Patent-Term Extension and the Pharmaceutical Industry

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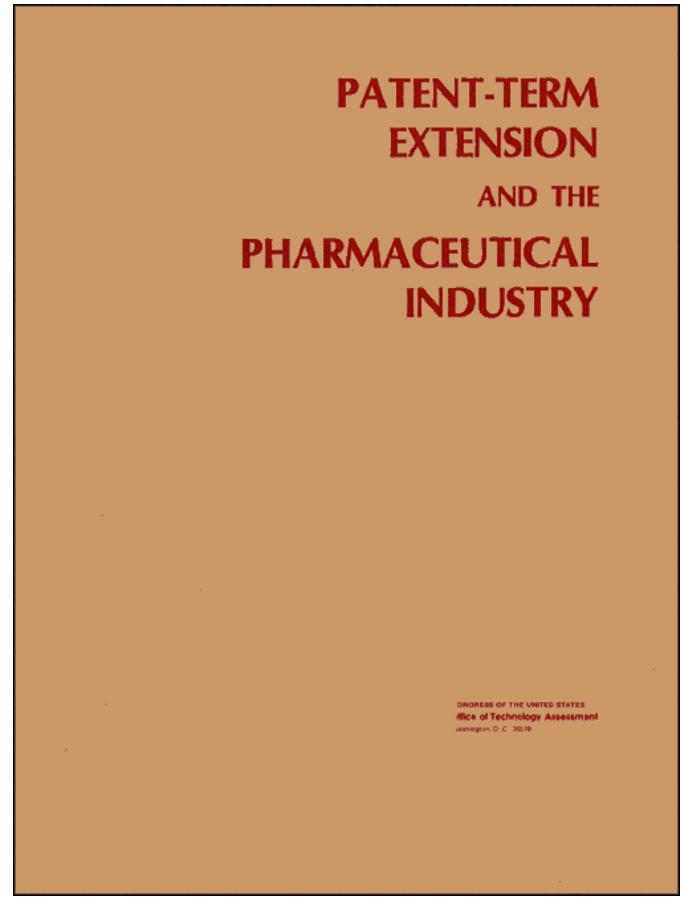

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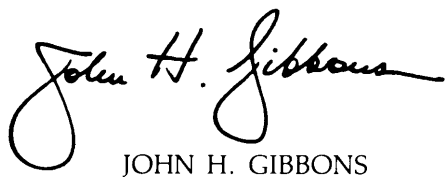
Foreword

This report examines the relationships between patent-term extension and pharmaceutical innovation. Particular attention is paid to the social implications of patent-term extension. The report was prepared in response to a request from the Chairman of the House Committee on the Judiciary and supporting requests from the Chairman and the Ranking Minority Member of the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce.

The Office of Technology Assessment was assisted by an advisory panel comprised of pharmaceutical industry representatives, consumer interest group spokesmen, medical professionals, lawyers, and others concerned with health care and pharmaceutical innovation. Reviewers from universities, Government, consumer interest groups, industry, and the law provided helpful comments on the draft report. The Office expresses sincere appreciation to all those individuals.



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Chapter 1
Executive Summary

Chapter 1

Executive Summary

INTRODUCTION

Patents were designed to promote innovation by providing the right to exclude others from making, using, or selling an invention. They enable innovators to obtain greater profits than could have been obtained if direct competition existed. These profits act as incentives for innovative activities.

Although the patent term in the United States is 17 years, the period during the patent term in which products are marketed (the effective patent term) is usually less than 17 years because patents are obtained before products are ready to be marketed.

Effective patent terms are influenced by many factors, including Federal premarketing and premanufacturing regulations. The products covered by these regulations include pharmaceuticals, medical devices, food additives, color additives, chemicals, and pesticides. These products are subject to different regulations that have had varying impacts on effective patent terms.

The regulations governing the pharmaceutical industry have contributed to a decline in the average effective patent term of prescription drugs. Pharmaceuticals cannot be marketed in the United States until they have been approved by the Food and Drug Administration (FDA). To obtain such approval, drugs must undergo extensive testing to prove they are both safe and effective. While the pharmaceutical awaits approval, its patent term keeps running.

Concern exists that the decline in the average effective patent term of pharmaceuticals may result in diminishing profits, decreased research and development (R&D) expenditures, and an eventual decline in the introduction of new drugs. Furthermore, to many, it appears inequitable that products subject to premarketing or premanufacturing requirements are marketed under patent protection for briefer periods than products that are not subject to such regulation.

To address the concerns that have arisen about innovation and equity, legislation has been proposed that would extend the patent terms for products affected by premarketing and premanufacturing regulations.

Although this report briefly describes the equity issue, its focus is on the relationship between patent-term extension and innovation in the prescription drug industry. The effects of patent-term extension on the members of the industry and on consumers are also examined.

THE CONTROVERSY

Pharmaceutical firms that are heavily involved in basic research (research-intensive firms) support legislation to extend patent terms. These firms claim that the costs of R&D are rising, effective patent terms are declining, and the rates of return to pharmaceutical expenditures are becoming unattractive. They maintain that, under these circumstances, a decline in innovation would not be unlikely and point out that future health care in the United States would suffer if pharmaceutical innovation declines.

Research-intensive firms believe that patent-term extension will provide encouragement for research activities, raise the profitability of drug research for successful innovations, and ultimately result in more innovative products. They contend that the additional drugs will increase pricing competition among different

products used fox the same or similar ailments and that the consumer will actually save money as a result of patent-term extension.

The firms that derive most of their revenues from nonpatented, generically equivalent drugs (production-intensive firms) believe that patent-term extension will delay their entry into the market and that they will be economically penalized for each year that the extension prevents them from marketing drugs. They also contend that for some drugs, the product life remaining after the extension may be too short to justify their entry into the market. They believe that competition will decline as a result of patent-term extension and that the costs of drugs will therefore increase.

The production-intensive firms contend that many drugs are covered by more than one patent and that the combined patent terms often result in patent protection for the drug in excess of 17 years. They also point out that as a result of nonpatent barriers to market acceptance of generically equivalent products, patented products often maintain an exclusive market position even after their patents expire.

Production-intensive firms believe that some extensions might be equitable in certain situations in which the combined period of protection from all patents on the drug during its marketing is significantly less that 17 years due to excessive regulatory delay. They urge that any legislation for patent-term extension minimize any adverse effects on their industry and facilitate their effective entry into the market upon expiration of the extension. They are opposed to any legislation that would enable products covered by more than one patent to be protected by patents for more than 17 years, and they believe that the duration of the extension for any product should not exceed the actual marketing delay caused by premarketing regulations.

