety. However, some of these reactions can negate the effectiveness of the biologic or even cause side effects that are more dangerous. Most of these reactions can only be observed through clinical trials with real patients.[17]

The problems can be subtle and difficult to resolve. Famous in the field is the case of Eprex, in which Johnson & Johnson, surely among the most sophisticated and respected companies in the world, made a minor change in the rubber stopper used with a particular biologic, which resulted in an increase in a form of anemia.[18] Tracking the cause of the increase to the

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[17] Statement of Rep. Anna G. Eshoo, *Introduction of H.R. 5629, the Pathway for Biosimilars Act*, U.S. House of Representatives (March 13, 2008) http://eshoo.house.gov/images//biosimilars%20intro%20statement.pdf.

[18] BIO, *The Difference with Biologics: The Scientific, Legal and Regulatory Challenges of Any Follow On Biologics Scheme* (April 25, 2007) http://www.bio.org/healthcare/followonbkg/WhitePaper.pdf (Paper written by Life Sciences attorneys at Sidley Austin).

stopper change took four years of investigation by 100 people, and the detectives are still not 100% certain of their conclusions.[19]

Despite these problems, pressure to create a regulatory route for the approval of FOBs is powerful. It comes particularly from the generic industry, which wants in on a good thing, and from the funders of medical care, who want to get costs down, *now*. Several bills are pending in Congress: Biologics Price Competition and Innovation Act (S.1695)**;** Affordable Biologics for Consumers Act (S. 1505); Patient Protection and Innovative Biologic Medicines Act (H.R. 1956); Pathways for Biosimilars Act (H.R. 5629); Access to Life-Saving Medicine Act (H.R. 1038 & S. 623).[20] These vary in the degree to which they would facilitate the recognition of FOBs as equivalent, or interchangeable, with the patented reference drugs, and of course the generic and conventional industries are split on the best approach.[21]

REVISITING THE INCENTIVE STRUCTURE FOR R&D

The current debate about a pathway for FOBs focuses on the scientific issues, with only a tip of the hat to economic issues. Some, but not all, of the bills provide for a period in which innovators retain exclusive use of their data. These are not particularly generous – 12 years seems to be par. The underlying assumption seems to be that Hatch-Waxman settled the economic issues, and that this settlement should automatically be transferred to the FOB arena.

In fact, the economic issues deserve a more careful look. Their assumed settlement is illusory, because the assumptions underlying Hatch-Waxman are dubious. In the 25 years since passage of that law, the models of competition on which it was constructed have come into increasing question. The difficult economic and policy issues attending FOBs actually need to be revisited.

The innovating companies can fairly make a series of over-lapping points about the complexity of the economic and policy calculations.

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[19] Fred Bader (VP at J&J), *Immunogenicity of Therapeutic Proteins: A Case Report* (Sept. 14 & 15, 2004) www.fda.gov/cder/meeting/followOn/Bader.ppt.

[20] All are available through the Library of Congress Thomas service http://thomas.loc.gov.

[21] For descriptions, see Judith A. Johnson, *FDA Regulation of Follow-On Biologics*, CRS Report for Congress (June 18, 2007) http://opencrs.cdt.org/document/RL34045; Wendy H. Schacht & John R. Thomas, *Follow-On Biologics: Intellectual Property and Innovation Issues*, CRS Report for Congress (May 21, 2008) http://opencrs.com/document/RL33901.

The True Nature of Consumers' Interest

Most public discussion starts from the premise the patients' interest is primarily in having the price of prescription drugs reduced. The need to maintain the incentives for innovation is noted, but this is portrayed as an interest of the manufacturers, not of the consumers.

Indeed, in connection with drugs, as with other types of creative products, the issue is often phrased as a need for a "balance" between producers and consumers, as if the two groups were locked in a zero-sum game, squabbling over a fixed pot, and as if no harm to innovation will occur as long as the innovative producers are earning a profit. [22]

This depiction is seriously misleading. Consumers' best interests would be served by a *strengthened* intellectual property regime that puts *more* revenue into the hands of the producers.

To explain this conclusion, one should start by recognizing that one of the more problematic statements now permeating the national debate is the repeated premise that "The U.S. spends too much on health care." Considering the absolute primacy of health and health care to quality and length of life, the nation should continually spend more on health care as it is able to afford it. More money is spent on health care than before because medicine has improved so much that it delivers very high value.

