

Chapter 9: The Pharmaceutical Industry

It is often argued that the best case for patents is in the pharmaceutical industry. The fixed cost of innovation is large, with estimates of the average cost of bringing a single new drug to market as high as \$800 million in year 2000 dollars.¹ Patent protection is more limited than in other industries: because of the lengthy gap between discovery and approval of a new drug, the effective monopoly protection is estimated to last only 12 years – plus the 3-5 year extensions, as allowed by the Drug Price Competition and Patent Term Restoration (Hatch-Waxman) Act of September 1984.² Indeed, according to the industry surveys mentioned in earlier chapters, the only industry in which patents are thought to play an important role in bringing new products to market is the pharmaceutical industry.

The pharmaceutical industry is worthy of special consideration also for another, complementary, reason. The technology operated by the pharmaceutical industry – the chemical and industrial processes through which medicines are produced, packaged, and shipped – seems to fit the constant returns to scale hypothesis almost perfectly. That is, the cost of shipping the ten millionth container of medicine is about the same as that of shipping the first. Thus the many complaints about the pharmaceutical companies not shipping medicines to poor countries – even poor African consumers would be willing to pay the actual few additional cents needed to produce the additional medicine.

Also, and again, since the Hatch-Waxman Act of 1984, producers of generic drugs have found it easier to enter the market, so much so that, according to the CBO, in the U.S. generic drugs reached 43% of the prescription segment in 1996, versus 19% twenty two years earlier. The Pharmaceutical Research and Manufacturers of America (PhRMA) reports their share to be in the interval 42%-58% in 2006³. In areas such as Latin America, Europe, India, and other Asian countries, the portion of the drug market occupied by generics is even higher. Consequently, as soon as the patent expires, the incumbent monopolist may expect to face competition by a growing number of generic producers, selling at prices a lot closer to marginal cost than the patented medicine did. In the U.S. generic drugs are available at prices that are between 30% and 80% lower than the originally patented product.⁴

Finally, the global drug market is geographically concentrated, with sales in the US accounting for about 48% of the

total, followed by Europe's 29% and Japan's 11%. Why is this? The fixed cost of creating a new medicine is very high, it is argued, as a consequence, new drugs are expensive and only consumers in rich countries can afford them. Nevertheless, other markets are growing, and the economic development of China and India will soon lead to a substantial change in the world distribution of market shares.

This description of the pharmaceutical industry is much like the textbook description of a traditional Schumpeterian industry. The model we have been criticizing as unrealistic and misguided until now seems to fit almost perfectly the situation of the pharmaceutical industry. Under these circumstances, the traditional model predicts that there should be many potential producers of a medicine, that the industry should be dynamically competitive, and therefore highly innovative with newcomers frequently challenging incumbents by means of innovative superior drugs. Which, in some sense, describes the global pharmaceutical industry. But, in some other equally if not more important sense, it does not.

Some people esteem the pharmaceutical industry and some people despise it: there is little middle ground. The pharmaceutical industry is the poster-child of every intellectual monopoly supporter. It is the vivid example that, without the sheltering patents provide inventors with, the outpouring of new wonder drugs we have grown accustomed to would have not materialized, our life expectancies would be a lot shorter, and millions of people would have died of the diseases Big Pharma has instead managed to cure. In the opposite camp, Big Pharma is the scourge of humanity: a club of oligopolistic white men that, by controlling medicine around the globe and refusing to sell drugs at their marginal cost, are letting millions of poor people die. Withdrawal of supply by the big pharmaceuticals is as close to economic crime as anything can be, we are told. The wonders of contemporary medicine and biotechnology are the fruits of intellectual property, it is countered.

This sounds utterly complicated, so let us handle it with care and, for once, play the role of the wise fellows: *in media stat virtus, et sanitas*. The pharmaceutical industry is a complicated beast to vivisect, which can be approached from many contradictory angles and viewpoints. We will keep to ours, narrow that it may be, and ask – how strong is the case for patents in pharmaceuticals? Is there substantial evidence that without patents we would not have the medicines we have, or at least we would have a lot fewer and worse medicines? Would the industry shut down and talent move to some other, more rewarding, enterprise if

patents on drugs were more or less abolished, that is, if the world became like Switzerland until 1978 or Italy until a year later?

In fact, we shall see that while Big Pharma is not necessarily the monster some depict, the case for patents in pharmaceuticals is a lot weaker than most people think – and so, apparently, even under the most favorable circumstances patents are not necessarily good for society, for consumers, or in this case, for sick people. Patents are good for monopolists, but that much we knew.

World Shortest History of Pharmaceutical Patents

Pharmaceuticals are a significant industry, and of growing significance. Its market size is approaching \$700 billion worldwide and it grows at annual rates between 5 and 8 per cent. In the United States, where drug sales run at \$275 billion in 2006⁵, the share of prescription drugs in total national health care expenditure increased from 4.9% in 1980 to 10.0% in year 2004, corresponding to 1.6% of GNP. New drugs are extremely costly to develop. Hansen, Grabowski, and Lasagna⁶ provide the following estimates of the cost in millions of 1987 dollars of bringing a “new chemical entity” to market, assuming a success rate of 23% for patented drugs.

	<i>0% interest</i>	<i>8% interest</i>
<i>pre-clinical</i>	66	142
<i>Clinical</i>	48	72
<i>Total</i>	114	214

Notice that the pre-clinical component of cost is large, and especially so when the interest rate is taken into account, since the pre-clinical costs must be paid before going to clinical trials. More recent estimates by Di Masi, Grabowski, and Hansen⁷ place the total cost of bringing a new drug to market at around \$800 million, in year 2000 dollars. Even if a number of researchers have questioned their methodology, this figure suggests a spectacular increase in the cost of innovating. This increase is due, mostly, to the capitalization of the longer and more expensive clinical trials the FDA requires. In a very recent and publicized case, Pfizer announced the writing off of almost \$1 billion of expenditure sunk into the development of a new drug, Torcetrapib, which fell dramatically short of its expectations⁸. Of the billion dollars involved, \$800 million went to pay for clinical trials, while the Irish plant where the drug was supposed to be produced cost just

\$90 million.⁹ With R&D costs of such magnitude, it seems impossible to even dream of a pharmaceutical industry that could properly function and innovate in the absence of a very strong patent protection. It was not always this way.

Historically, intellectual monopoly in pharmaceuticals has varied enormously over time and space. To summarize: the modern pharmaceutical industry developed faster in those countries where patents were fewer and weaker. Since WWII, and the upheaval of the worldwide distribution of power within the chemical industry it brought about, patent lobbyists have lobbied long and successfully to increase patent protection for pharmaceutical products. Here are the details of their accomplishments.

In the U.S. drugs have been patentable since the writing of the U.S. Constitution, for the very simple reason that chemical products have always been patentable. The U.S. recognizes two distinct forms of patent: the process by which a drug is produced may be patented independently of the chemical formula for the drug. Until 1984 U.S. patent law treated medical discoveries in the same way as other innovations, and no special treatment was reserved for drugs. In more recent years longer and more frequent extensions for drug patents have been allowed than for other patents. As we already mentioned, the Hatch-Waxman Act of September 24, 1984, was designed to compensate for regulatory requirements that delay the introduction of new drugs. It is estimated that it increased effective length of patent protection for pharmaceuticals by about 3 to 5 years.

In most of continental Europe, until recent years, only the process of producing a drug could be patented, so once a drug was discovered, a second firm could also produce it provided they found a different way of doing so. The rationale behind process versus product patents is given by the German Association of the Chemical Industry in a memoire to the Reichstag.¹⁰ They point out that the same chemical product can be obtained by different processes and methods and even starting from initially different materials and components. Hence, there is social value in patenting a new process, as it rewards the innovator without preventing further innovation. There is negative social value in patenting a specific product, as this would exclude all other from producing it, even through different processes. It should be noted, though, that this did not prevent German chemical companies from patenting their products where possible, in the United Kingdom and the United States especially.¹¹

In France, under the law of July 5, 1844 pharmaceutical inventions could not be patented. Legislation then evolved, keeping the prohibition for patenting products but allowing patents for processes. The executive Order of February 4, 1959, and, then, the law of January 2, 1966 finally introduced limited patents for pharmaceutical products in France; the ban on patenting drugs was completely lifted only in 1978. In Germany, the law of May 25, 1877 introduced patents for both chemical and pharmaceutical processes, while products were explicitly excluded. The Law of April 4, 1891 extended patent protection to products obtained via a patented process. Finally, the law of September 4, 1967 introduced general patentability of chemical and pharmaceutical products also in Germany.

