Intellectual Property Rights and the Pharmaceutical Industry

The Consequence of Incomplete Protection

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Intellectual property rights (IPRs) are described as "the rights given to persons over the creations of their minds" (WTO 1999). The rights conferred give creators an exclusive right over the use of their creations for a specified period of time. These rights are administered and controlled by national legislation, within a framework of international law.

In December 1993, the Uruguay Round of negotiations on the General Agreement on Tariffs and Trade (GATT) completed an Agreement establishing the World Trade Organization (WTO). This included a subsidiary Agreement on Trade-Related Aspects of Intellectual Property Rights, Including Trade in Counterfeit Goods (TRIPS). This built on the existing multi-lateral treaties such as the Paris Convention for the Protection of Industrial Property (1883), the Berne Convention for the Protection of Literary and Artistic Works (1886), and the Treaty on Intellectual Property in Respect of Integrated Circuits (Washington, 1989), and the Patent Cooperation Treaty. Another important body in this context is the World Intellectual Property Organization (WIPO) and since the formation of the WTO there has been collaboration between these two bodies; e.g. in July 1998, in a joint press release, the

Note will be found on page 104.

WTO and WIPO announced a joint plan to help developing nations meet their year-2000 commitments on intellectual property.

Patent rights and data exclusivity are two separate and distinct parts of the intellectual property rights required to protect inventions such as a new chemical entity (NCE). The patent protects the inventor from others who might wish to create, use, or sell the patent during the patent period. However, the patent does not prevent another manufacturer from conducting the necessary laboratory, animal, and human tests and then applying for a license to market the product. If the second manufacturer gains access to the originator's data this creates an unfair situation because much of the original experimentation can be bypassed, thereby saving the second manufacturer a large investment. TRIPS provides for the maintenance of the originator's exclusive access to this research data.

A third right, which is not covered under TRIPS but is nevertheless important, is the right to market a product in a competitive environment without undue government regulation or control. From time to time, governments perceive the need to control prices. Various types of price control are sometimes attractive to politicians and bureaucrats because they appear to provide a simple and easy fix for prices that appear to be escalating at a rate perceived to be excessive and potentially injurious to the economy.

This paper examines these issues of intellectual property rights and the manufacturer's right to sell goods in a free competitive market. The benefits of ensuring free and fair competition will be outlined as well as some of the penalties incurred when these conditions are not adhered to.

The nature of intellectual property rights

For over a hundred years, there has been a general recognition that there must be a balance between the interests of inventors who create products or techniques and the interests of society at large: the inventors are entitled to be rewarded for their genius and creativity while society, by creating an environment within which the inventor is rewarded is also, in due course, entitled to benefit from the invention. This concept of balancing the interests of inventors with the interests of society at large has permeated the civilized world since the mid-nineteenth century. Without this arrangement, many, if not most, of the advances observed since the industrial revolution could not have occurred. Sensible manufacturers would not develop and market a product if they knew that a competitor could immediately steal the product design and begin to market it, thereby eliminating any realistic hope of reasonable reward.

These simple concepts of rewarding both inventive genius and society at large remain as valid today as they were a hundred years ago. They are the cornerstones of technological advancement throughout the world and they have become important factors in the economic development of nations.

Traditionally, Intellectual Property Rights (IPRs) have referred to copyright, design right, trademarks, and patents. All of these have an impact upon the pharmaceutical industry but most of the disputes arising around IPRs are focused on patents and patent protection. In recent years, another aspect of IPRs is beginning to assume significant proportions. This is the matter of the protection of research data accumulated during the process of obtaining regulatory approval for the marketing of a new chemical entity (NCE). This "data exclusivity" has become a matter of international concern and it appears that it may become the substance of international trade disputes within the near future.

Patent protection

Articles 27 to 34 of TRIPS set out the basic requirements for patent protection in member countries. Article 33 specifies that the basic term of patent protection is 20 years from the date of filing. This was a change for some countries, which had previously recognized the first to invent as the legitimate patent holder.

Other important aspects of the patent regulations of the TRIPS agreement include the prohibition of discrimination against foreigners and the option for countries to exclude from patent protection diagnostic and therapeutic methods for the treatment of humans, plants, or animals. In addition, member countries may require compliance with reasonable procedures but patents must be issued within a "reasonable time" so as to prevent unwarranted shortening of the period of patent protection.

Article 31 specifies certain circumstances under which a country has the right to issue compulsory licenses and make other exceptions, provided that these do not unreasonably conflict with a normal exploitation of the patent and do not unreasonably prejudice the legitimate interests of third parties. These exceptions cannot be invoked on a trivial basis and the conditions under which they can be introduced are carefully spelled out in the details of article 31. Despite the limitations, nations do have reasonable leeway, within the constraints of TRIPS, to adapt their legislation to local circumstances.