Spokesmen for consumer interest groups believe that patent-term extension will result in higher drug prices without providing better health care. They point out that increased drug costs will fall disproportionately on the elderly and chronically ill (whose incomes tend to be lower than average). They argue that the pharmaceutical industry is extremely profitable and needs no additional incentive to conduct research, These groups are concerned that the legislation proposed to date provides no guarantees that additional revenues derived during patent-term extensions will be invested in R&D activities. Concerns are also expressed that expenditures made for R&D may not be directed toward research areas that provide the greatest benefit to society. Therefore, many consumer spokesmen oppose patent-term extension.

FINDINGS

This study examines the issues raised by the various interest groups. Unfortunately, much of the data needed to differentiate between belief and fact are unavailable or unreliable. The evidence that is available neither supports nor refutes the position that innovation will increase significantly because of patent-term extension. Thus, the net effects of patent-term extension on pharmaceutical innovation cannot be ascertained. However, findings have been developed that should serve to clarify or explain many of the individual factors that have played, or will play, a role in pharmaceutical innovation.

The following is a list of our major findings, which will be discussed in more detail in the later sections.

- The costs of R&D for the average new chemical entity drug have increased.
- Since *1966,* average effective patent terms have declined; some factors influencing effective patent terms are, however, changing and there is reason to believe that the decline may be halted in the future.
- Revenues of the pharmaceutical industry have increased steadily and the relationship between revenues and R&D expenditures has remained stable.
- The effects of governmental actions that encourage use of generically equivalent drugs have thus far been minimal on the postpatent revenues of research-intensive firms but could become substantial in the future.

- The prices of drugs whose patents are extended are likely to be higher during the extended period than they would have been if patent protection had ended.
- Competitive pressures on patented drugs from generically equivalent drugs will be delayed and in some cases prevented by patent-term extension.
- The extension will increase the attractiveness of research on drugs that have large markets but will not increase the economic attractiveness of research on drugs whose potential markets are small.
- The effects of patent-term extension on innovation, the industry, and society will depend in part on the nature of the patent rights during the extension.

INNOVATION IN THE PHARMACEUTICAL INDUSTRY

Pharmaceutical innovation has resulted primarily from the activities of private industry, most of the expenditures being made by large, multinational companies.

In the pharmaceutical industry a long period exists between the initiation of research and the marketing of new products. Thus, the rate of innovation observed today may reflect decisions made 10 or 15 years ago, and decisions made today will affect innovation for the next decade.

The results of the innovative process in the pharmaceutical industry are often measured by the number of new chemical entity (NCE) drugs that are introduced into the market. By this measure, a sharp decline in innovation occurred with the adoption of the 1962 amendments to the Food, Drug, and Cosmetic Act, which substantially increased the stringency of the drug approval process. The number of NCEs judged by FDA to offer important or modest therapeutic gain has, however, been relatively stable. Although different measures produce different results, by most measures innovation does not appear to be increasing.

TRENDS IN THE FACTORS AFFECTING PHARMACEUTICAL INNOVATION

Innovation will not occur unless industry undertakes R&D activities. Many factors that influence R&D decisions appear to favor innovation: the industry continues to enjoy high and stable profits in terms of return to stockholder's equity; research techniques have improved; and competitive pressure for innovation has not diminished.

Nonetheless, there is a widespread belief that the return to R&D investment is declining, and this belief can affect R&D decisionmaking. Because data are insufficient to measure accurately the return to research investment, we have focused on the underlying factors influencing the returns. The major factors are the costs of R&D activities, the amount invested in R&D, and the revenues and profits of the firms conducting research.

The costs of R&D activities associated with an NCE drug have been increasing rapidly as a result of inflation and more stringent and time-consuming testing requirements. Because the time spent in obtaining FDA approval may be leveling off and new research techniques are being developed, R&D costs should increase more slowly in the future.

Real growth has occurred in expenditures for R&D. The relationship between revenues and R&D expenditures has remained highly stable over the past 15 years. For the years 1965 through 1978, research expenditures averaged about 8.5 percent of total sales.

The revenues and profits are influenced by the competitive pressures exerted on drugs. The competition may be from other patented drugs,

from nondrug therapies, or from generically equivalent drugs that are produced by either research-intensive firms or production-intensive firms. Of the drugs having generic competition, about 80 to 85 percent are sold by research-intensive companies.

Despite the decrease in the average effective patent term that may have allowed generic competition to enter the market earlier, the revenues and profits of research-intensive firms have thus far not been significantly affected by generic competition. But recent governmental actions could result in increased competition from generically equivalent drugs. Most States now have laws that allow or require generic equivalents to be substituted for brand-name drugs specified in prescriptions. FDA has adopted procedures to facilitate approval of generically equivalent drugs. The Federal Government now bases its reimbursements for prescriptions paid for under medicaid on the lowest wholesale price of generically equivalent drugs. Furthermore the Supreme Court has ruled that laws prohibiting the advertising of drug prices are unconstitutional.

Despite Government action to encourage use of generically equivalent drugs, barriers to the acceptance of these products still exist. Physicians, who determine the market for prescription drugs, tend to write prescriptions for the easily recalled brand-name drugs. Pharmacists fear they will be liable if they fill a prescription for a brand-name product with a generic equivalent that later causes injury. Furthermore, consumers tend to prefer drugs that look exactly the same as the drugs they are accustomed to using.

Thus, the effect of generic competition on the revenues and profits of research-intensive firms in the future is uncertain. If generic competition increases significantly, such revenues and profits could decline and R&D expenditures could be reduced. There is a possibility that additional generic competition could encourage research-intensive firms to increase their R&D expenditures in an effort to maintain their market shares through drug innovations.

IMPLICATIONS OF PATENT-TERM EXTENSION FOR PHARMACEUTICALS

Patent-term extension can encourage the development of new drugs through the incentives it provides to the patent owner (patentee). But by delaying use of the patented technology by the public, it may also delay some improvements in patented drugs.

Patent-term extension specifically addresses the prime concern of the research-intensive firms: the perceived decline in the rate of return to R&D investments attributed to the reduction in effective patent terms. Whether R&D activities actually increase as a result of longer effective patent terms will, however, depend on decisions made in the private sector.

Since patent-term extension will not provide additional revenues until original patents expire and extensions begin to run, the immediate incentive provided by extension legislation is the potential for obtaining greater returns on R&D investment in the future. Once extensions do begin, revenues for some firms will be greater than they otherwise would have been, thus providing additional incentive for R&D activity.