In Switzerland, patents for chemical and pharmaceutical products were explicitly prohibited by the Swiss Constitution. The Swiss pharmaceutical industry, whose strength does not need to be recalled, has, however, been a historically important competitor for the German. Constant German pressure, both political and legal, eventually led to the adoption of patents for chemical processes with the Swiss Law of June 21, 1907, which was nevertheless quite restrictive. The Law of June 25, 1954 continued to apply only to processes but extended the length of patents from 10 to 18 years. Patents for products were introduced in Switzerland only in 1977.

In Italy, pharmaceutical patents were prohibited until 1978, when the Supreme Court ruled in favor of eighteen pharmaceutical companies, all foreign, requesting the enforcement of foreign patents on medical products in Italy. Despite this complete lack of any patent protection, Italy had developed a strong pharmaceutical industry: by the end of the 1970s it was the fifth world producer of pharmaceuticals and the seventh exporter.

In Spain, the *Ley de Patentes* introduced patents for products in 1986, as a consequence of the country's entrance in the EEC. The law began to be applied only in 1992. Before that date, regulations dating back to 1931 explicitly prohibited the patenting of any substance and, particularly, of any pharmaceutical substance. Patenting of processes was instead allowed.¹²

Pharmaceuticals are also covered by a variety of international agreements. The contemporary era of patenting began with the Convention of the Union of Paris in 1883 following the Vienna Conference of 1873. More recently, the Patent Cooperation Treaty was signed in Washington on June 19, 1970, which started a process of international extension of stronger patent protection for medical products. The Munich Convention of October 3, 1973,

implemented in October 7, 1978 defines the notion of an “European Patent.” Further revisions and modifications of the original basic agreement led, eventually, to the definition of a Community Patent Convention, which was signed in Luxembourg on December 15, 1975. The latter was not ratified by various countries (Denmark, Ireland, Greece, Portugal and Spain) and the overall project eventually failed.

Nevertheless, the core idea of a unified European patent system was not abandoned and continued to be pursued in various forms, first under the leadership of the European Commission, and then under the European Union. In 2000 a Community Patent Regulation proposal was approved, which was considered a major step toward the final establishment of a European Patent. Things, nevertheless, did not proceed as expeditiously as the supporters of a E.U. Patent had expected. As of 2007 the project is still, in the words of E.U. Commissioner Charlie McCreevy, “stuck in the mud”¹³ and far from being finalized. Interestingly the obstacles are neither technical nor due to a particularly strong political opposition to the establishment of a continent-wide form of intellectual monopoly. The obstacles are purely due to rent-seeking by interest groups in the various countries involved, the number of which notoriously keeps growing. Current intellectual monopolists (and their national lawyers) would rather remain monopolists (legal specialists) for a bit longer in their own smaller markets than risk the chance of losing everything to a more powerful monopolist (or to a foreign firm with more skilled lawyers) in the bigger continental market.

It is worth pointing out that under E.U. patent law, programs for computers together with scientific discoveries and theories, mathematical methods, aesthetic creations, schemes, rules and methods for performing mental acts, playing games or doing business, and presentations of information are expressly not regarded as inventions and therefore cannot be patented. Since there is a large degree of ambiguity as to what a scientific theory or discovery is, it is unclear the extent to which a new medicine, or a new biologically engineered product is or is not independent of the underlying chemical and biological model that explains it. Through this ambiguity medical products and treatments have been increasingly patented in the E.U. in ways similar to the U.S.

Finally, in recent years and within the framework of the WTO-TRIPS agreement that came into effect on January 1, 1995, a steady process of worldwide harmonization of patent rules in the pharmaceutical, as well as other industries, has been undertaken.

Widespread controversies, both political and judicial, surrounding the modification of the Indian system of pharmaceutical patents in a direction favorable to intellectual monopoly, or the even more recent decision by the Brazilian government of “bypassing” a number of foreign patents covering the production and distribution of AIDS related drugs, are just two of the most visible aspects of this ongoing process, to which we return later and in chapter 10.

You may wonder why we are offering all these details about specific countries, patenting of chemical processes, and pharmaceutical products. For a very simple reason: if patents were a necessary requirement for pharmaceutical innovation as claimed by their supporters, the large historical and cross country variations in the patent protection of medical products should have had a dramatic impact on national pharmaceutical industries. In particular, at least between 1850 and 1980, most drugs and medical products should have been invented and produced in the United States and the United Kingdom, and very little if anything in continental Europe. Further, countries such as Italy, Switzerland and, to a lesser extent, Germany, should have been the laggards of the pharmaceutical industry until recently. Instead the opposite was true for longer than a century.

Chemicals Without Patents

Prior to the rise of the pharmaceutical industry, the most important form of chemical production was the paint and coloring industry. At its inception, the dye industry was a French-British business the same way that almost any industry was a French-British business until the second half of the nineteenth century. In both countries patent protection applied to all kinds of industrial products. In 1862 British firms controlled about 50% of the world market, and French firms another 40%, Swiss and German companies being marginal players. By 1873 German companies had 50% of the market, while French, Swiss and British firms controlled between 13% and 17% each. In 1913 German firms had a market share of more than 80%, the Swiss had about 8%, and firms in the rest of the world had largely disappeared. During this entire period there was no patent protection at all in Switzerland, while in Germany processes become patentable in 1877 but products did not. In France, the U.K. and the U.S. both products and processes had been patentable all along. Indeed, the strong patent protection for this industry in France and its absence in Switzerland was largely responsible for the development of the

important Swiss chemical, and then pharmaceutical, industry after 1864.

In that year, a judicial sentence favoring the French company “La Fuchsine”, in a fight over the scope of patents it held on the colorant by the same name, established its almost complete grip on the French dye industry. This put the many French companies constituting the paint and coloring industry on notice, resulting in a large movement of firms to Switzerland, where patents were instead illegal. From 1864 onward and for about two decades, “La Fuchsine” (“Poirrer”, after the 1868 acquisition) dominated the French market, thanks to its patents. During the same period it innovated little, if at all, while its Swiss and German competitors, unprotected by patents, did. “La Fuchsine” was therefore completely unable to compete outside of France and, once its patents expired, it disappeared into oblivion, together with its analogous patent-holders in Britain (among which, “Perkin” was the most well known). In case this reminds you of how the Hollywood movie industry was created by migrating entrepreneurs running away from Edison’s patents, you are beginning to see a pattern. The migrating French firms located in and around Basel and were rapidly followed by other chemical companies. The movement was so dramatic that just before the First World War, Haber observes that in France there was no production of chemical products, either organic or inorganic.¹⁴

Haber explicitly attributes the absence of a French chemical industry to the presence of patents stifling competition and making innovation impossible. He points out that, in a similar way, the slow growth of the coloring industry in the U.S. before the First World War was largely due to patent protection: most patents were held by large German companies such as Bayer, BASF, Hoechst and IG Farben. The chemical industry in the US was so underdeveloped, that during the First World War the U.S. was forced to import dyes from Germany via submarines to bypass the British blockade.