There are now 134 signatories to the WTO but not all are fulfilling the requirements of TRIPS. The European Union, Japan, the United States, and Canada are included amongst those that recognize the 20-year term of patent protection but not all these countries are free from controversy about the way in which they have implemented TRIPS. For

example, Canada is presently the subject of an appeal to the WTO because of a practice known as "early working." This arrangement permits a generic manufacturer to obtain regulatory approval to produce and stockpile a patent-protected drug while the patent is still in place. This places the generic company in a position to flood the market with its product as soon as the patent expires. The European Union, the United States, and Japan do not permit "early working" and they do not permit the generic manufacturers to stockpile product prior to the expiry of the original patent. Countries opposed to this procedure claim that permitting the generic manufacturer to apply for regulatory approval during the patent period and to manufacture the product prior to expiry of the patent is a breach of patent. This matter is currently (autumn 1999) before an active panel of the WTO and the decision will provide a new and useful guideline for Canadian legislators.

Recently Japan has been the focus of interest regarding some aspects of patent rights. Prior to 1997, the Japanese courts had held that any experiment or research by a generic manufacturer to test the commercial viability of a patented invention during the term of the patent constituted a violation of the inventor's patent rights. Beginning in 1997, this interpretation of Japanese law was reversed: five decisions of the Osaka and Tokyo courts interpreted the law so as to protect the generic manufacturers rather than the original patent holders (Otsuka Pharmaceutical Co. v. Towa Yakuhin K.K., Heisei 9 [ne] 3498 [Tokyo High Ct. March 31, 1998]; Kyorin Pharmaceutical K.K., v. Sawai Pharmaceutical K.K., Heisei 9 [wa] 138 [Osaka High Ct., April 15 1997]). Japan has a $41 billion pharmaceutical market and because of this the brand-name industry has a strong interest in maintaining the patent rights of innovative companies. The industry can be expected to continue to litigate these issues until the Supreme Court of Japan conclusively resolves the permissible scope of generic manufacturers to make experimental use of information during the period of patent protection.

Patent Term Restoration (PTR) is another contentious topic. This is a procedure whereby a manufacturer is compensated with an extension in patent protection for the time taken to obtain regulatory approval. The argument is that the manufacturer has little or no control over the government's bureaucratic process and should not be penalized for the time taken by that process. The European Union, the United States, Japan, and Australia all provide for patent extension through PTR; Canada and many other countries do not. Failure to provide PTR is perceived as unjust by those countries that make this provision. Consequently, there is growing pressure for non-compliant countries to harmonize their laws with those that do.

Disputes related to patent protection are an ongoing source of litigation in many countries and at the WTO. Many of the disputes arise

because national legislation is not sufficiently harmonized with the internationally agreed standards. This is an area that requires more work at the national level because it is in the interest of each country to modify and adapt their laws so that these national and international disputes are minimized.

Data exclusivity

In the process of preparing a new chemical entity (NCE) for regulatory approval, a pharmaceutical company conducts a massive array of laboratory, animal, and human trials. The data so obtained are the property of the company developing them but the patent rights that protect the NCE do not protect the data. In the normal course of events, the licensing process requires that much of these data be turned over to the regulatory body that provides the final approval to market the drug.

If these data, in whole or in part, are turned over to generic competitors who are seeking approval to manufacture a generic version of the original drug, an unfair situation is created. The cost of producing an NCE and taking it to market is approximately US$600 million (1997 dollars) (Kettler 1998: 1) but the cost of setting up a copycat generic production of a product is estimated to be about $1 million. If a regulatory body fails to protect data exclusivity, the consequences are far reaching. First, theft of the proprietary data has been legalized. Second, only about 30 percent of the drugs brought to market actually recover the R&D costs needed to get them there, and release of the research data further reduces the opportunity for the original inventor to make a fair profit. Third, such circumstances create a considerable disincentive for a manufacturer to operate in this type of environment.

The basic requirements for patent protection are set out in Articles 27 to 34 of TRIPS. However, the Trade Secrets portion of the agreement covers data exclusivity and this is included in Article 39. It is significant that TRIPS separates patent protection from trade secrets and in Article 39 requires the members of regulatory bodies to protect data against disclosure.

The 134 signatories to the WTO are required to comply with the TRIPS agreement by January 1, 2000. Some specified countries are permitted, under the agreement, to delay implementing of full patent protection until January 1, 2005. This delay does not apply to the protection of proprietary data. Failure to legislate and implement data protection required under TRIPS will leave countries open to complaint and resolution in accordance with the dispute mechanism.

At this time—autumn 1999—the European Union, the United States and Switzerland have implemented legislated protection of proprietary research data and New Zealand has indicated its intention of doing so. The Europeans have introduced a ten-year period of

exclusivity and the United States a period of five years. That is, no application using the inventor's data can be approved for a period of ten (or five) years after the approval of the originators application.