To take a personal experience, a few years ago I took a bad fall and severed a patellar tendon. The full armament of medicine was brought to bear -- a skilled surgeon backed by a medical team in a well-equipped hospital, a variety of drugs, a high-tech brace, physical therapy, acupuncture, massage. Within a relatively short time I was fine and fully mobile, recovered from an injury that, not so long ago, would have crippled me permanently.

Did this "cost too much" in the sense that I should have preferred to be crippled to save my money to buy a bigger house or car or more electronic toys? That would be an absurd statement. Did it cost too much in the sense that I, and society, would be better off if the option of repair had not been available so that I would not have been tempted to spend money on it? The suggestion is equally if not more ridiculous.

So how can anyone suggest that our current annual national health care bill of $2 trillion ($6,600 per capita) is "too high" without looking at the benefits? Would I have preferred to pay less for the insurance that covered the costs? Sure, but I would like to pay less at the grocery store, too, and I could use a rent reduction. Would I like to see waste and fraud eliminated? Of course, but that is not the same as the "we spend too much" conclusion. On a value-for-money basis, that knee repair was the best bargain of my life, and my major interests were that the treatment be available and of high quality. The cost mattered, but it was a tertiary concern.

[22] See, *e.g.*, Gitter, Note 14.

Transfer this example to the context of prescription drugs. Lower prices are a consumer interest, but far from the most important. It is much more important that a variety of effective drugs be available, that quality be assured, and that, if the stars of science are aligned so to make it possible, that a stream of new medicines be developed. Any public policy action that reduces costs at the expense of these other and more important interests is dubious indeed.

From this perspective, the rise of generics should give great pause to consumers and their representatives. The major fact about generics in the current system is that they make no contribution to the costs of the R&D that produced the innovation or to the operations of the testing and regulatory system that certified it. As a result, every increase in market share for generics means that the amount of money available for R&D is reduced.

A recent Congressional Budget Office (CBO) study found that "an FDA approval pathway for follow-on biologics . . . would cut federal government spending on health care by $5.9 billion and national expenditures on biologics by $25 billion over the next decade."[23] If CBO meant that this action would wring $25 billion in inefficiencies out of the health care system, that would be an excellent thing. But that is not what the statement means. It means that expenditures on drugs will be $25 billion less than would otherwise have been the case, and while this might *seem* to be an excellent thing – same quantity of drugs for $25 billion less – in fact it is troubling.

The introduction of generics will not reduce manufacturing costs, so the $25 billion must come primarily from three sources: R&D; profits; distribution/education. On balance, the consequences of this are not good:

- With respect to immediate R&D reductions, it is axiomatic that biotechnology is a promising field, and that research will produce payoffs that consumers will value highly. Taking research money out of the system removes these payoffs, by definition.

- Reducing profits will also reduce R&D. Investors put up money for R&D in anticipation of profits. If they know that revenues will be siphoned off to generic competitors, then many investments become uneconomic.

- Nor are reductions in distribution costs necessarily a blessing. Much "distribution" expense could be renamed as "education" of both medical professionals and patients. A source of savings from generics is that they usually do not perform this education function. As Henry Grabowski points out, biologics are more complicated than small molecule drugs, and require more education and informational support. So either the

[23] Congressional Budget Office, *Research and Development in the Pharmaceutical Industry* (Oct. 2006) http://www.cbo.gov/ftpdocs/76xx/doc7615/10-02-DrugR-D.pdf.

> savings will not be as large as promised, or functions vital to patients will go unperformed.[24]

There is considerable irony in the fact that every time the proponents of a pathway for FOBs increase their estimate of the savings that will be attained by allowing generics, they undermine their own argument. Their ideal case, the situation in which all drugs are sold at the marginal cost of production, would be a state of absolute stasis, with zero R&D, and zero innovation.

Furthermore, prescription drugs constitute only 10% of the total costs of the health care system,[25] and 20% of the expenditures of people under 65 years old.[26] The import is that even large percentage savings in drug costs would result in only minor savings for the health care system as a whole. At the same time, pharmaceutical R&D represents the best hope of achieving breakthroughs that will substantially reduce the costs of other health services, including hospital care (31% of all expenditures) and physician and clinical services (21%). So moving toward generic FOBs at the price of reducing R&D funding would achieve only minor current savings while sabotaging not only future health care quality but the possibility of major future cost savings in other sectors.