The price of drugs whose patents are extended will be higher during the extended period than they would have been if patent protection ended. The magnitude of the additional cost to the consumer will be significantly influenced by the extent to which generic competition would have existed had the patent term not been extended.

The bulk of revenues generated by patent-term extension will accrue to a few firms who have developed financially successful drugs. The increased revenues may serve to perpetuate their dominance in particular research areas, and other firms, lacking expertise, may be discouraged from entering these areas.

Since the economic incentives provided by patent-term extension will be greatest for drugs with high income potential, the tendency of firms to direct their research toward drugs with large market potential will be reinforced. Some therapeutic areas that are apt to produce economically marginal drugs may receive greater attention as a result of patent-term extension but patent-term extension will not affect research on drugs with small market potential.

The patent owner and the research-intensive firm will generally benefit from patent-term extension. To the extent that a research-intensive firm relies on revenues from the sale of generically equivalent drugs, its benefits may be reduced.

Patent-term extension poses risks for production-intensive firms. Although they depend on innovative new drugs to expand their product lines, the remaining product lives of drugs coming off patents will detemine their long-term revenues. In some cases product lives may be insufficient to justify their entry into the market.

Consumers will benefit if more and better pharmaceuticals are developed. These pharmaceuticals can provide substantial savings over other forms of health care. The cost of drugs for consumers will be higher than it would otherwise have been unless patent-term extension results in the introduction of more new drugs that exert a downward pressure on the prices of existing drugs. It is expected that both the benefits and the additional costs will affect the elderly and the chronically ill more than other segments of society; but patent-term extension will have no effect on either benefits or costs for at least a decade.

THE MECHANICS OF PATENT-TERM EXTENSION

The effects of patent-term extension can only be fully assessed in terms of specific proposals, because the effects will vary depending on the particular form the extension takes. This report has examined several proposed forms of patent-term extension to determine their possible implications for innovation.

Patent-term extension involves a modification of the present patent system. Therefore, in order to understand extension proposals, one must have a basic understanding of how the patent system works. In brief, a patent is granted for an invention which may be, for instance, a new drug, a new process for making a drug, or a new method for using a drug to treat an illness. A patent provides the right to the patentee to exclude others from making, using, or selling the invention in the United States for 17 years, In return, the patentee discloses his invention. Once the patent expires, anyone is permitted to use the invention.

The invention that is patented is defined by claims which establish the boundaries of the invention, much like a deed establishes the boundaries of a piece of land. A claim for a particular invention may thus include many potential products or processes. When a patentee attempts to enforce a patent, the claim is compared with the product or process against which the enforcement action is directed to determine whether it is included within the definition of the invention contained in the claims.

The effects of patent-term extension on the rights of the patentee and on the ability of others to use the invention will depend in part on whether patent protection is extended for the entire invention defined by the claims or for only a portion of the claimed invention. Effects will also differ depending on whether limitations are placed on the products, processes, and methods for use against which the patent can be enforced.

Numerous proposals that affect patent claims and their enforceability during the extension are examined in this report. Of these proposals, three enable the patentee to maintain an exclusive market position for the drug, while'

allowing others to use the invention for some purposes during the extension.

1. In the first of these proposals, the extension is provided for only those aspects of the claimed invention that involve the specific chemical contained in the drug approved by FDA and the patent is enforceable only against products, processes, or methods-for-use that must be approved by FDA. Of the three proposals, this one provides the greatest protection to the patentee.

   It permits others to use the patented invention for anything except drugs and allows others to make, use, or sell variations of the patentee's specific chemical for any drug therapy even though the variations may be included within the entire invention defined in the claims. It prohibits use of the patented invention for a drug therapy only if the patentee's specific chemical is used.

2. In the second proposal, the patent rights are extended for the entire invention defined by the claim, but enforcement is limited to the specific therapeutic use approved by FDA. This proposal is broader than the previous one in terms of the active chemicals that are protected, but the patented technology can still be used for other drug therapies.

   This proposal permits the development of the patented invention for all uses other than the specific therapy approved by FDA. Under this proposal, enforcement of the patent would be difficult. A competitor could manufacture and sell the identical drug for a different therapy; the competitor's drug might then be prescribed and used for the patentee's therapy. The only remedy available to the patentee would be to sue each of the prescribers or users for patent infringement.

3. In the third proposal, the extension is provided only for those aspects of the claimed invention which involve the specific chemical contained in the drug approved by FDA, and enforcement is limited to the specific therapeutic use approved by FDA. Of the three proposals, this one provides the least protection to the patentee.

   This proposal permits others to develop the technology for all uses and allows others to make, use, or sell variations of the patentee's specific chemical for any drug therapy. Furthermore, others can make, use, and sell drugs using the patented technology and the patentee's specific chemical for any drug therapy but the one for which the patentee obtained FDA approval. Enforcement under this proposal is difficult for the same reasons that it is difficult in proposal 2.

Chapter 2

The Issue in Brief

Chapter 2

The Issue in Brief

INTRODUCTION

The U.S. Constitution vests in Congress the power "to promote the progress of science and the useful arts by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries" (art. I, sec. *8).* Since 1861, U.S. patent law has specified that these rights shall be secured for a period of 17 years, beginning at the time the patent is granted by the Government. The period during the patent term in which a product is sold (the effective patent term) is, however, usually shorter than 17 years because patents are generally obtained before discoveries are ready to be marketed.

Thus, although all patented inventions receive protection for the same amount of time, the effective patent terms for the inventions vary. The length of an effective patent term depends on the amount of time needed to bring an invention to market; this time is influenced by numerous factors including the availability of capital, the pace of product development, and the ease with which distribution channels can be established.

In recent years, Federal premarketing and premanufacturing regulations have also played a role in determining the effective patent terms for particular products. These products, which include pharmaceuticals, medical devices, food additives, color additives, chemicals, and pesticides, are governed by different regulations that have varying impacts on effective patent terms. Although there are some exceptions, most of these products cannot be marketed until they have been approved by the Federal Government. In some cases, such as pharmaceuticals, this approval is granted only after the product has undergone lengthy clinical testing and extensive review to ensure its safety and efficacy. Since the patent term keeps running during the testing and review period, the effective patent term for the regulated product is reduced.

To remedy this situation, legislation has been proposed that would extend the patent term for products affected by premarketing and premanufacturing regulations. As proposed, these extensions would provide compensation for the period of time spent on testing and review of the product but would not exceed 7 years.