Many other countries have not yet met the standards required by TRIPS and there is a wide degree of non-conformity. For example, Japan has a legal requirement that the originator's test data be published in a medical article or journal. Canada's early working system enables generic manufacturers to file an abbreviated drug submission with the Health Protection Branch. This shortened submission relies heavily upon the innovators R&D and the innovating manufacturers claim that this contravenes the provisions of TRIPS. The magnitude of the deficiencies in the Canadian protection of patents and data exclusivity were illustrated recently by a case in which a generic manufacturer was given regulatory approval to manufacture and market generic *Enalapril* in spite of a Federal Court injunction prohibiting such licensing until 2007. This is now the subject of litigation.

Some other countries have not yet given legislated protection for the 20-year patent rights prescribed under TRIPS and, in the worst circumstances, some jurisdictions have failed to provide any patent protection for pharmaceutical products.

Access to free market competition

In recent years many nations have noted an increase in the total expenditure on state-purchased pharmaceuticals. All too often, politicians and bureaucrats have attributed these cost increases to escalating drug prices and, in reaction, have introduced a policy of "pharmaceutical cost containment," more accurately described as price controls.

Various arguments are made for the introduction of price controls. These include (Butler 1993: 4):

(1) *Inflation control*. The rationale for this stems from the belief that there are "cost-push" factors that cause inflation. The concept is that inflation stems from an increase in a rise in general costs, and these are then passed on to the consumer in the form of higher retail costs.

    This theory is no longer accepted by many economists who believe that the root cause of inflation is more often increased demand associated with an expansion in the money supply. While this latter postulate holds more credence, the possibility of stopping inflation through the use of legislative and regulatory controls on prices remains attractive to politicians and bureaucrats.

(2) *Ensuring fair prices*. This postulate holds that the greater social good requires that a just or fair price should be applied to goods and

services. Those who hold to this view often point to various aspects of health care as an example of how all should be deemed equal in their ability to obtain medical care. As Butler points out, this is a view that stems from medieval times (Butler 1993: 4) and is entirely rejected in market economics, which form the basis of the western economies. Nevertheless, the concept that all citizens should have equal access to a particular service is both beguilingly simple and politically attractive.

(3) *Unstable market conditions*. This concept holds that when unusual and unstable circumstances occur, these can be counterbalanced by price controls. War and widespread natural disasters may provide a backdrop for enthusiasm for this attempt to control the economy. There are numerous examples that illustrate that artificial measures such as price controls have been largely unsuccessful in controlling inflation, even in wartime (Schuettinger 1976: 91; Rockoff 1984: 186; Stein 1976: 68.). However, those who promote such measures bolster them with the argument that, "Extreme times require extreme measures."

There are two fundamentally different ways of approaching pharmaceutical price controls. First, an attempt can be made to influence the demand for drugs. These measures usually focus on encouraging physicians and other prescribers to use the lowest-cost drugs as well as discouraging patient's demand for drugs. Second, cost containment can focus on programs that influence the supply of pharmaceuticals to the consumer. Such programs tend to focus on the behaviour and performance of manufacturers, pharmacists, physicians, and other prescribers. Ideally, it is claimed, they have no impact on the consumer, who still receives high-quality products at the lowest cost available. The following classification of pharmaceutical price controls has been developed and explained elsewhere (McArthur 1997).

(1) Demand Side Measures
- Managed Care
- Education
- Cost sharing
- Mandatory budgets

(2) Supply Side Measures
- Assessed value criteria
- Profit limitations

- Legislated price controls
  - Price reductions
  - Maximum entry price control
- State formularies
- Prescription volume controls
- Professional fee controls
- Parallel importing
- Reference based pricing

Short or long term goals

In countries that are producers of pharmaceuticals but are striving to achieve front-line status, there is always a dilemma as to whether short term or long term goals should be pursued. The pharmaceutical industry presents an opportunity for substantial short-term gain. About $1 million and a handful of reliable technicians can quickly put together a generic production plant. By picking widely popular drugs and marketing them on the gray market at home and abroad, a producer can turn a tidy profit in a short time. Such activity requires a government that has little or no protection for intellectual property rights or, at least, is prepared to turn a blind eye to such activities.

The benefits of this type of production accrue to the investor only. The employees are soon out of work as markets dry up when the nature and source of the drug is identified by regulatory authorities in responsible countries. The country that permits this type of activity is damaged as it becomes recognized as a rogue nation in the international community. There are no long-term benefits, no gradual development of production and marketing skills, and no internal investment in R&D. The opportunity to create high-technology employment is lost and neither the country nor its citizens benefit.

Long ago, the leaders of the European Union, the United States, and Switzerland recognized these realities. They responded by developing just and enforceable rules to govern the protection of intellectual property rights. Others are following, and as they take each step forward, they begin to reap the industrial benefits. Vigorous protection of intellectual property rights brings substantial economic advantages but there is no successful short-term route to gaining these benefits.

The economic impact of incomplete protection for intellectual property rights

In the technologically advanced countries, and in those that are progressing toward higher levels of technological development, the phar-

maceutical industry is an important part of the economy. Table 1 reveals the pharmaceutical production per capita in some OECD countries.