This would be humorous, if it were not sad: German chemical companies competed heavily at home and across most European markets, where chemical products could not be patented. This situation forced them to innovate frequently and to develop production processes able to guarantee a very high productivity. Such intense competition already gave them a “competitive edge” relative to the Anglo-Saxon companies living in a world of generalized patenting. To this initial advantage was added the opportunity to patent products in the U.K. and the U.S., allowing

the German chemical companies to erect insurmountable barriers to entry in the chemical market. Do not get us wrong here; we are not claiming the German companies did not use patents in building up their worldwide dominance. They did, and there is no doubt whatsoever that the chemical industry worldwide was an assemblage of more or less loosely held together cartels until the late 1930s, cartels in which the German big chemical companies played a major leading and coordinating role. Still, the fact that they wiped out their French and Anglo-Saxon counterparts in the worldwide market, and that they did so in spite of having a lot less patent protection, speaks volumes in regard to the specific issue concerning us in this chapter.¹⁵

Thus, before the First World War, medicines and other chemical products were scarce and expensive in England. This led, in 1919, to the modification of the English Patents Act of 1907 with the addition of section 38A which introduced mandatory licenses for medicines. Again, the report of the Sargent Committee of 1937 pointed out the shortage of medicines and its relation to strong patents in England. In the Patents Act of 1949, section 41, No. 2, a new special procedure was introduced to favor mandatory licensing of food and drug products. The British government spent about forty years reworking its patent laws, without ever abolishing them, in the vain hope of lowering the prices of medicines and creating incentives for its pharmaceutical industry to catch up with the Germans. It did not succeed, as we all know: the German companies kept innovating, even if their new products were not protected by patents at home, and the British pharmaceutical industry never came close to being competitive. Aspirin, that wonder drug, was a German invention, not a British one and, while it was patented in the U.S., Britain, and France, it could not be patented in Germany. Bayer was forced to relinquish its patent on aspirin in the rest of the world by the Treaty of Versailles.¹⁶

Here is how Murmann summarizes the main findings from his historical study of the European synthetic-dye industries during the 1857-1914 period

British and French synthetic dye firms that initially dominated the synthetic dye industry because of their patent positions but later lost their leadership positions are important cases in point. It appears that these firms failed to develop superior capabilities in production, marketing and management precisely because patents initially

sheltered them from competition. German and Swiss firms, on the other hand, could not file for patents in their home markets and only those firms that developed superior capabilities survived the competitive home market. When the initial French and British patents expired, the leading German and Swiss firms entered the British and French market, capturing large portions of sales at the expense of the former leaders.¹⁷

It is only with the end of the two World Wars and the de-facto expropriation of German chemical knowledge, first by the French and British and then by the victorious Allies, that a degree of competition was restored in the chemical industry for a few decades. Indeed, in the end, the WWI blockade did work – allowing DuPont to enter the dyestuff market by pirating German products. The British government provided Du Pont with access to the industrial secrets found in a Hoechst plant in the U.K. that had been confiscated at the start of the WWI; the U.S government allowed Du Pont free access in 1919 to all German chemical patents, as these were confiscated at the end of the war.

From a theoretical point of view, it is not hard to understand the devastating impact of patents, especially of product patents, on innovation in the chemical industry. The chemical industry is a classic case of the innovation chains – new compounds and processes are built on the knowledge of existing ones. As we observed, patents are particularly harmful in this case, since the increased incentive to innovate that they may generate is, as in the chemical industry, more than offset by the increased difficulty of doing so.

It could be, and sometimes is, argued that the modern pharmaceutical industry is substantially different from the chemical industry of the last century. In particular, it is argued that the most significant cost of developing new drugs lies in testing numerous compounds to see which ones work. Insofar as this is true, it would seem that the development of new drugs is not so dependent on the usage and knowledge of old drugs. However, this is not the case according to the chief scientific officer at Bristol Myers Squibb, Peter Ringrose, who

told The New York Times that there were ‘more than 50 proteins possibly involved in cancer that the company was not working on because the patent holders either would not allow it or were demanding unreasonable royalties.¹⁸

Truth-telling remarks by pharmaceutical executives aside, there is a deeper reason why the pharmaceutical industry of the future will be more and more characterized by complex innovation chains: biotechnology. As of 2004, already more than half of the research projects carried out in the pharmaceutical industry had some biomedical foundation. In biomedical research gene fragments are, in more than a metaphorical sense, the initial link of any valuable innovation chain. Successful innovation chains depart from, and then combine, very many gene fragments, and cannot do without at least some of them. As gene fragments are in finite number, patenting them is equivalent to artificially fabricating what scientists in this area have labeled an “anticommons” problem. So it seems that the impact of patent law in either promoting or inhibiting research remains, even in the modern pharmaceutical industry.¹⁹

Medicines Without Patents

Patents for medicines were introduced in Italy, under pressure from foreign multinationals, in 1978. Today India, China and Brazil are, reluctantly, caving in to U.S. pressure to do the same. Proponents of IP argue that this will increase pharmaceutical innovation in those countries. So we may ask – did the strengthening of IP protection trigger a golden age of innovation in the Italian pharmaceutical industry?

During the period 1961-1980 a total of 1282 new active chemical compounds was discovered around the world. Of these, a total of 119 came from Italy (9.28%). During the period 1980-1983 a total of 108 compounds were discovered. Of these, 8 came from Italy (7.5%).²⁰ While we do not have data covering the most recent decades, the very clear impression of the informed observer is that innovations have decreased. Professors Scherer and Weisburst, in fact, took pains to carefully study the evolution of the Italian pharmaceutical industry after the adoption of patents. Here is the summary verdict, in Scherer’s own words

Research by Sandy Weisburst and mentored by me showed, for example, that Italy, with a vibrant generic drug industry, did not achieve any significant increase in the discovery of innovative drugs during the first decade after the Italian Supreme Court mandated the issue of pharmaceutical product patents.²¹

A number of historical and empirical studies makes it evident that, absent patents, the Italian pharmaceutical industry did not suffer particularly until 1978. On the one hand, foreign companies holding patents abroad entered the Italian market, via direct investment and the establishment of local production units, in order to protect the market share of their own products. On the other hand, the possibility of freely imitating products patented elsewhere favored the creation of a large number of Italian imitative firms, which improved upon existing products and, at the same time, allowed for their diffusion at much lower prices. In spite of this, the forty largest Italian firms (out of about 500, until the late 1970s) did not simply imitate but developed their own products and innovated extensively, either by using existing products as ingredients (25%) or by using products which were not patentable or with expired patents (31%).²²

In other words, a thriving pharmaceutical industry had existed in Italy for more than a century, in the complete absence of patents. That is point one. Point two is that neither the size, nor the innovative output, nor the economic performances of that industry have improved, to any measurable extent, during the thirty years since patents were adopted. Every indicator one can look at suggests that, if anything, the Italian pharmaceutical industry was hurt, not helped, by the adoption of patents, and every expert that has looked the matter has reached this same conclusion.

Since 1978, India has taken over as the primary center of pharmaceutical production without patent protection. The growth and vitality of the Indian industry is similar to that of the pre-1978 industry in Italy. In fact much more so, as the sheer size of the national market has turned Indian generic drug producers into big players in the global pharmaceutical industry. Within the framework of the WTO-TRIPS agreements, India has now been forced to introduce product patents on pharmaceutical products, which have become progressively more stringent (2005 having been the formal deadline for complete compliance). While a variety of researchers have speculated, partly on the ground of the Italian experience, about the consequences of this legislative shift for the Indian pharmaceutical industry, we are aware of very few studies addressing directly the Indian situation.²³ Only one study focuses directly upon India and asks the important welfare question: are Indian consumers going to be better or worse off after pharmaceutical patents are fully adopted in their country? By concentrating on the market for a specific drug – quinolones, for which very good micro time series data are available – Chaudhuri,

Goldberger and Jai reach the following conclusion (apologies for the jargon)

We [...] carry out counterfactual simulations of what prices, profits and consumer welfare would have been, had the fluoroquinolone molecules we study been under patent in India as they were in the U.S. at the time. [...] We estimate that in the presence of price regulation the total annual welfare losses to the Indian economy from the withdrawal of the four domestic product groups in the fluoroquinolone sub-segment would be on the order of U.S. \$305 million, or about 50% of the sales of the entire systemic anti-bacterials segment in 2000. Of this amount, foregone profits of domestic producers constitute roughly \$50 million. The overwhelming portion of the total welfare loss therefore derives from the loss of consumer welfare. In contrast, the profit gains to foreign producers in the presence of price regulation are estimated to be only around \$19.6 million per year.²⁴

Other observers, looking at the big picture, are less negative. Interestingly though, we have not been able to find a single independent analyst claiming that the additional amount of pharmaceutical innovation patents may stimulate in the Indian industry, will be substantial and large enough to compensate for the other social costs. More to the point, the positive consequence of patent adoption in countries like India is, according to most analysts, a consequence of beneficial price discrimination. The argument goes as follows: monopoly power allows price discrimination – that is, the selling the same good for a high price to people valuing it a lot (usually people richer than average) and for a low price to people valuing it little (usually people poorer than average). Due to the absence of patent protection, there are very many new drugs that are not marketed in poor countries by their original producer, as the latter is not protected by reliable patents in that country. If it were, the profit maximizing monopolist would have an incentive to quickly introduce those drugs, at prices lower than in rich countries, also in poor countries. This would increase the welfare of the poor country's residents, as they would receive the medicine earlier rather than later.