The purposes of the proposed legislation are twofold: to provide equitable protection to products whose marketing is delayed by regulatory requirements and to encourage innovation in industries affected by these requirements.

This study focuses primarily on the implications of patent-term extension for innovation in the prescription drug industry. The subject of equity to the patent owner is discussed only briefly to provide the reader with a background understanding of the issue.

THE PATENT SYSTEM AND PHARMACEUTICAL INNOVATION

Why are changes in the patent system viewed as a mechanism for addressing concerns about pharmaceutical innovation? The answer to this question is rooted in the basic relationship between the patent system and innovation. As used in this report, innovation means the introduction into the market of something new and excludes discoveries that do not reach the market.

According to theory, the primary incentive provided to the patent owner (patentee) by a patent is the ability to prevent for a limited time competitors from selling products of the same

type as the invented product. If the market accepts the product, the patentee can enjoy an exclusive market position, which enables him to charge prices that are higher than those he could have charged if direct competition existed. The potential for obtaining these higher prices can justify the risks and expenses involved in innovative activities.

The patent system has many attributes as a mechanism for promoting innovation. The patent system does not directly involve the Government in research and development (R&D) activities and does not necessitate complex regulatory or oversight activities on the part of Government. Whatever rewards occur derive from the marketplace. Because the patent system has undergone few changes in its 200-year history, a change in patent policy, such as patent-term extension, would probably be regarded as permanent, whereas a new program to provide incentives for innovation might be viewed as a temporary measure and therefore provide little security to the industry.

The use of patents as an incentive for pharmaceutical innovation does, however, have some limitations. Not all inventions can meet the standards established for patentability. Furthermore, although patents are granted for products, process for making products, and methods for using products, product patents can be more readily enforced than the other types of patents and are, therefore, more meaningful. The patent system may provide little or no incentive for the R&D of drugs that would be beneficial to society but that cannot be meaningfully patented. Furthermore, patent incentives alone may be insufficient to encourage the R&D of drugs that have a potentially small market.

In reading this report, the reader is cautioned to remember that the patent system is only one of many mechanisms available to the Government for promoting innovation. Innovation could be encouraged by changes in tax policy, increases in governmental funding of R&D, alterations in the Food and Drug Administration's (FDA) approval procedures, and improvements in the general economic climate. This report does not address these other policy options for promoting innovation, nor compare them with the patent options.

THE LIFECYCLE OF A SUCCESSFUL NCE PHARMACEUTICAL

Before effective patent terms and innovation are examined, it is useful to have a basic understanding of the drug development process. For this reason a description of the lifecycle of a drug from the discovery of a new chemical entity (NCE) to the end of its marketing life is provided. This description is not intended to be representative of all innovative activity within the pharmaceutical industry; rather, it is presented so that the reader will have a framework for understanding later chapters.

Although important pharmaceutical innovations may result [rem new therapeutic applications of existing chemicals, new processes for making chemicals, or new combinations or formulations of existing chemicals, this study concentrates primarily on innovations resulting from the discovery or synthesis of NCEs. This approach is used for several reasons. Many of the pharmaceutical breakthroughs that have occurred have resulted from NCE research and the development of NCEs generally has required more time and money than other types of innovation and has involved greater risks. Moreover, because FDA testing requirements generally have been more time-consuming for NCEs than for other types of innovation, they have had their greatest impact on the effective patent terms of NCEs. By focusing on NCEs, the most extreme reductions in effective patent terms can be determined, but these effects are not representative of the average effects for all new pharmaceuticals.

The drug development process for NCEs is time-consuming and expensive and is characterized by a high probability of failure. A decade or more may elapse between the time a chemical having promising biological activity is identified

and the time it is marketed as a new drug. The odds against developing a marketable pharmaceutical are great: on the basis of historic trends, only 1 out of *7,000* to **10,000** newly synthesized chemicals will be found to have promising biological activity.[1] Only 1 out of 10 promising chemicals will survive to marketing.[2] Taking into account the R&D costs of chemicals that fail to reach the market, one investigator has estimated that discovery and development costs per marketed NCE are in the neighborhood of *$33* million **(1976** dollars).[3] This estimate applies only to NCEs discovered, developed, and marketed by the same firm and includes only direct costs.

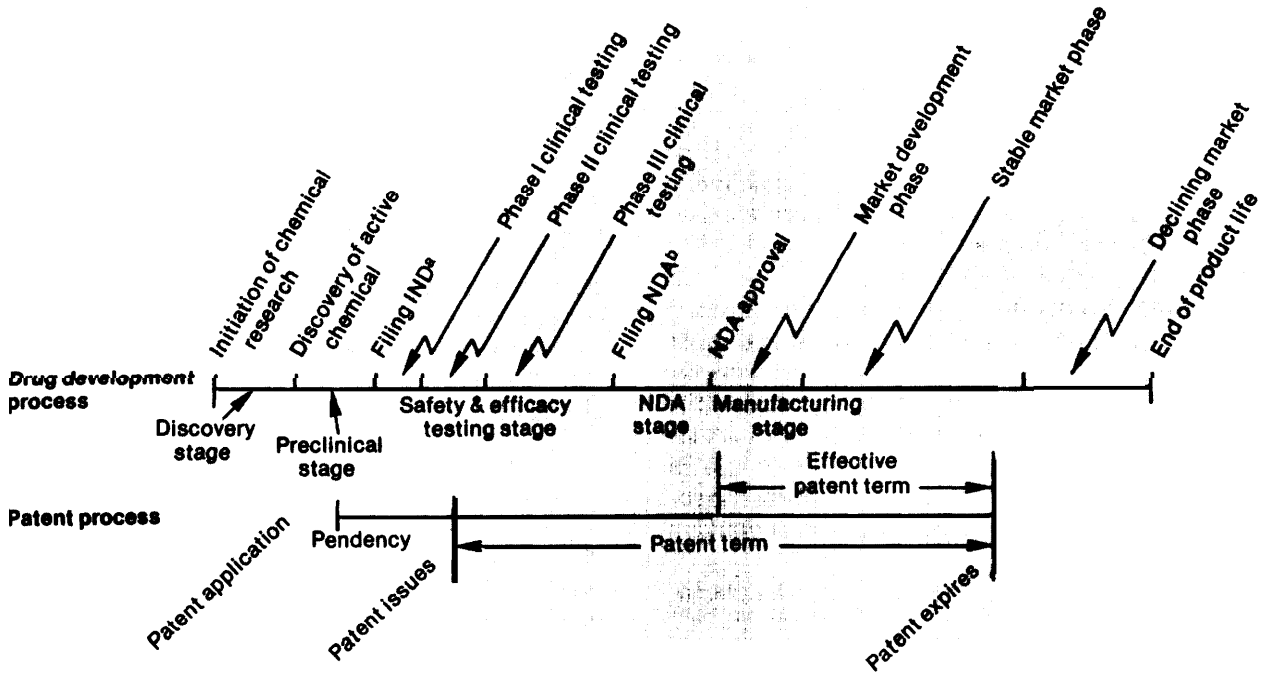
[1] William M. Wardell, "The History of Drug Discovery, Development and Regulation, " in *issues in Pharmaceutical Economics,* Robert I. Chien (cd.) (Lexington, Mass.: Lexington Books, 1979).