It is apparent that some of the European countries have the most productive economies with respect to pharmaceutical production. The United States, Japan, and Korea join them in this desirable position. The immediate question arises as to why this group of nations surpasses other technologically advanced countries such as Canada, Australia, and New Zealand which are also low end employers in pharmaceutical manufacturing.[1]

There may be several factors involved in the ascendancy of the more successful nations but it is not by chance that they have the most stringent laws protecting intellectual property rights. The pharmaceutical industry in Germany provides an illustration of the benefits that can accrue from this sector of the economy. Figures 1 through 6 provide an overview of some of these factors. Figure 1 shows capital spending on pharmaceutical production; note that this is 30 percent higher than in both the motor-vehicle industry and overall manufacturing and 73 percent higher than in the mechanical engineering industries.

Table 1: Pharmaceutical production per capita for selected OECD countries (US$ adjusted by purchasing power parity)

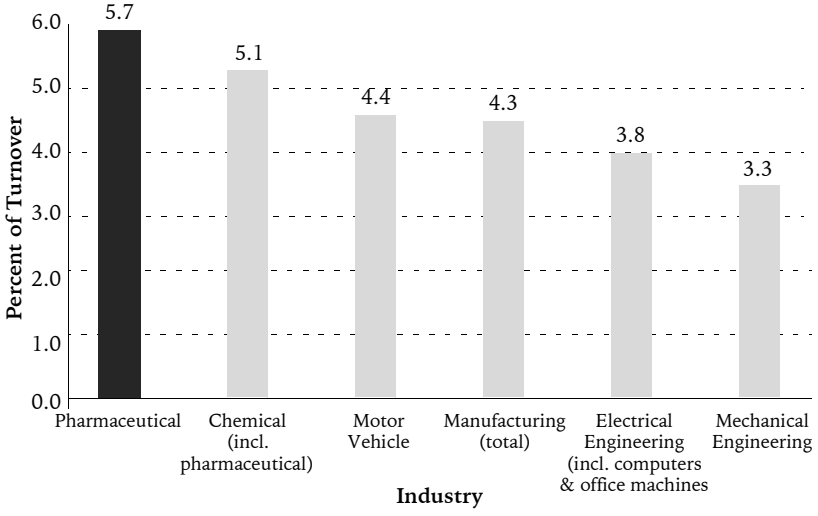
	1975	1992	1994
Australia	26	101	
Austria	34	218	235
Belgium	34	255	287
Canada	25	116	133
Denmark	31	238	290
France	58	251	257
Germany	47	190	195
Greece	15	59	
Japan	52	208	215
Korea	19	185	211
Mexico (1980)	25	64	72
Portugal	23	90	93
Spain	59	198	202
Sweden	25	189	289
Switzerland			600
United Kingdom	49	241	
United States	51	261	283

Source: OECD Data, CD-ROM (May 1998).

Figure 2 shows demand from within Germany and from abroad. This demonstrates how the existence of a high-quality product produced in a country with strong protection for intellectual property rights can result in an increasing export demand. Figure 3 also shows the impact of high-quality products and strong protection for intellectual property rights upon the economy of Germany, which is the world's leading exporter of pharmaceuticals. Also of interest in figure 3 is tiny Switzerland, a country with a highly educated and trained population, a very high standard of living, and a high standard of protection for intellectual property rights: it is the world's second-largest exporter of pharmaceuticals. Switzerland's position as an exporter of pharmaceutical products ahead of the United States, the United Kingdom, France, and Japan carries a powerful message for those interested in increasing national wealth through the export of high-technology products. At the same time, the Japanese legislation requiring the public disclosure of research data from patent research may be one of the factors contributing to the relatively lower export performance of the pharmaceutical industry in that country.

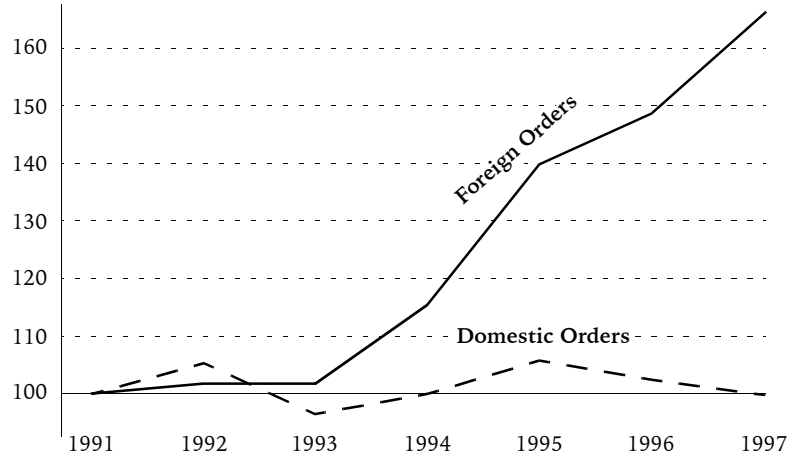
The level of skilled to unskilled employment as shown in figure 4 (using percentages of salaried employees and wage labourers as a proxy)

