

Generic Drug Companies: Competing at Boundaries of Time and Geography

Michael Gollin
Venable LLP
October 7, 2003

The generic drug industry is locked in a perennial struggle with the patented drug industry. Legal battles are being fought constantly across boundaries of time and geography. For the individual companies, these battles are distressing and costly, and to hear the lobbyists, each side is poised to destroy the other.

My view is more optimistic. I think that the fierce competition between the companies in the U.S. is a sign of a robust system at work. Indeed, I can not think of another system that would work as well at balancing the rival interests to achieve social benefit.

The Dilemma of Human Desires

At the core of the struggle are two fundamental human desires, which create what I call the dilemma of "medicine later vs. medicine now."

On the one hand, people want new and better medicines in the future, to make us healthier and therefore happier. Our societies prize innovation. We believe that new ideas will improve our lives, and the lives of our children. And so we reward medical researchers. The Nobel prize for medicine, just awarded to Paul C. Lauterbur and Sir Peter Mansfield for magnetic resonance imaging, is a reward that can be shared by only a few individuals. A much more widespread instrument of reward is the system of laws and practices we call intellectual property, and in particular, for medicine, it is patents that give the inventor the reward of limited exclusive rights over the invention.

On the other hand -- sick people want the best medicine they can get, now. This leads to the populist argument that patents keep the cost of medicine too high for poor patients, and so governments should help by granting compulsory licenses and importing less expensive generic drugs in order to protect the public health. The drug industry argues that weakening patents will reduce research, development, and improvements in health care, in effect robbing improvements from future patients. This argument is based on economics and is lost on people who frame the issue as a populist choice of 'patients vs. patents.'

The conflict between medicine later and medicine now raises issues of intergenerational and international equity. We deal with the intergenerational issue first.

Intergenerational Equity - Medicine Later vs. Medicine Now

The problem may be framed as follows:

How do we balance the needs of today's patients for today's medicine with the needs of future patients to have new medicine?

This balance may be referred to as "sustainable innovation," borrowing from the concept of sustainable development.¹ The answer must have to do with the specific boundaries of a patent in terms of its scope and its duration, but there is an appalling lack of guidance on the core issue - what is the **optimum** strength and duration of drug patents?

In the meantime, the answer to this question must take into consideration the complementary public roles of the generic industry and the patented pharmaceutical industry

Let us review the pharmaceutical ecosystem, and the generic industry's niche within it, as shown in the Figure 1.

THE PHARMACEUTICAL ECOSYSTEM

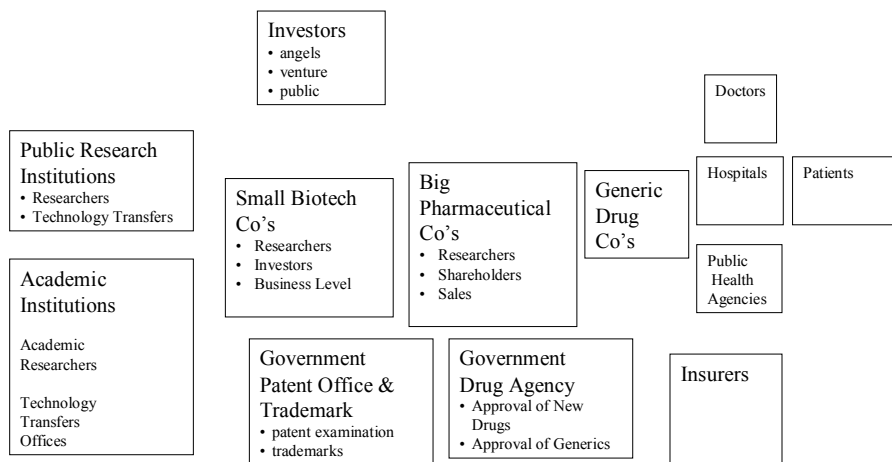


Figure 1

¹ Michael Gollin, "Sustainable Innovation for Public Health," *Food and Drug Law Institute Update Magazine* (January/February 2002)

This ecosystem has many "creatures" -- inventors, research institutions, corporations (biotechnology companies as well as patent holding "big pharma" and generics), funders (investors, insurers, donors), governmental regulators (patent offices and food and drug and health agencies), patients, doctors, nurses, hospitals, and insurance companies. Upon reflection it becomes clear that this is not a bipolar world of patented pharmaceutical companies vs. generic companies, but rather it is a rich and diverse community with many stakeholders. The competitive relationship between generics and patent holders is influenced not just by each other, but by all the other players. Generic competition arises at a crucial temporal boundary – when a patent expires – but that is in the context of many broader relationships.