[2] Ibid.

[3] R. W. Hansen, "The Pharmaceutical Development Process: Estimates of Development Costs and Times and the Effects of Proposed Regulatory Changes, " in *Issues in Pharmaceutical Economics,* Robert 1. Chien (cd.) (Lexington, Mass.: Lexington Books, 1979).

Knowledge of the relationship between the drug development process and the patent process is essential for an understanding of the issues surrounding patent-term extension. Figure 1 shows the steps involved in both of these processes and indicates that these steps are taken concurrently. The patent process and the drug development process are, however, independent of each other and each progresses at it own pace. Although the figure accurately depicts the stages that a patented drug will pass through, the duration of each of the stages varies. Therefore, the relationship between the timing of the drug process and the timing of the patent process will also vary. A successful NCE must pass through five stages of the drug development process: the discovery phase, the preclinical stage, the safety and efficacy testing stage, the NDA (new drug application) stage, and the marketing stage. In most cases, the NCE will also be subjected to the patent process.

Figure 1.— The Drug Development Process and the Patent Process



[a]IND notice of claimed investigational exemption for a new drug
[b]NDA new drug application

SOURCE Off Ice of Technology Assessment

Drug Development—The Discovery Stage

The discovery stage involves the synthesis or isolation of new chemicals.[4] Initial screening tests are conducted to determine whether the new chemicals possess sufficient biological activity to be worthy of further investigation. This stage may be relatively short if the research is quickly fruitful. On the other hand, many years or even decades may pass before a suitable candidate is discovered.

Drug Development—The Preclinical Stage

Once a promising new chemical is identified, the preclinical stage begins. In this stage, the new chemical is tested in animals to determine its short-term toxicity. Results of these tests are studied carefully for indications that the chemical might not be safe to use in tests on humans, The preclinical stage generally lasts from 1 to 2 years.

Patent Process—The Application

Although the patent process is independent from the drug development process, in many cases a patent application for an NCE will be filed in the U.S. Patent and Trademark Office (Patent Office) when a drug is at the discovery or preclinical stage. Sufficient information exists at this time to prepare a patent application which fully complies with the patent laws. An early filing of a patent application is encouraged by the patent laws of the United States and most foreign countries, since when two or more investigators independently arrive at the same discovery, the investigator who first files a patent application generally has an advantage in obtaining the patent. Also, early filing is encouraged since a disclosure of the invention before the patent application is filed can bar a patent. (For clarification, see ch. 5.)

Several inventions may be made when an NCE is discovered and developed such as the chemical itself, the process for making the chemical, and the method for using the chemical to treat an illness. Separate patent applications could be filed on each of these inventions.

Drug Development—The Safety and Efficacy Testing Stage

The third stage of drug development involves clinical testing and long-term animal toxicity testing. These tests are conducted to satisfy the premarket approval requirements of FDA. These requirements that include the types of tests, the procedures to be used, and the standards to be met, may vary among therapeutic classes (groups of drugs used for similar purposes) and even among drugs for use within a therapeutic class.

The third stage begins when a request for authorization to begin human testing is filed with FDA. The request is termed a notice of claimed investigational exemption for a new drug (IND). Once authorization is received, the first of three clinical testing phases can be initiated. In phase I chemical testing, a small group of volunteers receive dosages of the investigational drug for a short period of time. The primary purpose of the phase I clinical testing is to look for evidence of toxicity or undesirable reactions. Phase I clinical testing can usually be conducted in less than 1 year. Only about one-half of the promising new chemicals identified in the discovery stage survive through phase I clinical testing.

Phase 11 clinical testing is similar to phase I testing, but more human subjects are used and the investigational drug is administered for a longer period of time. The primary purpose of phase II testing is to ascertain the effectiveness of the investigational drug. Phase 11 clinical testing may require about 2 years to complete.

Phase III clinical trials are conducted on a large scale; they often involve several hundred human subjects and are conducted for substan-

[4]For a more detailed discussion of the discovery stage, the preclinical stage, the safety and efficacy testing stage, and the NDA stage, see: R. W. Hansen, 'Pharmaceutical Development Process, " William Warden, "History of Drug Discovery, " and J. R. Virts and J. Fred Weston, "Expectations and the Allocation of Research and Development Resources, " in *Drugs and Health*, R. B. Helms (cd.) (Washington D. C.: American Enterprise Institute for Public Policy Research, 1980).

tial periods of time. These tests are designed to determine the efficacy of the investigational drug and to uncover any unanticipated side effects that the drug may have. Generally, phase 111 clinical trials last about 3 years.

While the phase III trials are underway, long-term animal toxicity studies are also conducted. The purpose of these studies is to determine the effects of prolonged exposure and the effects on subsequent generations, The duration of the studies and the animals used vary widely among therapeutic classes. For drugs that affect the reproduction system or that will be used over long periods of time, the animal toxicity studies will be expensive and of long duration.

Patent Process—Examination and Grant

If the patent application was filed during the discovery or preclinical stage, it is not unlikely that the patent will be issued during the safety and efficacy testing stage. Before a patent can be issued, a patent application is examined by the Patent Office to determine whether the invention is patentable (e. g., novel and not obvious in view of the state-of-the-art). If the invention meets these requirements, a patent is granted (issued) by the Patent Office. The average pendency of a patent application in the Patent Office is about 2 years; however, the pendency is subject to wide variations as will be discussed in chapter 5. If more than one patent application *were* filed in order to cover several inventions made during the discovery and development of a drug, these applications could issue as patents at different times.