Figure 1: Comparison of capital spending in various german industries (percent of turnover, 1995)



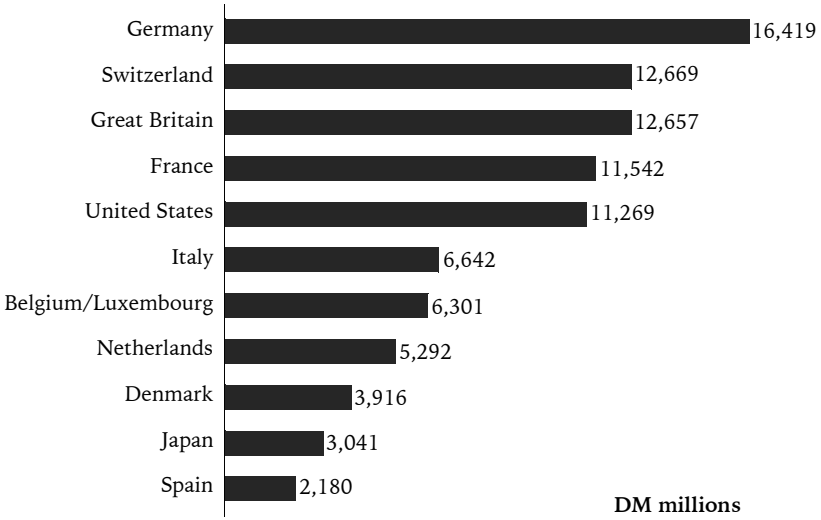
Source: German Statistics Bureau; Verband Forschender Arzneimittelhersteller e.V. (VFA) (www.vfa.de/extern/index_c.html).

Figure 2: Domestic and foreign orders for German pharmaceutical products (1991= 100)



Source: Verband der Chemischen Industrie; after Verband Forschender Arzneimittelhersteller e.V. (VFA) (www.vfa.de/extern/index_c.html).

Figure 3: Exports (1996) of pharmaceutical products (less primary pharmaceuticals) from Europe, Japan, and the United States



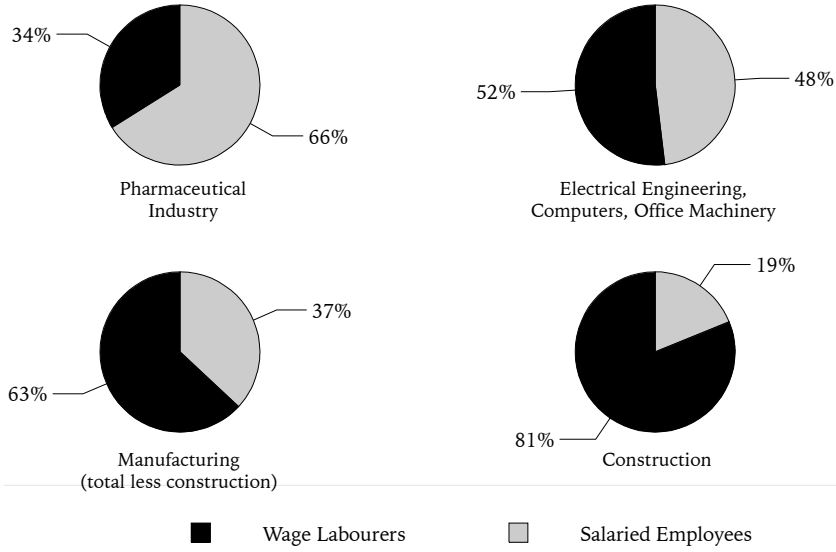
Source: Verband der Chemischen Industrie; Verband Forschender Arzneimittelhersteller e.V. (VFA) (www.vfa.de/extern/index_c.html).

is higher in the pharmaceutical industry than engineering, general manufacturing, or construction. This complements the high added value per employee and net value-added numbers shown in figures 5 and 6.

The experience in Canada also illustrates some of the benefits of implementing vigorous protection of intellectual property rights. Prior to 1987, Canada had poor patent protection for pharmaceuticals and in that year pharmaceutical R&D spending totaled $106 million. In 1987, the Canadian parliament enacted Bill C-22, which improved patent protection, and by 1993 R&D spending had increased to $504 million. Bill C-91 was passed in 1993, bringing Canadian patent protection closer to accepted world standards. Over the next 4 years, spending on R&D increased to approximately $825 million. This increase in spending on research when intellectual property rights are strengthened is a pattern that has been seen many times, in many countries, and once again illustrates the economic benefits that flow from improving the protection of intellectual property rights.