While the argument sounds perfectly logical (leave aside the issue of how large the gains from this earlier marketing of new medicines would be) there are two points its advocates either do

not notice or underplay. The first has to do with re-trading, otherwise known as “parallel import”, or free trade if you like. If a drug is sold more cheaply in country X than in country Y, there is an incentive to set up a firm shipping the drug from X to Y, as many Americans and Canadians have recently discovered. Hence the full requirement for poor countries is not just to adopt Western-style patents, so that price discrimination by the monopolist can benefit them, but also to restrict free trade. An interesting twist, given that the idea comes from the WTO, an international organization erected and financed to support and expand free trade worldwide! The second doubt comes from the following observation: if it were really true that imitating and “pirating” new drugs is that easy, absent patent protection local firms would be already producing and marketing such drugs in the country in question. Hence, the arrival of the foreign patent-holder’s output could not really increase the welfare of local consumers as it would purely replace existing local suppliers. This conclusion seems unavoidable, unless one is willing to argue that the marginal cost of producing drugs is not constant, or that imitation and reverse-engineering are not all that cheap, or that the initial inventor has some cost advantages over its imitators. But then, once either of the last three points is admitted, the whole argument for patent protection fails in the first place, and we are back to square zero: *qui prodest?*

The Pharmaceutical Industry Today

In spite of the fact that between 1985 and 2005 a long string of almost fifty mergers and acquisitions has led to a progressively more concentrated pharmaceutical industry, it is hard to argue, from a worldwide perspective, that this is a monopolized industry. True, a few large companies – about fifteen and possibly shrinking soon – hold a dominant position throughout the world, all of them based in USA, Germany, UK, Switzerland and France. Still, the difference in sales between number 15 and 16 in 2004 was \$600 million, out of about \$10 billion, and the list of the top 50 pharmaceutical and biomedical company looks more like a smooth continuum, starting at \$52 billion with Pfizer, and ending at \$1.5 billion with Tanabe Seiyaku, with the two biggest percentage drops in sales between number 2 (Johnson and Johnson) and number 3 (Glaxo SmithKline), of about -21%, and number 12 (Eli Lilly) and 13 (Bayer), of about -27%. Furthermore, the post 1985 merger wave runs parallel to the emergence of new biotech companies and, as documented above, of a growing

number of generic drugs producers. These two factors have prevented monopolistic concentration in the industry; the combined worldwide market share of the top 30 pharmaceutical and biotechnology firms is just over 50%. The sales of the two largest ones covered about 15% of the global market for drugs in 2004. Relative size and market share are not the sources of monopoly power, if there is any, in this industry. Furthermore, while the wave of mergers may have erected substantial barriers for reaching the top, it would be a stretch to claim that there are substantial barriers to entry into the industry per se. In every country we have considered there are often hundreds of competing pharmaceutical firms, and new biomedical startups are appearing and being financed, especially in the U.S., on a monthly basis.²⁵

A few additional facts may help the reader get a better understanding of why, at the end, we reach the conclusion we do. Sales are growing, fast; at about 12% a year for most of the 1990s, and still now at around 8% a year; R&D expenditure during the same period has been rising of only 6%. A company such as Novartis (a big R&D player, relative to industry's averages) spends about 33% of sales on promotion, and 19% on R&D. The industry average for R&D/sales seems to be around 16-17%, while according to the CBO [1998] report the same percentage was approximately 18% for American pharmaceuticals in 1994; according to PhRMA [2007] it was 19% in 2006. The point here is not that the pharmaceutical companies are spending "too little" in R&D – no one has managed (and we doubt anyone could manage) to calculate what the socially optimal amount of pharmaceutical R&D is. The point here is that the top 30 firms spend about twice as much in promotion and advertising as they do in R&D; and the top 30 are where private R&D expenditure is carried out, in the industry.

Next we note that no more than 1/3 – more likely 1/4 – of new drug approvals are considered by the FDA to have therapeutic benefit over existing treatments, implying that, under the most generous hypotheses, only 25-30% of the total R&D expenditure goes toward new drugs. The rest, as we will see better in a moment, goes toward the so called "me-too" drugs. Related to this, is the more and more obvious fact that the amount of price discrimination carried out by the top 30 firms between North America, Europe and Japan is dramatically increasing, with price ratios for identical drugs reaching values as high as two or three. The designated victims, in this particular scheme, are apparently the U.S. consumers and, to a lesser extent, the Northern European

and the Swiss. At the same time, operating margins in the pharmaceutical industry run at about 25% against 15% or less for other consumer goods, with peaks, for US market-based firms, as high as 35%. The U.S. pharmaceutical industry has been topping the list of the most profitable sectors in the U.S. economy for almost two decades, never dropping below third place; an accomplishment unmatched by any other manufacturing sector. Price discrimination, made possible by monopoly power, does have its rewards.

Summing up and moving forward, here are the symptoms of the malaise we should investigate further.

- There is innovation, but not as much as one might think there is, given what we spend.
- Pharmaceutical innovation seems to cost a lot and marketing new drugs even more, which makes the final price for consumers very high and increasing.
- Some consumers are hurt more than others, even after the worldwide extension of patent protection.

Where do Useful Drugs Come From?

Useful new drugs seem to come in a growing percentage from small firms, startups and university laboratories. But this is not an indictment of the patent system as, probably, such small firms and university labs would have not put in all the effort they did without the prospect of a patent to be sold to a big pharmaceutical company.

Next there is the not so small detail that most of those university laboratories are actually financed by public money, mostly federal money flowing through the NIH. The pharmaceutical industry is much less essential to medical research than their lobbyists might have you believe. In 1995, according to a study by two well reputed University of Chicago economists, the U.S. spent about \$25 billion on biomedical research. About \$11.5 billion came from the Federal government, with another \$3.6 billion of academic research not funded by the feds. Industry spent about \$10 billion.²⁶ However, industry R&D is eligible for a tax credit of about 20%, so the government also picked up about \$2 billion of the cost of “industry” research. That was then, but are things different now? They do not appear to be. According to industry’s own sources²⁷, total research expenditure by the industry was, in 2006, about \$57 billion while the NIH budget in the same year (the largest but by no means the only source of public funding for biomedical research) reached \$28.5 bn. So, it seems, things are

not changing: private industry pays for only about 1/3rd of biomedical R&D. By way of contrast, outside of the biomedical area, private industry pays for more than 2/3rds of R&D.

Many infected with HIV can still recall the 1980s when no effective treatment for AIDS was available, and being HIV positive was a slow death sentence. Not unnaturally many of these individuals are grateful to the pharmaceutical industry for bringing to market drugs that – if they do not eliminate HIV – make life livable.

the "evil" pharmaceutical companies are, in fact, among the most beneficent organizations in the history of mankind and their research in the last couple of decades will one day be recognized as the revolution it truly is. Yes, they're motivated by profits. Duh. That's the genius of capitalism - to harness human improvement to the always-reliable yoke of human greed. Long may those companies prosper. I owe them literally my life.²⁸

But it is wise to remember that the modern “cocktail” that is used to treat HIV was not invented by a large pharmaceutical company. It was invented by an academic researcher: Dr. David Ho.