Drug Development—The NDA Stage

Before **a** drug may be marketed, an NDA must be submitted to and approved by FDA. Frequently, the NDA is filed before phase III clinical tests and long-term animal toxicity tests are completed. However, all the safety and efficacy tests must be completed before FDA will approve an NDA. During the NDA stage, FDA may require additional clinical or animal tests to be conducted. The time required for processing an NDA depends on the completeness of the testing data, the performance of the drug, and the speed with which FDA reviews the data. In **1980,** the duration of the NDA phase (for NCEs) varied from about 1 to 7 years and averaged slightly less than 3 years. [5]

The NDA is approved by FDA for a specific drug that will be made by a specific process and used for a specific therapy. If the innovator wishes to change the composition of the drug or its manufacturing process or if he desires to sell the drug for a different therapy, he must file a supplemental NDA and obtain FDA approval for these changes.

Drug Development—The Marketing Stage

By the time the NDA is approved, part of the patent term usually has expired. The remaining patent term may be the only time that the drug has an exclusive market position.

The marketing stage is usually characterized by three periods: the market-development stage, the stable-market stage, and the declining-market stage. In the market-development stage, the demand for the new drug increases. In the stable-market period, the demand for the drug is relatively steady. Later, the market for the drug declines as new and better therapies and drugs are discovered, and eventually the manufacturer takes the drug off the market. Depending on the length of the effective patent term and the product lifecycle, the patent may expire during the market-development stage, the stable-market stage, the declining-market stage, or after the product has been removed from the market. Once the patent has expired, others can manufacture and sell the drug if they have secured premarket approval from FDA. The approval procedure for generically equivalent drugs is discussed in chapter 3.

[5]Departmen t of Health and Human Services, *New Drug Evaluation Project. Briefing Book* (Washington, D. C.: Food and Drug Administration, Bureau of Drugs, 1980).

AN OVERVIEW OF THE PHARMACEUTICAL INDUSTRY

Pharmaceutical innovation has resulted primarily from the activities of private industry. Of the new drugs introduced in the United States between 1960 and 1969, 91 percent were discovered and developed by the industry. [b] Government, nonprofit research organizations, and universities were responsible for the remainder of the new drugs. Because the public relies so heavily on the industry for improvements in drug therapy, efforts to increase innovation must be based on a thorough knowledge of how the industry operates.

Throughout the past four decades, pharmaceutical sales have increased steadily, with the greatest growth occurring in the sales of ethical drugs (products prescribed by health care professionals). The **1978** sales revenues (wholesale) for ethical drugs were approximately $9.5 billion. Total U.S. expenditures for health care were **$192** billion of which **$15** billion or 7.9 percent were for drugs and medical sundries.[7] Although drug expenditures have increased dramatically over the past decade, they have increased much less rapidly than total health care expenditures.

Since the 1950's, the U.S. pharmaceutical industry has been considered one of the most profitable of all major manufacturing industries. As shown in table 1, the industry's after-tax rate of return on average stockholder's equity has remained stable at a relatively high level and has exceeded the average after-tax rate of return for all manufacturing.[8]

Table 1.—After-Tax Rates of Return on Average Stockholders' Equity 1956-79 (in percentages)

Year	Pharmaceutical industry	All manufacturing	Year	Pharmaceutical industry	All manufacturing
1956	17.6	12.3	1969	18.4	11.5
1957	18.6	11.0	1970	17.6	
1958	17.7	8.6	1971	17.8	9.7
1959	17.8	10.4	1972	18.6	10.6
1960	16.8	9.2	1973	18.9	12.8
1961	16.7		1974	18.7	14.9
1962	16.8	9.8	1975	17,7	11.6
1963	16.8	10.5	1976	18.0	13.9
1964	18.2	11.6	1977	18.2	14.2
1965	20.3	13.0	1978	18.8	15.0
1966	20.3	13.4	1979	19.3a	16.4
1967	18.7	11.7	1980 (1st 3 quarters)	20.8	13.9
1968	18.3	12.1			

[a] Industrial classifications were changed The percentage of companies reclassified in the drug Industry is unknown

Note For the purpose of this table, the pharmaceutical industry is defined as corporations primarily engaged in manufacturing biologicals, inorganic and organic medicinal chemicals, pharmaceutical preparations, and grading, grinding, and milling of botanicals

SOURCE: Quarterly Financial Reports, U S Federal Trade Commission

The Industry Members

In 1979 the Federal Trade Commission staff estimated that the U.S. pharmaceutical industry consisted of *1,300* Firms, of which about *750* produced prescription drugs. ' The prescription drugmakers generally fall into two categories: 1) firms specializing in branded drugs (including patented and generically equivalent drugs), and 2) smaller firms specializing in nonbranded generically equivalent drugs. Throughout this report, firms in the first of these categories are referred to as research-intensive companies and firms in the latter category are referred to as production-intensive companies.

It should be noted that the line between research- and production-intensive firms cannot be easily drawn. Many research-intensive firms produce generically equivalent drugs as well as their own patented branded drugs. Both research- and production-intensive firms manufacture pharmaceuticals for each other, and both may purchase the active chemicals that they use in their products from other firms. In

"Federal Trade Commision, "Drug Product Selection," Washington, D. C., 1979 (staff report to FTC).

[7] U.S. Department of Health, Education, and Welfare, *Health United States—1979*, HEW publication No. (PHS) *80-1232* (Hyattsville, Md.: Public Health Services *1980*, Office of Health, Research, Statistics, and Technology).

"The rates of return shown in table 1 were determined using an accounting procedure that treats R&D expense as current expenditures rather than capital investments. Regardless of the accounting procedure employed, the rate of return for the pharmaceutical industry is higher than that for all manufacturing. For further discussion see: Kenneth Clarkson, *Intangible Capital and Rates of Return* (Washington, D. C.: American Enterprise Institute, *1977)*, p. *64.*

'Federal Trade Commission, "Drug Product Selection, " op. cit.

some instances production-intensive firms, such as Generics Corp. of America, Biocraft Laboratories, and Philips-Roxane Laboratories, Inc., have engaged in NCE research.

Among the research-intensive firms, the size, type, and scope of research activities vary considerably. Based on these activities, research-intensive firms can be divided into three rough groupings:

1. *The large multinational companies.* — These firms account for the dominant share of pharmaceutical R&D expenditures. About a dozen domestic companies fall into this class, including Eli Lilly, Merck, SmithKline, Upjohn, and Pfizer. Together, the companies account for over one-half of U.S. ethical drug sales and well over two-thirds of the private- pharmaceutical research in the United States.
2. The *midsized companies,* —These firms are primarily domestic, have research programs of a much smaller scale, and account for about one-quarter of the U.S. ethical drug sales. Included within this group are A. H. Robins and Richardson Merrell (Merrell National Division was recently purchased by Dow).
3. *The small research companies.* —These firms often conduct research in a limited therapeutic area. Firms, such as Marion Laboratories, that license drug technology and develop drugs for marketing in the United States also fall in this class.