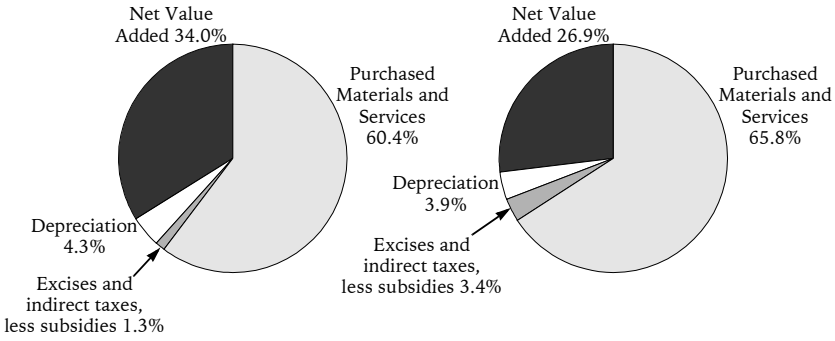
Canada presents another side of the coin as well. Why would this nation of some 30 million people, a democratic country with a long established and impartial judiciary, with an enviable record in world trade,

Figure 4: Comparison of percentage salaried employees and wage labourers in various German industries (1995)



Source: German Statistics Bureau; Verband Forschender Arzneimittelhersteller e.V. (VFA) (www.vfa.de/extern/index_c.html).

Figure 5: Output and added value per employee in the pharmaceutical and in all manufacturing industries of Germany (DM. 1995)

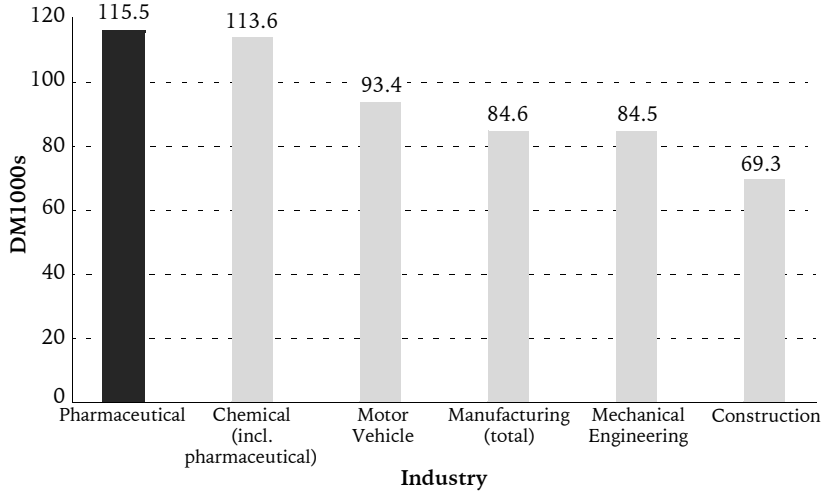


Pharmaceutical Industry
Gross Output = DM 340,000

All Manufacturing Industries
Gross Output = DM 315,000

Source: German Statistics Bureau; Verband Forschender Arzneimittelhersteller e.V. (VFA) (www.vfa.de/extern/index_c.html).

Figure 6: Comparison of added value per employee in various German industries (DM1000s, 1995)



Source: German Statistics Bureau; Verband Forschender Arzneimittelhersteller e.V. (VFA) (www.vfa.de/extern/index_c.html).

perform so poorly in pharmaceutical production compared with its southern neighbour? The weaker protection of intellectual property rights may be a factor. As noted above, Canada permits "early working," and generic stockpiling and does not provide for patent-term restoration. Countries that surpass Canada in pharmaceutical production do not permit protection of intellectual property rights to be weakened in these ways, a factor that probably contributes to their superior performance.

Japan presents an interesting scenario. In 1975, it was second only to France and Spain as a per-capita producer of pharmaceuticals. By 1998, it had fallen to ninth position, far behind Switzerland and significantly behind several countries from the European Union. While impossible to prove, it seems that this fall in ranking may be related to the countries poor protection of data exclusivity.

Viewed from another perspective, the response of the innovative pharmaceutical industry to a jurisdiction that does not protect and enforce intellectual property rights is fairly predictable. Development of each new chemical entity requires a huge financial investment and, on average, less than one in every thousand new drugs discovered will finally get to market. These factors make it imperative for manufacturers to focus their energies and investment in jurisdictions that create the best opportunity for success. Conversely, jurisdictions that fail to provide solid and reliable protection of intellectual property rights are regarded as poor locations for investment and manufacturing of pharmaceuticals and the pharmaceutical industry will respond accordingly. These responses include the following:

(1) *Failure to invest* The large manufacturers of innovative drugs are constantly on the lookout for places to construct new plants for R&D and manufacturing. They seek, among other things, locations where there are solid, long-term assurances of protection of their intellectual property rights. Unless these exist, a company will not invest there and the economy will not have the benefit of the investment and job creation that goes with such a program.

(2) *Relocation* If a plant is located in an environment where there is a perceived economic or social instability, the prudent manufacturer will avoid entering into the production of new drugs there and will instead assign such production to another plant in a location perceived to be more stable.