Still, one may say, the issue we are debating here is patents and if, in particular, medical patents are socially beneficial or not. Lots of, even most of, important medical discoveries may come from publicly sponsored research laboratories, but it is a fact that, without the strong incentive the prospect of a successful patent induces, those researchers would not be working as hard as they do. That is true, so let us think the issue through once again. We observe that, while the incentive to patent and commercialize their findings should have been increased by the Bayh-Dole act allowing patentability of such research results, there is no evidence whatsoever that, since 1980 when the act was passed, major medical scientific discoveries have been pouring out of American universities' laboratories at an unprecedented rate. Good research was done previously, good research is done now. Medical and biological scientists comparing “then” and “now” may complain, more often than not, about the direction of research (more commercially oriented “now”, less directed toward big problems and pure scientific discovery than it was “then”) but they are not claiming the quality has gone visibly down. At the same time, we are not aware of anybody claiming, let alone documenting, that after the Bayh-Dole Act took effect, the quality of biomedical

research in U.S. universities and federal sponsored laboratories visibly increased. It has remained roughly where it was, meaning that patentability made no difference as far as general incentives are concerned.

Let us proceed, though. Because there are not just general incentives, but also specific ones, it may be that patents have biased biomedical research in a more socially valuable direction. The substantive findings emerging from Petra Moser's research discussed in Chapter 8 suggest that the opportunity patents offer of achieving large private gains may push innovation in certain directions instead of others. Interesting as this question may sound, apparently it has not been investigated or, at least, we could not find any trace of an answer to it. It therefore remains an open question: did patentability of basic biomedical innovations create an incentive for engaging in more socially valuable research projects and investigations?

Even more telling, we also could not find anything in the field of health economics addressing what, in our view, is an even more basic question: where do medical and pharmaceutical discoveries of high social value come from? This left us on our own, trying to figure out what a fundamental medical discovery or a truly innovative medicine were. Being two theoretical economists, we appealed to the law of comparative advantages to figure out whom to ask: Doctors, medical doctors more precisely. Consulting a large number of medical journals leads to the pleasant discovery that the *British Medical Journal*, a most distinguished publication, has decided to inaugurate a new series by asking colleagues and readers something very close to our fundamental question: which medical and pharmaceutical discoveries are truly fundamental and where do they come from? In their own words

*We asked readers to nominate milestones, which you did in good numbers. A panel of editors and advisers narrowed the field down from more than 70 to 15. We invited champions to write on each one; their contributions make up the commemorative supplement we are publishing on 20 January. And we are now inviting readers to vote for which you think is the most important of these medical milestones (see bmj.com). The result will be announced on 18 January [2006].*²⁹

In no particular order, here are the selected fifteen (we could not get hold of the group of seventy, which, we suspect, would have not moved the bottom line an iota):

*Penicillin, x rays, tissue culture, ether (anaesthetic), chlorpromazine, public sanitation, germ theory, evidence based medicine, vaccines, the pill, computers, oral rehydration therapy, DNA structure, monoclonal antibody technology, smoking health risk.*³⁰

How many entries in this list were patented, or were due to some previous patent, or were obtained during a research project motivated by the desire to obtain a patent? Two: chlorpromazine and the pill. Is this a fluke? We do not think so. In the same issue (freely available on line) of the *BMJ* you can find references to other similar lists. A particularly interesting one was compiled since 1999-2000 by the US Centers for Disease Control and Prevention (CDC): a top 10 list of public health achievements of the 20th century in the United States. How do medical patents score on this one? Zero. The editor of the *BMJ*, recognizing the intrinsic arbitrariness of any top-N list, somewhere in the editorial presentation names her three beloved ones among the excluded, “Where are Aspirin, Helicobacter pylori, and Medline?” Good point, and we ask: do they owe anything to patents? Not at all.

Even if one tries to stack the odds in favor of patents as much as possible, the bottomline changes only slightly. To do this we went to the web site of the *Chemical and Engineering News* magazine³¹ where a “List of Top Pharmaceuticals”, divided by therapeutic categories, can be found.³² These are the current pharmaceutical products selling the most worldwide, and there are 46 of them. Each entry in the list links to a well documented page telling the story of the drug and a number of other scientific and commercial details related to it. Using this abundant information we counted how many of these wonder-drugs of today do not owe their existence to patents in any meaningful sense, either because they were never patented and those inventing them did not have a patent as their aim, or because they were discovered by companies operating in countries where drugs could not be patented at all. One would expect that nearly all of the entries in this list were patented at one point in time or another. Here is the summary of our reading about all kinds of modern medicines.

Patents had pretty much nothing to do with the development of 20 among the 46 top selling drugs (aspirin, AZT,

cyclosporine, digoxin, ether, fluoride, insulin, isoniazid, medical marijuana, methadone, morphine, oxytocin, penicillin, phenobarbital, prontosil, quinine, ritalin (methylphenidate), salvarsan, vaccines, vitamins). For the remaining 26 products patents did play an important role (allegra, botox, cisplatin, crixivan, erythropoietin, fentanyl, fosamax, hydrocortisone, ivermectin, l-dopa, librium, lovastatin, oral contraceptives, premarin, prozac, rituxan, salbutamol, tagamet, taxol, thalidomide, thorazin, thyroxine, viagra, vioxx, RU-486, 6-mercaptopurine). Notice though that of these 26, 4 were discovered completely by chance and then patented (cisplatin, librium, taxol, thorazin), 2 were discovered in university labs before the Bayh-Dole Act was even conceived (cisplatin and taxol). Further, a few were simultaneously discovered by more than one company leading to long and expensive legal battles, however, the details are not relevant to our argument.

The bottom line is rather simple: even today, more than thirty years after Germany, Italy and Switzerland adopted patents on drugs and a good half a century after pharmaceutical companies adopted the policy of patenting anything they could develop, more than half of the top selling medicines around the world do not owe their existence to pharmaceutical patents. Are we still so certain that valuable medicines would stop to be invented if drug patents were either abolished or drastically curtailed?

This is not particularly original news, though. Older American readers may remember of the Kefauver Committee of 1961, which investigated monopolistic practices in the pharmaceutical industry.³³ Among the many interesting findings reported, the study showed that 10 times as many basic drug inventions were made in countries without product patents as were made in nations with them. It also found that countries that did grant product patents had higher prices than those who did not, again something we seem to be well aware of.

The next question then is, if not in fundamental new medical discoveries, where does all that pharmaceutical R&D money go?

Rent-Seeking and Redundancy

There is much evidence of redundant research on pharmaceuticals. The National Institutes of Health Care Management reveals that over the period 1989-2000, 54% of FDA-approved drug applications involved drugs that contained active ingredients already in the market. Hence, the novelty was in

dosage form, route of administration, or combination with other ingredients. Of the new drug approvals, 35% were products with new active ingredients, but only a portion of these drugs were judged to have sufficient clinical improvements over existing treatments to be granted priority status. In fact, only 238 out of 1035 drugs approved by the FDA contained new active ingredients and were given priority ratings on the base of their clinical performances. In other words, about 77% percent of what the FDA approves is “redundant” from the strictly medical point of view.³⁴ The New Republic, commenting on these facts, pointedly continues

If the report doesn't convince you, just turn on your television and note which drugs are being marketed most aggressively. Ads for Celebrex may imply that it will enable arthritics to jump rope, but the drug actually relieves pain no better than basic ibuprofen; its principal supposed benefit is causing fewer ulcers, but the FDA recently rejected even that claim. Clarinex is a differently packaged version of Claritin, which is of questionable efficacy in the first place and is sold over the counter abroad for vastly less. Promoted as though it must be some sort of elixir, the ubiquitous “purple pill,” Nexium, is essentially AstraZeneca's old heartburn drug Prilosec with a minor chemical twist that allowed the company to extend its patent. (Perhaps not coincidentally researchers have found that purple is a particularly good pill color for inducing placebo effects.)³⁵

Sad but ironically true, me-too or copycat drugs are largely the only available tool capable of inducing some kind of competition in an otherwise monopolized market. Because of patent protection lasting long enough to make future entry by generics nearly irrelevant, the limited degree of substitutability and price competition that copycat drugs bring about is actually valuable. We are not kidding here, and this is a point that many commentators often miss in their “anti Big Pharma” crusade. Given the institutional environment pharmaceutical companies are currently operating in, me-too drugs are the obvious profit maximizing tools, and there is nothing wrong with firms maximizing profits. They also increase the welfare of consumers, if ever so slightly, by offering more variety of choice and a bit lower prices. Again, they are an anemic and pathetic version of the

market competition that would take place without patents, but competition they are. The ironic aspect of me-too drugs, obviously, is that they are very expensive because of patent protection, and this cost we have brought upon ourselves for no good reason.