In **1978, 24** firms had U.S. prescription drug sales that exceeded $100 million.[10] Foreign-based firms, such as Roche and Ciba Geigy, accounted for at least **25** percent of the firms in this group. In recent years foreign-based firms have increased their share of the U.S. market, but these efforts by foreign firms are not surprising since the United States represents the largest single market for pharmaceuticals.

In terms of worldwide sales, 10 of the **20** largest multinational pharmaceutical firms are based in the United States. U.S.-based firms and their affiliates account for more than 30 percent of total world sales .1' Pharmaceutical R&D of U.S.-headquartered firms is, however, increasingly being carried out in other countries, which may have less stringent controls on R&D activities than our own. In **1978,** more than $220 million was spent for R&D conducted by U.S. firms in foreign countries. *[2]

In contrast with the research-intensive firms, about 600 production-intensive companies derive revenues primarily from the sale of nonpatented products marketed under the generic name of the drug, rather than under a trademarked brand name.[13] Consequently, these companies are often referred to as generic companies. Most of these companies have sales amounting to less than $10 million per year. They usually sell within limited territorial areas and together account for only about 15 to 20 percent of the sales of drugs available from more than one firm. *[4] Because these firms generally do not engage in research or heavy drug promotion, the price of their products need not reflect such expenditures. Furthermore, the markup on these products may be lower. Therefore, production-intensive firms frequently sell drugs at prices that are considerably lower than the prices charged by innovator firms. Although some of these firms do engage in R&D activities for the purpose of formulating and compounding existing drugs to improve their activity and benefit to the patient, they generally do not direct their research activities toward finding NCEs.

The sales of U.S. production-intensive firms are generally exclusively domestic. Many production-intensive firms purchase drugs from foreign manufacturers.

In recent years, the market for generic drugs has been increased by some Government actions. For example, many States now allow or require pharmacists to fill prescriptions for

"'Henry Grabowski and John Vernon, "Government Policy and Innovation in the Pharmaceutical Industry, " draft report (Durham, N. C.: Duke University, 1980).

[1] 'Private communication with Henry Grabowskion July 3, 1981.

''Charles River Associates, "The Effects of Patent Term Restoration on the Pharmaceutical Industry, " Boston, Mass., May *4, 1981* (report to OTA).

[13]Federal Trade Commission, "Drug Product Selection, " op. cit.

[14]Ibid.

brand-named drugs with generically equivalent drugs. Under medicaid, reimbursements to pharmacists are limited to the cost of the lowest priced drug among; generic equivalents plus a dispensing fee. The FDA approval procedure for drugs that are generically equivalent to existing drugs has also undergone changes favorable for generic competition. FDA plans to reinstate its "paper NDA" procedure in which published data of reliable safety and efficacy tests will be accepted in lieu of actual tests conducted by the second entrant. Also, in *1970,* FDA adopted an abbreviated NDA (ANDA) procedure for certain drugs approved prior to the **1962** amendments to the drug regulation law. Under the ANDA procedure some drugs are able to obtain premarket approval without the submission of safety and efficacy data.

The Market for New Drugs

Industry undertakes R&D in areas that it believes will be profitable. The size of the potential market plays an important role in the selection of these areas. Two factors that influence the market size for any particular new drug are the number of people suffering from the ailment treated by the drug and the advantage the drug provides **as** compared with other drugs for the same ailment.

For an ailment that is relatively uncommon, the potential market may be so small that any drug, regardless of its therapeutic value, will have little chance of financial success. On the other hand, drugs offering significant or moderate therapeutic advantages to a large number of potential users will generally be financially successful because their advantages will enable the drugs to capture significant market shares. Even drugs that offer little or no therapeutic advantage to most users may be commercially attractive in a large market. Because physicians, rather than consumers generally determine the financial success of a drug, the creation of markets involves a great deal of advertising directed at physicians. On occasion, these marketing strategies can create a large market for a drug that offers only minimal advantages. 's

Drugs are frequently divided into categories according to the types of ailments they are designed to treat. The market share of different therapeutic categories varies over time, but in **1978,** sales of drugs directed at central nervous system disorders were *23,6* percent of total U.S. ethical drug sales; sales of anti-infectives were 15 percent. [16]

Drugs that obtain major shares of the market can meet with extraordinary success. Table 2 shows a ranking of the top eight prescription pharmaceuticals in the United States by sales in *1980.* Although the sales figures have not been confirmed, they provide a relative indication of total sales.

The sales figures for the most successful drugs give little indication of average sales. In a study of a group of 119 NCE pharmaceuticals introduced in the United States between *1967* and

[15] Ronald Bond and David Lean, "Sales Promotion, and Product Differentiation in Two Prescription Drug Markets, " Washington, D. C., 1977 (staff report to the Federal Trade Commission.)
[16] Charles River Associates, op. cit.

Table 2.—Sales Ranking of the Top U.S. Pharmaceuticals in 1980[a]

Drug (trade name)	Therapy	Manufacturer	U.S. sales (in millions of dollars)
Tagamet	Duodenal ulcers	Smith Kline	$250
Valium	Antianxiety	Roche	$230
Inderal	Antiarrhythmic	Am. Home Pdts. (Ayerst)	$200
Motrin	Antiarthritic	Upjohn	$150
Aldomet	Hypertension	Smith Kline	$145
Dyazide (dyrenium)	Hypertension	SmithKline	$145
Keflex	Antibiotic	Lilly	$140
Clinoril	Antiarthritic	Merck	$125

[a] By revenues.

SOURCE: *New York Trees,* Sunday, May 17, 1981, quoting Oppenheimer and Co.

1976, the sales data (wholesale) were collected for the years during which the drugs were sold. Sales figures for products which were sold for less than 10 years were projected on the basis of historical trends. The top **25** percent of the new drugs had average annual sales of $21.1 million, and the lower 75 percent had average annual sales of $2.3 million. 17 By doubling these figures, one can approximate their value in *1980* dollars.

There are two important points that are not portrayed by the simple sales average. First is the extraordinary range of sales revenues for different drugs. Second is the large percentage of sales, attributable to a small percentage of drugs. According to the study cited in the previous paragraph, **25** percent of the drugs on the market accounted for about **90** percent of sales revenues. These figures suggest that there is a very large difference between the market shares and earning power of the few top drugs and the great majority of drugs. Throughout this study, drugs that have sales of more than $75 million per year will be termed high-income drugs.