The Hand Off to Generics

Next we focus in particular on that boundary – the time for a particular drug when the generic company steps in. The boundary is clear in Figure 2, which shows the life cycle of a drug.

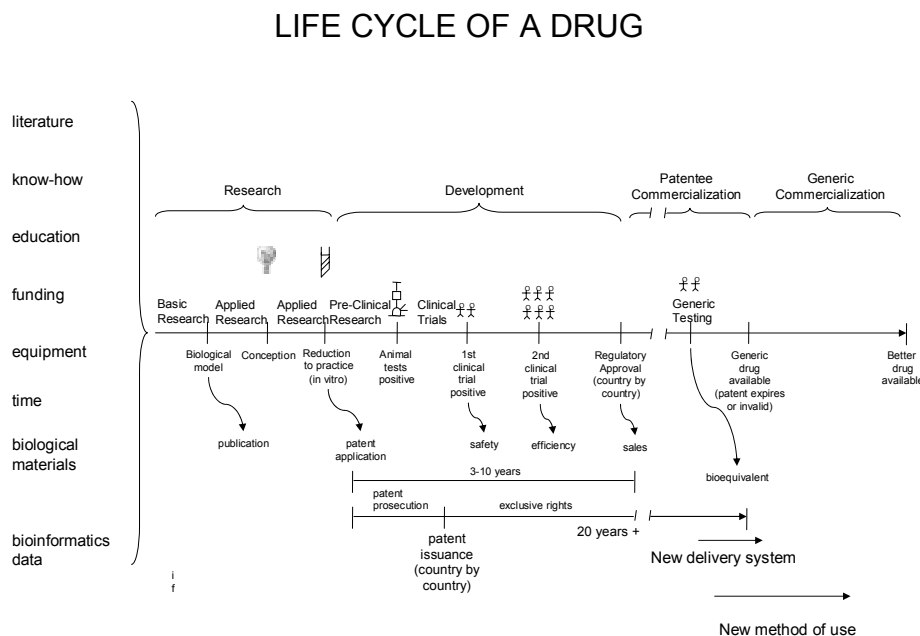


Figure 2

Again, it is important to note that "big pharma" (as the patented industry is sometimes referred to) is not the only source of new medicines. Much of the starting material for a new drug comes from publicly funded research. There is then a handoff of sorts from public research institutions to big pharma, either by

a technology transfer agreement, as with Bristol-Myers Squibb's license of Taxol from the NIH, or by publication of the basic science. Research progresses to the clinical stage, and a drug is developed and approved for market, thus beginning the patentee commercialization phase.

In the U.S. system, generic companies begin preparing early so they are ready to enter the market immediately upon patent expiration. Rules of fair play govern this hand off, such as the Hatch-Waxman Act, which allows generic companies to develop their manufacturing capability and to conduct clinical trials prior to patent expiration, and in effect to "free ride" on the patent holder's clinical data, by showing only that the generic drug is bioequivalent to the patented drug.

Meanwhile, there is extensive skirmishing around that hand-off. Patent-holding big pharma has a strong incentive to innovate and patent new dosage forms, formulations, and chemical variants on successful drugs, bringing a stream of improvements to patients, improvements which may be more modest than a blockbuster, but are nonetheless important. Generic companies, too, innovate to optimize chemical synthesis processes, and they have an incentive to timely enter the marketplace when a patent expires, and even to challenge a weak patent so they can enter the market earlier.

Let us consider what would happen without such a mechanism? One example is the new generation of so-called "biologics," such as therapeutic proteins. Examples are erythropoietin, human growth hormone, insulin, and interferon. The Hatch-Waxman Act does not apply to these drugs. Many people are concerned that because it is harder for generic companies to enter the market for a biologic, big pharma will have less incentive to make constant improvements on existing drugs (a variant of the economic argument for "medicine later"). Also, the generic companies will have to replicate the full clinical data instead, at great cost, and with no social benefit except to clinical research organizations, instead of investing in other more valuable projects (interfering with "medicine now").

The False Dichotomy

This discussion raises another important point about the relationship between generics and patent-holding pharmaceutical companies -- it is a false dichotomy.