This expensive creation of redundancy also has two implications relevant for our final argument. As in the computer software industry, it suggests that indivisibility is not such a significant factor in the innovation process; in other words, the true fixed cost to be recouped via monopoly profits is probably small. Second, it suggests a substantial amount of socially inefficient rent-seeking, artificially created by the patent system itself. One often finds, in the public debate over the rising cost of health care, a misplaced insistence on the huge profits of Big Pharma. Yes, those profits are abnormally large and persistently so. A signal, we agree, of a highly monopolistic industry. But they are not the main cause of the rising cost of health care, because in the end they are just 10% of the whole pie. The much larger amount of resources the patent system forces us to waste in the me-too drugs business, its advertising and its legal support, *that* is a sizeable share of the pie. When you add them together, the research cost, the legal cost, the advertising and promotion cost get you to possibly more than 50% of the whole pie!

Now consider this: assume we can cut Big Pharma's profits to the average level in the manufacturing sector. As a percentage of sales that would be about 5%, meaning 5% off the cost of drugs. Make the pharmaceutical industry a competitive one, and get rid of the resources wasted in the monopolistic competition monkey business. That is a substantial 50% off the cost of drugs. Making the pharmaceutical industry a more competitive one will probably reduce its profit margins to more common level, giving you the extra 5% cost reduction for free. The U.S. Congress should note this.

Insofar as new drugs are replacements for drugs that already exist, they have little or no economic value in a world without patents – yet cost on the order of \$800 million to bring to market because the existence of patents forces the producers to “invent something” the USPO can pretend to be sufficiently different from the original, patented, drug. Where does that money go? What are the social gains from this kind of investments? None: the only social gain from introducing a “me-too” drug is that the supply of the beneficial active ingredient increases, and average prices possibly decreases somewhat. But this could be achieved, much more rapidly and at a cost orders of magnitude smaller, by

simply copying the old drug, and improving upon it. Money spent in obtaining a “me-too” drug that can be patented is money denied to society and charged to consumers: Rent-seeking and monopoly profits can be very costly for all of us, indeed.

Redundancy and Bribing

A different way of looking at the same problem stresses the emphasis on the marketing of drugs over the R&D to search for new ones.

A better explanation for the pharmaceutical slump is a shift in priorities toward marketing, particularly since the FDA first allowed companies to directly target consumers five years ago. According to data collected by Alan Sager, a professor at the Boston University School of Public Health, the number of research and development (R&D) employees at companies making patented drugs declined slightly between 1995 and 2000, while the number of people working in marketing shot up 59 percent. “Drug companies trumpet the value of breakthrough research, but they seem to be devoting far fewer resources than their press releases suggest,” says Sager.³⁶

Libraries have been written on the obvious connection between marketing and the lack of competition. The pharmaceutical industry is no exception to this rule, and the evidence Professor Sager, and many others, point to has a simple and clear explanation: because of generalized and ever extended patenting, large pharmaceutical companies have grown accustomed to operating like monopolies. Monopolies innovate as little as possible and only when forced to; in general they would rather spend time seeking rents via political protection while trying to sell at a high price their old refurbished products to the powerless consumers, via massive doses of advertising.

[Pharmaceutical] Companies today have found that the return on investment for legal tactics is a lot higher than the return on investment for R&D,” says Sharon Levine, the associate executive director of the HMO Kaiser Permanente. “Consumers today are paying an inordinate premium under the guise of the creating the stream of innovation in the future. But it's actually funding lawyers.”³⁷

Economists call this “socially inefficient rent-seeking.” It is ugly, but the polite academic jargon of “rent-seeking” includes “corruption” and all that comes with it. We have already mentioned the music industry, where corruption has become the standard marketing practice, as exemplified by the sorry story of Payola. In industries that are highly monopolized and in which the returns from capturing the main distribution and information channels are enormous, the temptation to bend and then break the rules is too strong to resist, as public choice theory and economic common sense suggest. In the pharmaceutical industry the main distribution and information channels are not the radio and TV stations, but the medical profession. Hence, the unavoidable and continued temptation to capture the doctors, to induce them to “promote” a particular drug, and to be silent about other drugs. We have started to learn, more and more frequently, that “As Doctors Write Prescriptions, Drug Companies Write Checks”, as Gardiner Harris aptly titled his report on how drug companies mail large checks to doctors in exchange for “consulting activities” that amount to ... doing nothing beyond prescribing a particular drug.

In Boston, federal prosecutors have been attempting to crack down on these marketing practices. From the cases they have brought, it appears that this is not just the usual story of the few rotten apples

Last month, Pfizer agreed to pay \$430 million and pleaded guilty to criminal charges involving the marketing of the pain drug Nuerontin by the company's Warner-Lambert unit. AstraZeneca paid \$355 million last year and TAP Pharmaceuticals paid \$875 million in 2001; each pleaded guilty to criminal charges of fraud for inducing physicians to bill the government for some drugs that the company gave the doctors free.

Over the last two years, Schering-Plough, which had sales of \$8.33 billion last year, has set aside a total of \$500 million to cover its legal problems – mainly for expected fines from the Boston investigation and from a separate inquiry by federal prosecutors in Philadelphia who are investigating whether Schering-Plough overcharged Medicaid.³⁸

The case is overwhelming, and there is not much value added in repeating further stories of this kind.³⁹ What is the point of bringing this kind of scandal into an otherwise serious debate? We are not trying to score some cheap moral points here – even if, it should be said, the fact that “business is business” cannot be used to put up with every kind of conceivable immorality. We are stressing, instead, a dramatically poignant policy implication. The drug industry is monopolized because patents are the core and foundation of the business method adopted. Such an industry must end up practicing rent-seeking and bribery, it must conceal or suppress relevant research findings, it must monitor doctors’ prescription behavior, it must employ a sales force three times the size of its research team, it must, finally, become one of the top donors of “political campaign contributions.”

If this were the radio industry and the bribery affected the quality of the tunes played on this station or the other, there would be only a very mild case for social concern. But this is the health industry, and the bribery is affecting the medicine you take.

How Steep is the Tradeoff, Then?

A recent NBER paper, by Hugh, Moore and Snyder and sponsored by Aventis Pharmaceuticals, attacks directly the costs and the benefits of drug patents.⁴⁰ They conclude that if the appropriate rate of interest for discounting the social benefits of new drugs is greater than about 5%, then social benefit of eliminating patents is greater than the cost. Since the social benefits of pharmaceuticals are risky, and indeed in this study they are assumed to be perfectly correlated with private risk, an appropriate interest rate is the rate of return in the pharmaceutical industry. Indeed, the interest rates used for cost-benefit calculations for government projects, is usually around 15%, which is the same as the rate of return Hugh, Moore and Snyder assume for pharmaceutical R&D. This is substantially in excess of 5% for eliminating patents.

Since Hugh, Moore and Snyder are among the few who have attempted to quantify the costs and benefits of intellectual monopoly, it is worth reviewing their calculations.

Hugh, Moore and Snyder assume that demand for pharmaceuticals is linear. From the perspective of cost-benefit analysis, this assumes that as output expands past the monopoly level, demand falls off at a constant rate. If demand falls abruptly, then the loss of consumer surplus is much smaller than would be estimated by a linear demand function, and we would get a more

favorable case for patents. However, there is some reason to think that demand for pharmaceuticals depends upon income, and if this is the case, the linear demand assumption is a reasonable one. Other parameters of the Hugh, Moore and Snyder model are calibrated to the data. They assume that 75% of pharmaceutical revenue is generated by drugs still under patent; that market exclusivity lasts 9 years; and that the lifetime of a new drug is 25 years. They assume that it will take generic manufacturers one year to enter after innovation. Also based on data about competition between generic and non-generic drugs after patent expiration, they attribute a first mover advantage to the innovator by assuming that they will be able to charge the monopoly price and still serve 20% of the market. In fact, evidence from India suggests that it takes closer to four years for generics to enter; and relatively unbiased sources such as the Congressional Budget Office suggest that market share after the entry of generics is substantially larger than 20%.