Problems in Communicating the Nature of Consumers' True Interest

Given the realities of the true nature of the interests of consumers, the conundrum is why discussion of the medical care system has become so fixated on the costs of prescription drugs. Six factors come to mind:

> The effect of the limited time for recovery of R & D costs;
> Pharmaceutical research as a winner-take-most tournament;
> Interest group and academic opposition to Intellectual Property;
> Incentive structures of third-party payers and governments;
> Static versus dynamic efficiency and the myth of marginal cost pricing; and
> Concerns about market power.

These will be taken up in order.

The Effect of the Limited Time for Recovery of R & D Costs

A fundamental problem permeating the field of pharmaceutical development is that the entire cost of developing a drug must be recaptured through sales during the relatively brief period

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[24] Henry Grabowski, *Statement to the House Oversight and Government Reform Committee*, March 26, 2007 http://oversight.house.gov/documents/20070416132526.pdf.
[25] U.S. Bureau of the Census, *Statistical Abstract of the United States*, Table 124 (2008).
[26] J. P. Sommers, *Prescription Drug Expenditures in the 10 Largest States for Persons under Age 65, 2004.* Statistical Brief #158, Agency for Healthcare Research and Quality (January 2007) http://www.meps.ahrq.gov/mepsweb/ data_files/publications/st158/stat158.pdf.

of patent protection and data exclusivity. Inevitably, this pushes up the prices, because the basic pricing formula is inexorable – Price (X) Volume (X) Time must equal the $1.7 billion development charge plus all the costs of production, distribution, and post-launch monitoring. If the time over which costs can be recovered becomes longer, or the number of patients larger, then prices will decline.[27]

So if the system limits the time during which the innovator maintains its exclusivity, then this forces the prices higher, which creates intense moral and political pressures on the system. Because all the development costs are loaded onto the first few years of a drug's life, the price must be kept high. Then the patent expires and generics enter, and the price inevitably falls off a cliff. The immediate reaction of consumers seems to be, "Hey, you must have been cheating me all those years!" Then the initial high prices are used to justify the need for generics, and to inflate the estimates of the savings that will be produced by their introduction.

Similarly, if foreign nations put price controls on drugs, the rational manufacturer will still sell in the foreign markets as long as the price exceeds the marginal costs of production. That way, it gets at least some contribution toward recoupment of development costs. But this leaves most of the development cost on the U.S. consumers, who then look at the lower prices overseas and say, again, "Hey, you're cheating me!"

These reactions encourage actions such as approval of generics or reimportation. These then reduce the patient base over which the R&D and regulatory costs can be spread, which requires that the initial prices be even higher, which then increases the public irritation at the high price of prescription medicines, in a continuing vicious circle.

Another dysfunction should be noted. As development costs increase and the time-for-cost-recovery decreases, the innovators are forced to focus on finding "blockbusters," drugs with very high, quick demand. They are often criticized for this, but it is the inevitable result of the pricing equation. The high costs of R&D, regulatory review, and education must be spread over a large base of users if prices are to be kept down. For example, assume a drug has a million users. The sunk costs of $1.7 billion for development mean that the producer must get $1,700 in revenue from every one of them, plus additional sums for actually making and distributing the drug, plus time costs of money. Take the number of users down to 100,000, and the price tag goes to $17,000 per person for development alone.

Pharmaceutical Research as a Winner-Take-Most Tournament

Outraged reactions over the consequences of loading all the costs of R&D, regulatory approval, and education onto a brief initial term of patent protection are accentuated by the nature of the business. As noted earlier, drug development is a winner-take-most tournament,

[27] This is a bit over-simplified because price discrimination is possible, a phenomenon that raises distinct and complicated problems of its own.

in which a small number of successes must pay the costs incurred by the large number of failures.

Such industries are very vulnerable to attack, because those who pay for the successes do not much like subsidizing the losers. Thus the patient who needs drug X is unimpressed when you point out that he is also paying for drugs Y and Z, which did not work and had nothing to do with his condition anyway.