- Generic companies innovate and patent their inventions in areas such as chemical synthesis, new methods of use, and new delivery systems, and as they grow, they even do basic research.
- Patent-holders compete with each other by producing alternatives of other blockbuster products – such as cox-2 inhibitors (Vioxx by Merck and Celebrex by Pfizer), and PDE5 inhibitors (Viagra, Cialis, and Levitra).
- Patent-holders run their own generic companies to take advantage of the separate market niche (as with Novartis with generic subsidiaries Sandoz and Geneva).

So we see that generic companies hold patents and innovate, and patent-holders challenge other innovators, and sell generic drugs. The two industries have a substantial amount in common.

The System at Work

Some examples of the skirmishes at the temporal boundaries will illustrate that this is not a bad system, even if it is hard on the players.

In recent patent litigation over the antihistamine Loratidine, Schering Plough owned a patent on a metabolite of the original patented drug, des-loratidine. The patent was ruled invalid in a challenge by Teva and other generic companies. As a result, generics entered the market, and Claritin lost most of its market share, and faced huge price erosion. Schering is still trying to recover.

Also, GlaxoSmithKline's Paxil (paroxetine hydrochloride) was patented as a particular "polymorph" or crystal form. A trial court ruled the patent invalid this Spring, and without waiting for the appeal, generic company Apotex last month launched sales of the antidepressant. This will surely result in lower costs, making the drug more widely available. And it puts new pressure on GSK to innovate to find new blockbuster drugs, instead of optimizing existing drugs.

A third example is Bayer's Ciprofloxacin. During the anthrax scare in 2001, US Secretary of Health and Human Services Thompson briefly threatened that the U.S. might assert compulsory license to gain access to Cipro at below market prices. At the same time, a generic company, Danbury, was challenging the

extension of the Cipro patent, but that challenge failed, giving the Cipro patent additional life.

Another aspect of skirmishing involves heightened antitrust oversight of generics and big pharma. Without going into detail here, it is worth observing that the gist of the recent Federal Trade Commission efforts to block collusion between generics and patent holders is the desire to maintain robust competition - the same goal that I am suggesting makes this system work well.

International Equity -- Medicine Here vs. Medicine Elsewhere

The second problem characterizing the role of the generic industry, and its competitive relationship with patented pharmaceutical companies, is the issue of international equity, or "medicine here vs. medicine elsewhere." The question may be framed as follows:

How can we balance the needs of patients in rich countries like the U.S. with those of poor countries?

This is an aspect of the overall North-South dynamic. Our concern here should be, what is the role of generic companies in striking such a balance? Increasingly, there are global markets for making and selling drugs, and patent-holding companies are seeking markets in all corners of the world. However, patients in poor countries can be at a terrible disadvantage because of the small markets, low purchasing power, lack of incentive for development of drugs for their worst public health problems (e.g. malaria, tuberculosis, leishmaniasis), and the absence of intellectual property expertise, which is concentrated almost entirely in the rich countries.

One solution has been to promote a globalization of the generic industry. Some drugs are patented in some countries but not in others. Here, a generic version of the drug can be sold in any country where there is no patent in force. The only obstacle is to determine that no patent exists that would block sale of the drug, what we patent attorneys call "freedom to operate." That determination, in turn, requires patent expertise too often lacking in developing countries.

As the WTO's agreement on Trade Related Aspects of Intellectual Property comes into force in developing countries, patents will become more valuable and the number of countries where patents for a particular drug are obtained may increase. So the international scope of freedom to operate is likely to diminish and the need for careful analysis of existing patents will grow.

An organization like Public Interest Intellectual Property Advisors (PIIPA) can help developing countries pursue their interests in the globalization of competition between patented pharmaceutical companies and generic companies. PIIPA is a global non-profit resource for developing countries and public interest organizations seeking expertise in intellectual property matters to promote health, agriculture, biodiversity, science, culture, and the environment. PIIPA provides worldwide access to a network of IP professionals who can advise and represent such clients pro bono publico (as a public service).² A second way to promote globalization of the generic industry is via compulsory licensing consistent with the WTO agreements. We have seen skirmishes at the geographical borders with respect to anti-retrovirals in South Africa and Brazil, as well as the US as mentioned before. This, too, requires extensive expertise. The country that decides to exercise a compulsory license must then decide whether to make the drug domestically, or to import from a generic company in another country. The 2001 Doha declaration and the August 30, 2003 statement of the TRIPS council made it clear that countries have many avenues to encourage generic competition in their countries if the patent-holder does not make a drug available on acceptable terms.³

Countries such as India, Brazil, South Africa, and Thailand are well-positioned to build a local generic industry for domestic use and export. This endeavor can serve many national development goals. Indeed, India's generic companies are growing rapidly and becoming important players in the global pharmaceutical market, due to skills and capacity dating from before patent laws there were strengthened. This kind of competition is likely to be very effective at bringing about supplies of drugs at a suitable price, and may reduce the need or interest for price controls.