(3) *Reassignment* If the regulatory environment deteriorates, making production of brand-name pharmaceuticals unprofitable, the manufacturer may choose to reassign plant production to another phar-

> maceutical product such as an over-the-counter medication or a veterinary medication that is subject to little regulation; alternatively, the manufacturer may begin making an entirely different product. The result is the loss of pharmaceutical R&D, the probable loss of employment for highly skilled technical workers and researchers combined with a decrease in investment. The jurisdiction so affected will also lose the capability to compete in the lucrative international pharmaceutical trade, thus resulting in a weakening of the nation's export capability.

The industrial response to price controls can be equally devastating. Examples are provided by New Zealand, which some years ago introduced a price control mechanism known as Reference Based Pricing, a scheme that substitutes older and less expensive drugs for the newer and often more effective products. The result of this program has been to have pharmaceutical manufacturing move out of New Zealand to less hostile jurisdictions. Again, in the Canadian province of British Columbia a similar program of Reference Based Pricing was introduced in 1995. The results have been devastating. The provincial government claims to be saving about 40 million dollars per year. However, more than that amount is being withheld in medical research funding from the province by the pharmaceutical industry, which takes the position that it will not supply research funding in jurisdictions where they are impeded in marketing their products fairly and freely. In addition to the loss of research funding, independent analysts have calculated that this venture designed to save money is actually costing the province as much as $300 million per annum. This amounts to an annual loss of nearly $100 for every person in the British Columbia.

The counter-productive economic nature of price controls, in many jurisdictions, for many products forms the basis of a substantial literature and one is hard pressed to find an example where price controls have not, in the long term, created a substantial increase in prices. The pharmaceutical industry is no exception to this experience.

The pharmaceutical industry is a significant net contributor to the economy of many of the technologically advanced countries. Looked at from another perspective, the countries with high levels of production of pharmaceutical products also tend to have high standards of living and generally lower levels of unemployment. This suggests that countries aspiring to achieve front-line status in terms of economic stability and productivity should consider the steps that must be taken to improve industrial performance to these levels.

Overall, it appears that there is a clear correlation between national prosperity, high standards of living, and the strict protection of

intellectual property rights. It would be erroneous to conclude that focusing solely on development of the pharmaceutical industry will, in itself, bring prosperity. Rather, the creation of an environment where the pharmaceutical industry prospers will provide opportunity for high technology, intellectually based, general industrial development.

Impact of incomplete protection for intellectual property rights upon health

There are human consequences to weak protection for the intellectual property rights of pharmaceutical manufacturers. There is an erroneous belief that the vigorous protection of IPR somehow inhibits the development of new and better drugs at a rapid rate; often, the reverse is true.

While patent laws prevent imitators from making and marketing copies of a newly identified product, they do not create a monopoly. Indeed the creation of a successful new drug with potent action to benefit a large number of people often stimulates considerable inventive effort to achieve the same means through a different process, using a different chemical compound. A case in point are the drugs for combatting peptic ulcers. Prior to 1975, the recognized treatment for serious peptic-ulcer disease was an operation known as a vagotomy and pyloroplasty (V&P). This major intra-abdominal surgery takes 2 to 3 hours to perform, the patient is hospitalized for a week or more, and the procedure has uncertain results. In 1975, a new drug called *Cimetidine* came to market and reduced the need for V&Ps considerably. In 1983, another new drug with a different mode of action called *Ranitidine* became available and further improved the treatment of peptic-ulcer disease. Then in 1989, *Omeprazole*, a drug with a previously unknown mode of action became available and the result was that V&Ps became an unneeded procedure.

Patents, as in this example, provide an umbrella under which innovative companies can compete and conduct research and development to create and produce new and different drugs that benefit society and, in the process, create profit for those who choose to invest in the producing company. Discovery of the initial drug did not create a monopoly but rather vigorous competition aimed at achieving the same result through different means. The beneficiaries were those patients who gained relief from the newer and more effective drugs, the governments and other insurers who were saved the cost of paying for the previously required surgery, and the investors in the producing companies, who made a profit from these efforts.

This type of competitive research is likely to become more common as the industry moves into the development of vaccines with the

potential to cure or even prevent diseases that are presently untreatable. Debilitating and expensive disorders such as diabetes, osteoporosis, and arthritis may be curable within the next ten to 15 years. In fact, within the foreseeable future, we may be able to prevent or cure many of the diseases that now afflict mankind. It is certain, however, that this will only occur if the research and development is permitted to advance without the interference of excessive regulation.

Failure to protect intellectual property rights and the imposition of price controls can have a serious adverse impact upon the care of the ill. R.A. Levy and D. Cocks (1996) present one of the most comprehensive analyses of this topic. Part V of their report describes:

- a Louisiana study that showed markedly increased patient hospitalization in response to increased formulary restriction
- a West Virginia study by Bloomb and Jacobs that revealed increased surgical rates for peptic ulcer patients when access to newer peptic ulcer drugs was restricted
- a report from Smith and Simmons that showed that, when minor tranquilizers were restricted, there was a substantial increase in the prescribing of more potent, more expensive, and potentially more dangerous drugs such as barbiturates
- a study by DeTorres and White that showed restrictions on newer antibiotics for patients resulted in increased renal damage in the patients affected
- a report by Richton-Hewett *et al*. that revealed an example of how substituting a cheaper generic, *Warfarin*, in Boston City Hospital produced a significant increase in morbidity and health costs
- several authors who point out that the people most adversely affected by formularies and other restrictive practices are those with low income and complex illnesses, truly the most vulnerable and frail in society.