Finally, a critical assumption is the connection between producer surplus and the number of new drugs discovered. That is, higher expectations of profit due to monopoly lead to more pharmaceutical research, and consequently more drugs. Notice, however, that this effect can be negative, since the monopolization of existing drugs may also make it harder to discover new drugs, and we saw that this was empirically important in the history of the chemical industry. Hugh, Moore and Snyder assume that the number of new drugs discovered is proportional to producer surplus. That is, since they estimate that without a patent profits are about 25% of what they would be with a patent, they assume that there will be 25% as many drugs discovered without patents. Even without the problem of innovation chains and the cost of “inventing around existing patents” discussed earlier, this assumption is very favorable to the patent system. The number of discoveries is scarcely likely to drop 25% if profits are reduced to 25%. Based on survey data from industry interviews (which, in turn, probably understates the number of drugs that would be developed without patents) a figure of 40% would appear to be closer to the mark. We should also note that our own estimate is that without patents, firms would earn closer to 80% of what they earn with patents, rather than 25%.⁴¹ Despite these apparent biases, Hugh, Moore and Snyder still find that, even with an interest rate as low as 5%, the immediate benefit of wider drug availability exceeds the long-term cost of having fewer new drugs.

How steep is the tradeoff society faces, then? Not too steep, apparently, if a 5% discount rate is high enough for even a pharmaceutical industry sponsored study to conclude we would be better off without patents.

The Cost of New Drugs, Revisited

Much of the case for drug patents rests on the high cost of bringing drugs to market. Most studies have been sponsored by the pharmaceutical industry and are so quite suspect. In our previous analysis we have already seen one huge reason for suspicion: the cost of new drugs includes not only the cost of failed projects; that would be reasonable. It includes also the R&D cost for me-too drugs, which is about 75% of all R&D cost; and that is a lot less reasonable. The story does not end here, though. Let us proceed with the accounting.

The Consumer Project on Technology⁴² examined the cost of clinical trials for orphan drugs – good data are available for these drugs because they are eligible for special government benefits. A pharmaceutical industry sponsored study estimated the average cost of clinical trials for a drug at about \$24.5 million 1995 dollars. However, for orphan drugs where better data are available, the average cost of clinical trials was only about \$6.5 million 1995 dollars⁴³ – yet there is no reason to believe that these clinical trials are in any way atypical.

A 2002 report of the Center for Economic and Policy Research⁴⁴ also estimates costs orders of magnitude less than those claimed by the pharmaceutical companies. It also finds that, holding output of pharmaceutical products constant, private companies tend to spend twice as much as public medical research centers to develop new drugs. As one might suspect, the report documents that the additional costs of the private drug monopolists are mostly legal and advertising costs: the first to get patents and defend them, the second to convince doctors to prescribe “their drug” instead of the alternative, most often a generic and cheaper alternative.

Last, but not least is the issue of clinical trials. Even after accounting for the money spent on me-too drugs, and the resources expended on the legal and marketing costs induced by the patent system, it is still a fact that, on December 5, 2006, Pfizer had to write off \$800 million of expenses on clinical trials when it gave up on the production and commercialization of Torcetrapib. Somehow, somewhere the pharmaceutical industry must recoup such costs. By common admission, by both pharmaceutical firms

and outside observers, the cost of clinical trial now amounts to about 80% or more of the total cost of developing a new drug. While clinical trials related to imitative drugs are almost a complete waste from a social point of view, those related to truly innovative and therapeutically beneficial drugs are not so. On the contrary, they are socially very valuable and they need to be recouped. Are pharmaceutical patents necessary to accomplish this?

No, they are not. We will be brief and leave the details of this argument for the next, final chapter, in which we address a few proposals for reform. Clinical trials are the step in the process of developing a new drug during which information is produced about the effect of a given chemical compound on a large sample of humans. The cost of distributing and absorbing this information being low, and the cost of acquiring it being high, it has a strong public good component. There is also no reason, either of by way of economic efficiency or equity, why this should be paid for by the pharmaceutical firms developing the new drug – indeed, as they will be first to market they have a strong conflict of interest. The cost of clinical trials cost would better paid from the public purse, for example, by competitive and peer-reviewed NIH grants. At that point, patents on drugs would no longer have any reason to exist.

The Ultimate Virus

The pharmaceutical malaise has many ingredients – the FDA system of regulation, the entire idea that some drugs should be available by prescription only, the broader problem of health insurance, and who pays for drugs. To argue that the system could be fixed by eliminating patents on pharmaceutical would be foolish. It would be foolish also to think that it would make sense to abolish patents on pharmaceuticals without also reforming the infrastructure – such as the way clinical trials are paid for and made available – at the same time.

That said, we have seen that patents do not play a helpful role in pharmaceutical innovation. Far from encouraging great new health and life-saving products, the system instead produces too much innovation and expense of the wrong kind – “me-too” drugs to get around others’ patents and get a share of a lucrative monopoly, and all the advertising and marketing expenses attendant upon monopoly power.⁴⁵ In the play that is life, health is the ultimate commodity – we all want to live longer and stay

healthier. As we have just seen, patents do not have a useful role in this play.

Comments

The point of view we take here is a very narrow one, and this chapter should not be read as an overall evaluation of the current functioning of the pharmaceutical industry and of the impact that reducing patentability of new drugs would have on it. In particular, it does not ask, as a complete analysis instead should, if, under an alternative system, doctors, medical researchers, and shareholders of Big Pharma will be better or worse off than they are now.

Notes

¹ Hansen et al [1991] report the 1987 cost of developing a new drug. The department of commerce reports an implicit GDP price deflator in the first quarter of 1987 of 72.487 and in 2000 of 99.317, which is used to convert the \$200 million year 1987 dollars of the earlier estimate to year 2000 dollars.

² The estimate length of medical patent protection is from Grabowski [2002], while the impact on it of the Hatch-Waxman Act is from Grabowski and Vernon [1986, 1996].

³ PhRMA [2007], p. 2.

⁴ Basic information about the current structure of the drug industry and its economic performances are widely available on line. The specific data we quote are taken from El Feki [2005], healthguideusa.org/NationalCosts.htm and various online reports freely available at www.imshealth.com.

⁵ Up from \$253.7 billion in 2005, as reported by IMS Health at their website, <http://www.imshealth.com>. The Top-10 drugs accounting for about \$41 billion.

⁶ Hansen, Grabowski, and Lasagna [1991].

⁷ Di Masi, Grabowski, and Hansen [2003]. This study also explains the interest rates used in capitalizing and discounting costs and benefits in the pharmaceutical industry.

<http://www.fda.gov/bbs/topics/NEWS/2006/NEW01514.html> for the FDA official announcement.

⁹ These figures are from the Pfizer's press report on December 3, 2006 and are still available from the many websites reporting the announcement.

¹⁰ Dutfield [2003], p. 78.

¹¹ In fact, a number of large chemical companies wanted to let the industry completely free of any patent protection to avoid the fate of the French dye industry (see below) and favor its development. Apart for Dutfield [2003], see also Seckelmann [2001] for additional details about the German patent system at the end of the nineteenth century, and Arora et al [1998] for various historical studies on the growth of the chemical industry.

¹² Again, Dutfield [2003], especially chapters 4 and 5, is our main source of information. Zorina Kahn's online history of patent laws, at <http://eh.net/encyclopedia/article/khan.patents>, provides a useful and easy to access summary of the main facts.

¹³ As quoted in http://en.wikipedia.org/wiki/Community_patent, and in various media sources.