Again, the path to being able to obtain or produce a drug, by purchase from the manufacturer, license, independent production with freedom to operate, or compulsory licensing is extremely complicated. Figure 3 shows some of the decisions that need to be made to reach the goal of providing access to a particular medicine.

² See www.piipa.org.

³ http://www.wto.org/english/tratop_e/trips_e/implem_para6_e.htm

IP DECISION TREE FOR ACCESS TO ESSENTIAL DRUGS

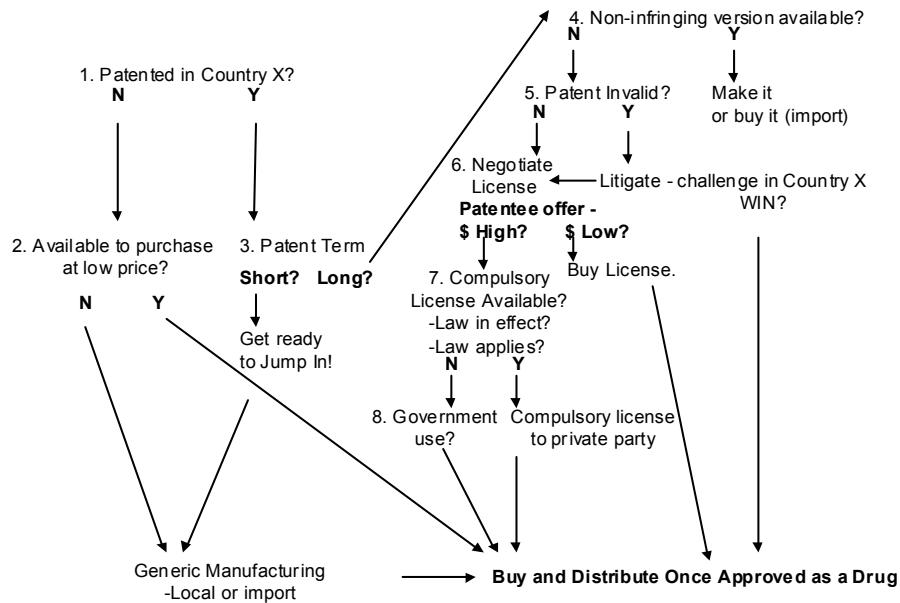


Figure 3

Again, the complexity of this approach requires intellectual property expertise lacking in most developing countries. As noted above, this has been the driving demand for the non-profit service called Public Interest Intellectual Property Advisors, which makes IP professionals available to developing country clients who need their services.

Meanwhile, the U.S. Congress is contemplating legislation that would permit the importation of drugs from foreign countries where the prices are lower, to bring increased price competition. One thing to be very cautious about is the possibility that importing will increase the amount of counterfeit "bad" drugs on the market, because it is more difficult to enforce quality standards on foreign companies.

The flip side of importing, of course, is exporting. In Canada, a proposed amendment to the patent law would permit Canadian generic drug makers to produce medicines for export, even if they were listed and patent-protected in Canada, so long as they are directed to poor countries grappling with pandemic diseases.⁴ Apparently Canadian patent drug makers are willing to work with the government "to frame any legislative proposal to assist in humanitarian relief." Presumably the generic companies would compete on price, and the patent-holding companies would rather not go down that path. This is a fitting final

⁴ http://www.pbs.org/newshour/updates/canada_11-06-03.html

example, as it promises some collaboration between generic and patent-holding drug companies.

In conclusion, society needs to support both those who innovate in medicine, and those who disseminate the best medical innovations. Social benefit is maximized by a framework that first, rewards innovator drug companies with patent rights that are limited by specific boundaries of time and geography, while second, encouraging generic drug companies to compete vigorously outside those boundaries. The consequence of this system may be furious policy battles over the optimal strength of medicine patents in general, and specific legal battles at the temporal and geographical boundaries. This leaves much hard work for lawyers, but this is an inherent part of the system, and can promote sustainable innovation, balancing our desire for the best medicines here and now with the desire for better drugs everywhere tomorrow.