In this, the pharmaceutical industry is much like another industry that is heavily dependent on intellectual creativity – the music business. And the unfortunate recent experience of that business is instructive. There, too, thousands of new works are released each year; and very few are successful. Since determining *ex ante* what will succeed is impossible, the costs of the failures must be recompensed by high returns from the hits.

The music business is characterized by poor relations between the labels on the one hand (who supply the finance, production, and marketing) and the artists and customers on the other. The successful artists forget that their success was improbable *ex ante*, and think the labels are collecting an excessive amount of their earnings. The customers look at the margin between the cost of a plastic CD or an MP3 download and its price, and assume they are being cheated. These grievances have been an important factor in the confiscation of the industry's property that has occurred via the medium of P2P file sharing. Comparable feelings are an important part of anti-intellectual property sentiment in the context of pharmaceuticals.

Tournament economics are not impossible to understand. The public has a basic familiarity with the principles, from their own lives and from the world of sports salaries, where winner-take-most applies with particular force.

However, the principles are somewhat counter-intuitive, so public understanding and acceptance is vulnerable to being undermined if there are institutions which have an interest in doing so.

Interest Group and Academic Opposition to Intellectual Property

In the case of pharmaceuticals, two sets of institutions have an interest in undermining the IP system.

- The first is, obviously, the generic manufacturers. These have a strong interest in painting themselves as white knights, and they have been remarkably successful in establishing the narrative that they are reducing prices for consumers. *A priori*, one might have thought that the theme "free riders want to destroy the R&D system" would have had as much bite with the public, and thus with Congress, but that is not how it is playing out.

- Second, there exists a strong international anti-intellectual property movement, based in academia and foundations, remote from and distrustful of the realities of the market and real world economics, grounded in an ideology that decisions should be made by governments acting in the best interests of the hive, and very well funded.[28]

The efforts of these groups to demonize the innovators have been quite successful. They have been helped considerably by genuine weaknesses in the IP system, such as overly broad and vague patents, high transaction costs, and concerns about ambush – discovery of a pre-existing patent after a company has developed a successful product, such as in the Blackberry case. These issues are real, but they are far less important in the pharmaceutical field than in other areas of technology. They can also be addressed directly, not through the over-kill mechanism of repudiation of the basic institution of intellectual property.

Incentive Structures of Third-Party Payers and Governments

Many have commented on the distortions introduced into the health care system by the ubiquity of third-party payments. The area of imitators versus innovators presents another one. The consumers' interests are in availability, quality, innovation, and price, with the last of these lower on the scale of concern. For the third-party payer, price assumes a much higher priority. As an economic matter, a third-party payer is interested in a price/efficacy trade-off only if the drug will reduce other costs that would otherwise fall on the payer. If the drug does not do this, if it simply alleviates an otherwise intractable condition, then the real economic interest of the third party payer is that the drug not exist.

On the whole, creating an approved biologic is probably somewhat less expensive than creating a small molecule drug. But a few instances of very expensive treatments, such as $100,000 per patient year, have received heavy press play.

Faced with such expensive treatments, governments and other third-party payers face unpalatable choices: either ration drug availability in some fashion, thus telling some people that they simply do not get the treatment, or find some way to transfer the money to pay the bill from one sector of the populace to support the medicinal needs of another. Given the political unattractiveness of both alternatives, their optimum political course is:

(1) If such expensive drugs are developed, to introduce generic substitutes as quickly as possible;

(2) To avoid any need to face the problem in the future by discouraging the development of such expensive drugs.

[28] See Mark Schultz & David B. Walker, How Intellectual Property Became Controversial: NGOs and the New International IP Agenda. *Engage*, Vol. 6, Issue 2, p. 82 http://www.fed-soc.org/doclib/20080313_IPSchultz.pdf.

Allowing introduction of generics at an early stage accomplishes both these ends. While no one would ever admit to acting on these incentives, and most participants may be unaware of them, one must recognize that governments and third-party payers have strong motives to avoid difficult political and moral choice, even at the cost of having people suffer for lack of drugs that would otherwise have been developed, and that such incentives have a way of shaping behavior even when denied or unrecognized.