In November 1998, P. Authier and J. Robinson recently published details in the *The Montreal Gazette* of a heretofore-secret study reporting death and illness resulting from a cost-containment plan introduced in Quebec in 1997 (Authier and Robinson 1998). This bombshell came in the middle of a provincial election and told of 3,926 extra hospitalizations as well as increased mortality. The plan, which involved a substantial increase in drug costs for 93,950 seniors and 55,333 welfare recipients, gives an indication of the effects of the sudden implementation of a poorly conceived cost-containment program.

Other well known reports include that by Stephen B. Soumerai *et al*. (1994), who described the impact of withholding drugs from schizophrenic patients—increased admissions and increased utilization of medical services. Susan D. Horn *et al*. (1996) have demonstrated that health maintenance organizations (HMOs) that employ rigorous cost-containment measures have more unintended outcomes than HMOs using less rigorous constraint measures. These unintended consequences include more visits to the emergency department, more hospital admissions, and overall increased utilization of health-care resources. Recently J.E. Calfee (1999) has described how pharmaceutical price controls in the United States are causing economic inefficiencies as well as reducing the quality of care available.

These and other papers provide evidence that patients suffer when pharmaceutical cost containment is imposed. There appears to be no evidence in the literature to suggest that patients have improved medical outcomes when attempts are made to reduce spending on drugs.

Summary

Over the past 10 years, there has been a vigorous international effort to increase the protection of intellectual property rights. These efforts culminated in the TRIPS agreement, which is now the standard by which all nations are judged.

Patent protection has been stabilized at 20 years from the date of filing but other constraints have been added to this 20-year minimum. Patent-term restoration has become the norm in Europe, the United States, Japan, and some other countries. Discrimination against foreigners is no longer permitted and procedures such as "early working" and the practice of manufacturing and stockpiling generic products prior to patent expiration are no longer acceptable to the international community.

The protection of data exclusivity is also becoming a focus for more attention. The unfairness of permitting generic manufacturers to gain access to the research data of the original patent holder prior to the expiration of patent expiry is addressed in article 39 of TRIPS. The 134 signatories to the WTO agreement are required to put a stop to such disclosure by January 1, 2000 or face the penalties that can be imposed under the agreement. There is little doubt that complaints regarding this will be filed with the WTO early in 2000; Japan and Canada appear to be two countries that may become the focus of complaint.

Many countries have imposed different types of pharmaceutical cost containment, or price controls. Some of these are benign and do little to effect market access while others are more draconian. While some of these measures are probably subject to appeal under interna-

tional treaty, no appeal has been launched to date. The probable reason for this is that price controls appear to cause more economic harm to the countries that introduce them than to other countries. Under these circumstances, the industry appears willing to let the countries concerned learn the painful lessons of experience.

An examination of some of the countries of the European Union, the United States, and Japan reveals that they have been quick to capitalize on the new international treaties concerning the manufacture and sale of pharmaceuticals. These countries have passed legislation harmonizing the national law with the TRIPS agreement. As a result, they are now reaping the rewards of increased skilled employment, increased exports of these valuable products, and an escalating industrial investment in this high-technology industry. Another important benefit is increasing investment in R&D, which tends to improve overall industrial R&D.

Apart from the economic impact, there is also an impact upon the health of the citizens of these countries. It is not by chance that some of the best and most sophisticated health care in the world is observed in those countries that have adapted rapidly to the changing international environment in pharmaceutical production. The improved employment, the increase in high-technology R&D, and the rapid availability of the newest and most effective medications are characteristics that complement and contribute to high-quality health care.

These countries also seem to be recognizing the futility of pharmaceutical cost containment. The overwhelming evidence to date is that the most effective method of controlling the price of drugs is to permit the manufacturers to compete on a free and open market for the opportunity to sell their product. There are still attempts being made to control pharmaceutical prices, particularly in the United States, but as more studies reveal the negative effects of this upon both economics and health care, these efforts will probably diminish.

Overall it is clear that countries that seek front-line status in the pharmaceutical industry have huge gains to make, both economically and in terms of improved health outcomes for their citizens. To achieve these goals they must make an irrevocable commitment to:

- establishing long-term goals for the pharmaceutical industry
- introducing legislation to protect intellectual property rights, including patent protection and data exclusivity that conforms with TRIPS
- creating a free, competitive market for pharmaceuticals
- avoiding price controls and other artificial distortions of the market place.

Note

1 OECD data reveal that pharmaceutical employment per capita in Australia, Canada, and New Zealand is less than half that in France, Germany, and the United Kingdom.

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