¹⁴ To begin learning about the history of the dye industry and the crucial, if not necessarily positive, role patents played in it see Morris and Travis [1992] and the references therein. For why patents and monopoly did not allow "La Fuchsine" to thrive, see Van den Belt [1992]. For similar stories of not-so-useful patents in other sectors and countries, such as the U.S., see Murmann [2004], where the initial stages of the dye industry are also carefully analyzed. If you are curious about the nature of the mysterious "fuchsine", Wikipedia can tell you about its chemical composition.

¹⁵ Meyer-Thurow [1982] provides additional information about both the dye industry and the development of the German chemical industry. The absence of both organic and inorganic chemical production in France is noted by Haber [1958, 1971], from which other details about the history of the chemical industry are also

drawn. The demise of the British coloring industry is also discussed by Penrose [1951, pp. 102-105].

¹⁶ As confirmed by any of the hundreds web sites reporting the history of aspirin.

¹⁷ Murmann [2004], p. 3.

¹⁸ Pollack [2001].

¹⁹ Together with its label, the “anticommons” problem in medical research was pointed out first in a much debated article by Heller and Eisenberg [1998]. More recent appraisals are in Scherer [2002], Epstein & Kuhlik [2004], who argue that patents on gene fragments are still growing and patent holders will want to make money, hence there should be no anticommons problem at all, and in Benkler [2004], and Clark et al [2000], who argue that patent pools, as in the software industry, will solve the problem: an oligopoly is better than a monopoly, after all; and the dozens of references these articles contain. A conference at the University of Illinois College of Law, home.law.uiuc.edu/iple/conferenceJune06.html, provides a good picture of where the debate stood as of 2006. Information about the growing number of scientists and medical or biological research labs willing to share their results can be found in a variety of journalistic sources, among which Begley [2006], Leaf [2005], Maurer et al [2004].

²⁰ Information and data about the Italian pharmaceutical industry are from Campanella [1979], Ferraguto et al. [1983], and Paci [1990].

²¹ Scherer [2003] p. 122. This is Scherer’s study of the welfare impact that worldwide drug patents may have, the conclusion of which is that medical patents are bad for our health.

²² One may ask why we did not look more carefully at the Swiss pharmaceutical industry. It also grew without patents in its home country to become more successful than the Italian industry, and still is, even if patents were adopted in Switzerland just one year earlier than in Italy. That would have been more than mildly unfair, though equally so to both sides of the debate, as the Swiss

did exceedingly well both without and with patents. While it is quite true, as pointed out in the chapter, that the Swiss chemical industry was created by French firms running away from French patent controls, the size of the internal Swiss market is too small to be relevant. That the chemical, first, and, then, pharmaceutical Swiss firms could not use either process or product patents to protect their home turf is of little relevance, given that they could use patents, and use them they did, in most other countries the market size of which dwarfed that of Switzerland. In this sense, and apart for its inception, the successful Swiss pharmaceutical industry – championed today by Novartis and Hoffman-La Roche at number 5 and 6 respectively of the world scale, but also by Alcon (29) and Serono (35) – is neither a “pro” nor a “counter” patent story. It is nevertheless significant that from Alexander Clavel and his fellow French “patent runners” came great firms such as CIBA-Geigy and Hoffman-La Roche. That until the late 1960s the leading pharmaceutical countries were Germany, Switzerland and Italy (that is, those either without patents or weak patents) is recognized even by Wikipedia in its entry on “pharmaceutical company.”

²³ Readers interested to learn more about the Indian pharmaceutical industry and how it grew without patents may consult the Wikipedia’s entry on “Pharmaceuticals in India.” It is particularly informative, well written and reporting abundant references and data sources. The late Jean Lanjouw was probably the leading world expert on the impact that the adoption of patents may have on India’s drug industry. In her [1997, 2002, 2005] papers, she casts a very balanced view of the pros and cons faced by low and middle income countries adopting pharmaceutical patents. As far as our limited question is concerned, though, the answer coming from her empirical work is fairly clear, if technically phrased

There is some evidence that high levels of protection might encourage more frequent entry of innovative products in the short term, particularly in countries where multinationals might otherwise hesitate because local technical capacity might create competitive pressures. On the other hand, in the longer term that same domestic capacity could be an alternative source of entry, and we find that a country offering extensive patent protection may

lose the benefits of that activity and have fewer new products in the market overall as a result. [2005, p. 25]

Admittedly, Lanjouw is one of the analysts that, albeit in a very tentative form, have advanced the idea that patent adoption may help poor countries by making price discrimination more effective. A substantially more robust statement in this direction can be found, in Maskus [2001]. The paper focuses mostly on parallel imports and advocates the strange charity argument according to which rich countries should be allowed to export drugs to poor ones when the prices are higher in the poorer than in the richer countries, or at best equal, but not vice versa. Which piece of economic logic and which social welfare function support this asymmetric free trade rule escapes us, but maybe we missed the whole point. Why this would be “benevolent” toward poor countries, is even more mysterious. To see why we say so, try applying the same logic to agricultural products. That is exactly what the EU agricultural trade policy amounts to.

²⁴ Chaudhuri, Goldberg, Jia [2003], excerpt from the Abstract.

²⁵ Our general information about the current status of the pharmaceutical industry comes from various sources, CIPR [2002], El Feki [2005], IFPMA [2004], Maskus [2001], NIHCM [2002], Wikipedia and the C&E News special issue available at <http://pubs.acs.org/cen/coverstory/83/8325/index.html>.

²⁶ Murphy and Topel [1999].

²⁷ PhRMA [2007], “Key Facts”.

²⁸ Andrew Sullivan's Blog Friday, July 01, 2005 12:12:00 pm.

²⁹ Godlee [2007], p. 1.

³⁰ Godlee [2007] p. 1. The special issue of the BMJ in which this editorial piece appears lists the top 15 medical milestones and is available at their site, www.bmj.com.

³¹ <http://pubs.acs.org/cen/>.

³² <http://pubs.acs.org/cen/coverstory/83/8325/8325list.html>.

³³ Information about the 1961 Kefauver Committee leading, among other things to the Kefauver-Harris or Drug Efficacy Amendment of 1962, is abundantly available on line, beginning as usual from Wikipedia.

³⁴ NIHCM [2002].

³⁵ This and the following most amusing string of quotations on “me-too” drugs and their distinctive purple color, on the ratio between R&D and marketing employees in pharmas, and on what consumers are financing with the outrageous prices they are forced to pay for drugs are all from the same *The New Republic* piece. The [link](http://www.thenewrepublic.com/docprint.mhtml?i=20021007&s=tompson100702) is <http://www.thenewrepublic.com/docprint.mhtml?i=20021007&s=tompson100702>.

³⁶ Ibidem

³⁷ Ibidem

³⁸ Harris [2004].

³⁹ A long, if incomplete, list of rent-seeking practices bordering the highly improper, if not the strictly illegal, is in Baker and Chatani [2002]. Additional information on the development and patenting of imitative drugs are in Hubbard and Love [2004] and references therein, whereas more details about their “marketing” to the medical profession, are in Angell and Relman [2002].

⁴⁰ The Hugh, Moore and Snyder study is [2002]. We should note that their stated conclusion is the opposite of ours: they conclude that drug patents should not be abolished. The reason is that they apparently believe that the relevant interest rate is less than 5%.

⁴¹ The 40% estimate of the fraction of drugs that would be developed without patent is from the Levin et al [1987] survey. Information about generics in India is from Lanjouw [1997], information about market share after generic entry is from CBO [1998], and our own calculations are in Boldrin and Levine [2005b].

⁴² <http://www.cptech.org/>

⁴³ The orphan drug study is Love [1997].

⁴⁴ <http://www.cepr.net/> The CEPR study comparing the cost of inventing new drugs for private and public research centers is Baker and Chatani [2002].

⁴⁵ Excessive “me-too” imitation is explored theoretically in the market for textbooks by Boldrin and Levine [2002], where we show that under certain circumstance – not dissimilar from those in the pharmaceutical industry – the result can be the “Pareto Worst Outcome.” This idea is not very distant from that advanced in the, apparently now forgotten, literature on patent races and excess R&D spending, see, for example, Fudenberg and Tirole [1991].