The phenomenon is similar to the oft-noted reality that the regulators' incentives are to be absolutely sure that dangerous drugs do not slip through the net, even if the cost is delay and false negatives that cost lives. People who die from a drug that turned out to be risky are highly visible; those who die from delay and excessive caution are not. That regulators respond to these incentives is hardly surprising, given that rational risk/benefit decision-making is often sabotaged by "truly vitriolic criticism from leading medical journals, Congress, and the news media." [29]

Of course, the cost of allowing these incentives to operate is high. While Moore's law is limited to semiconductors, biotech is also subject to learning curves, and costs will come down with time. Also, a significant characteristic of the field is that new uses are found for existing substances. Obviously, increasing the number of uses of a substance increases the number of users, and allows cost spreading that reduces the price.

Lest this analysis be regarded as overly-cynical, a forthcoming empirical analysis appears to confirm the assessment. The abstract says:

> [T]third parties (insurance or government) . . . reimbursement levels . . . tend to sacrifice future drug development because they limit profits to be made and therefore discourage manufacturers from investing in useful innovation. . . .
>
> Based on the careful empirical analysis of drugs used to treat HIV/AIDS, [the authors] conclude that drug manufacturers glean only about 5 percent of the mammoth returns brought about by these life-saving therapies. As a result, patients may be worse off than they would be with policies based less on cost-savings and more on incentives to develop new technologies. The implications of these findings, when taking account of other valuable drug classes, suggest that we face the prospect of paying less money for drugs now while getting far fewer new drug treatments later.[30]

[29] John Calfee, Book Review, 10 *DePaul Journal of Health Care Law* 513-522 (Spring 2007) (citing the Vioxx example) http://www.aei.org/publications/filter.all,pubID.26921/pub_detail.asp.
[30] Cato Institute, Description of Book Forum for *Innovation and Technology Adoption in Health Care Markets* (Sept. 2008) http://www.aei.org/events/filter.economic,eventID.1795/event_detail.asp.

Static versus Dynamic Efficiency and Marginal Cost Pricing

Policy discussions of the pharmaceutical industry are heavily influenced by the concepts of antitrust law, particularly as interpreted by the Federal Trade Commission, which, under the division of antitrust authority between the FTC and the Department of Justice, supervises this area.

The intellectual construct that dominates the practitioners of antitrust is that price should equal marginal cost, and that prices in excess of this are somehow "anticompetitive." While there is some recognition that in the real world prices must be set at level that allows recovery of investment costs, this necessity receives mostly lip service.

This misapprehension and its impact has been described by the distinguished economist William Baumol:

> Economists have generally been careful to point out that perfect competition is an artificial concept, albeit a useful and powerful analytic device. . . But the optimality properties long associated with this market form … **have tempted some who are not as careful as they should be to invite regulators and antitrust authorities to use perfect competition theory for guidance in their rulings**, as a way to promote the public interest. For example, only this year I heard a conference presentation dealing with the economic and legal principles of copyright suggest that the innovating Schumpeterian entrepreneurs are automatically to be deemed proper subjects for antitrust attentions because in the period before imitators enter the market, they can charge prices that exceed the marginal-cost levels of perfect competition. Never mind that this is a prescription for undermining intertemporal efficiency. **Never mind that marginal-cost pricing would generally preclude recoupment of the research and development (R&D) costs of the innovations at issue, costs that will have to be incurred many times again if innovation is to continue.** And never mind that a world of perfect competition requires constant returns to scale and firms so small that they would never attract the attention of regulatory or antitrust personnel.[31] [Emphasis added.]

Because intellectual property is so crucial to the pharmaceutical industry, the misapprehension has particularly deleterious effects in this context. Policy Analyst Solveig Singleton has expanded on the issue, focusing on the specific context of intellectual property:

> [T]he difference [is] between static and dynamic efficiency. The efficiency measure of the [marginal] cost models described above is static, in the sense that it does not allow for change over time. The model offers a definition of "efficient" or "inefficient" to which a snapshot of reality at a given instant conforms or does not conform. If prices fail to be set at marginal cost, one is done; one has found static inefficiency.

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[31] William Baumol, *Regulation Misled by Misread Theory: Perfect Competition and Competition-Imposed Price Discrimination,* American Enterprise Institute, Mar. 16, 2006, p. 1. http://www.aei.org/books/bookID.850/book_detail.asp.

> . . . .
> Since the real economy must deal with incentives to invest over time, dynamic efficiency is more relevant than static efficiency. A firm with market power earns high profits; this creates an opportunity for a new entrant into the market to come in and undercut the first price. No large firm has more than a transitory advantage. In Schumpeter's well-known description of creative destruction, he notes that during the period when a large firm does enjoy an advantage, it is able to pour extensive resources into research and innovation. Empirical business studies such as the *The Rule of Three* recently confirm the vulnerability of large firms to competition, even as markets tend to mature around a few dominant players and some small niche firms. There is no perfect competition, but neither is there stagnation of the sort that harms consumers. [Footnotes omitted][32]

The idea that marginal cost pricing is a desirable state of affairs should be expunged from all discussions of pharmaceutical markets. Nor should antitrust lawyers be making life-and-death decisions about pharmaceuticals on the basis of the antitrust industry's rather cartoonish view of the world.

The natural dynamic of a field like biotechnology should be for capital to flood in, lured by the prospect of high profits achieved through the protection granted by patents. A few would succeed; most would not. The overall impact would be a rapid advance in knowledge and a build-out of both R&D and production facilities. Thereafter, a number of companies would go bust, and their assets would pass on to new owners who would have lower costs, and would thus be able to charge less for the final products. Sufficient numbers of research facilities would exist to encourage the production of me-too drugs that provided a check on any monopolies.

The generics movement short circuits this dynamic process for the sake of a crabbed version of static efficiency, concerned solely with minor price savings in the short-term, and not at all focused on the long term.

Concerns About Market Power.

A logical question: Why has national thinking about the drug industry has taken such a perverse turn? A logical answer: in the pharmaceutical field, concern about monopoly prices and profits has real bite.

Professor Edmund Kitch has noted that, for the most part, patents do not confer undue market power. People find substitute products, or they do not want the product enough to pay for it, or competitors invent around a patent.[33]

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[32] Solveig Singleton, *Is Cheaper Always Better? Misusing the Concept of Marginal Cost in Policy Discussion*, Convergence Law Institute (Discussion Draft, July 23, 2008) http://convergencelaw.com/Jargon_Anonymous.__by_Solveig_Singleton_(00186370).pdf.

[33] Edmund W. Kitch, Elementary and Persistent Errors in the Economic Analysis of Intellectual Property, *Vanderbilt Law Review*, Vol. 53, p. 1727 (2000).

With pharmaceuticals, the fear of monopoly is acute, because the choice not to use the drug has serious impacts on life itself, or at least on its quality. Usually, substitutes do not exist, in part at least because the regulatory system has discouraged development of what it calls "me-too" drugs, even though it would seem logical to encourage these.

Looking at the history of other areas of economic life, such as transportation, power generation, and telecommunications, it is clear that the fear of monopoly has had serious results, and has often triggered government intervention in the form of regulatory regimes that discouraged innovation and investment.

Savvy industries, when faced with such threats, can defuse the drive for regulation by ceding some of their formal legal rights to charge monopoly rates.[34] The innovative pharmaceutical industry has been thinking along the same lines, developing programs to ensure that people in need are able to get drugs without excessive economic sacrifice. Finding mechanisms to turn such programs into formal commitments could be a powerful argument for allowing the industry the pricing freedom necessary if the goose of pharmaceutical R&D is to keep on laying the golden eggs, in the form of a continuing stream of new products.

The industry also needs to publicize these efforts more effectively, because the word is not penetrating through the fog of attacks on intellectual property rights.

CONCLUSION

The civil law of liability for negligence has a doctrine called "attractive nuisance." It covers a situation in which a property owner creates a situation that is both enticing to children and dangerous for them.

The current focus on creating FOBs is the health policy equivalent of an attractive nuisance. It looks appealing and resonates with current public concerns about health costs. It lends itself to sound bites, especially by those whose judgment is immature. But it also poses dangers to overall progress toward creating new pharmaceuticals in particular and improving and rationalizing the total health care system in general.

Certainly, improvements in the intellectual property system can and should be made. But changes should be approached with a clear understanding that the protection of intellectual property is a keystone of the system, and that the ancient medical maxim applies: *Primum non nocere.*

[34] James V. DeLong, Avoiding a Tech Train Wreck, *The American* (May/June 2008) http://www.american.com/archive/2008/may-june-magazine-contents/avoiding-a-tech-train-wreck.

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