Purchasers of Drugs in the United States

In the United States, ethical drugs are purchased by patients, Government agencies, and by pharmacists and hospitals (which resell them to patients). In *1979, 53* percent of manufacturers' sales were made to wholesalers (who distributed mostly to retail pharmacies), *22.5* percent were sold directly to retailers, 14.9 percent to private hospitals, 6.3 percent to Government (including State and local government hospitals), 1.4 percent to other Federal Government agencies, and 1.2 percent directly to physicians. 18

The users of drugs do not necessarily reflect the population as a whole. People over *65,* who are generally on fixed and limited incomes, constitute 11 percent of the population but make *25* percent of all drug purchases. Similarly, persons with chronic diseases such as arthritis, angina, or epilepsy, will have above average health expenditures, but, because of their ailments, may have below-average earnings.

Although third-party payments (Government, philanthropy, industry, and private health insurance) constituted about two-thirds of the payments for personal health care in 1978, only about 16 percent of the payments for drugs and medical sundries in 1979 were covered by insurance or by Government reimbursement programs. 20

[17] Virtsand Weston, op. cit.

[18] Pharmaceutical Manufacturers Association, "20th Annual Survey Report," Washington, D. C., 1980.

[19] The Office of Technology Assessment Workshop on Mar. 24, 1981, American Association of Retired Persons.

[20] Freeland and Schendler, "National Health Expenditures: Short-Term Outlook and Long-Term Projection," *Health Care Financing Review (winter* 1981).

THE ISSUE OF EQUITY

A major argument for patent-term extension is that it is unfair that products subject to premarketing regulations have shorter effective patent terms than products that are unregulated. The point is made by proponents of patent-term extension that industries required to act in a socially beneficial manner should not be penalized for their actions.

On the basis of this argument, it would appear that the patent period should be extended purely as a matter of equity. Undoubtedly if patent-term extension involved no costs to anyone, there would be little disagreement that regulated products deserve extensions. But there are costs and there are disagreements.

Critics of the extension argue that what is equitable for the larger pharmaceutical firms may not be equitable for society. They urge that the issue of patent extension not be decided solely on the basis of equitable treatment to the large manufacturers but also on the basis of the social costs and benefits that will result from the extension.

Although this report focuses on the innovation issue, nonetheless, it is useful to have some understanding of both the nature and extent of any inequities that may exist.

The Nature and Extent of the Inequity

There is concern that industries subject to premarketing regulations are not receiving equitable treatment from the Government. The extent of the inequity is often equated with the extent to which premarketing regulations delay commercialization of the product. However, by issuing a patent, the Government grants the patentee the right to exclude others from making, using, or selling the invention; it does not grant the patentee the right to sell, use, or market the invention himself. Thus, even when a patentee is awaiting premarketing approval, his patent rights are exactly the same as the rights of patentees who are not required to seek premarketing approval.

However, the research-intensive firms do not believe that the inequity derives from their patent rights, but rather from the marketing delays caused by FDA regulations. Estimates of delays caused by FDA are based on the average duration of the FDA approval process. One study found that, on average, NDA approval for a patented NCE was granted *6* to *9* years after an IND had been filed.[21] As seen earlier, however, few products are ready for commercialization at the time an IND is filed. Thus, that portion of the FDA review period that would, even without FDA regulations, be used for testing and development cannot fairly be included in the FDA-induced marketing delay. Although the actual marketing delays attributable to FDA (e. g., through regulatory proceedings, testing procedures, and performance standards) are not precisely known, one can conclude that, in most cases, the delays are less than the *6* to 9 years consumed by the drug approval process.

Whether these delays actually result in an inequity is probably best determined by a comparison of the average effective patent terms for pharmaceuticals and the average for all products.

According to a study of patented NCE drugs receiving NDA aproval, the average effective patent term for drugs approved in 1979 was less than 10 years .22 Unfortunately, there are no figures for the average effective patent terms for all products, but a rough estimate can be made, based on data on average lag time (the time that elapses between the discovery and marketing of a product). One study showed that the average lag time for **319** significant innovations originating in the United States and introduced between 1953 and 1973, was about 7 years.[23] If it is assumed that in most instances the time between the conception of the invention and the granting of the patent was about 4 years, it can be hypothesized that the average product was not marketed for 3 years of its patent life and that the average effective patent life was, therefore, probably greater than 13 years but less than 17 years. Based on these calculations, the conclusion can be drawn that the average effective patent term for significant innovations in general is probably 3 to 7 years longer than the average term for NCE pharmaceuticals.

This differential in the effective patent terms of pharmaceuticals and other products has led many to believe the extension should be provided, purely as a matter of equity. Others point out that marketing of products is delayed by many types of Government regulations, such as those governing zoning permits or environmental impact statements and that the Government cannot possibly guarantee equitable treatment to all industries at all times.

Because of the time value of money, the revenues generated during an extension that was equal to the actual delay caused by the FDA approval process would not fully compensate firms for the revenues lost during the period that marketing was delayed .24

[21] Charles River Associates, op. cit., p. 3-2.

[22] M. Eisman and W. Wardell. "The Decline in Effective patent Life of New Drugs," *Research Management*, January 1981.

[23] Gellman Research Associates, "Indicators of International Trends in Technological Innovation," Jenkintown, Pa., April *1976* (final report to the National Science Foundation).

[24] Private communication with Henry Grabowski on Mar. 24, 1981.

THE POSITIONS OF THE PARTIES INTERESTED IN PATENT-TERM EXTENSION

Legislation to extend patent terms has been proposed and supported by the research-intensive firms. They argue that the FDA premarket approval procedure for new drugs has inequitably and unintentionally shortened the effective patent lives of pharmaceutical products. These firms further contend that the costs of pharmaceutical R&D have been escalating rapidly, effective patent lives have been declining, and the rates of return to pharmaceutical R&D expenditures are becoming unattractive. They point out that the ratio of R&D funding (deflated by the NIH biomedical deflator index for research costs) to total sales (deflated by the producer price index for ethical pharmaceuticals, Bureau of Labor Statistics) has declined by over *35* percent from **1963** to **1979.** They express concern that incentives for R&D are eroding at the very time that advances in science have created the possibility of major improvements in drug therapy. In view of these trends, they contend that the rate of R&D investment will be insufficient for the rapid transition of scientific advances. In such circumstances, they believe that the user of drugs, and not necessarily the pharmaceutical industry, will be the loser.

Some research-intensive firms argue that the present trends have driven many companies away from pharmaceutical R&D and diminished the commitment of others. Many research-intensive companies have shifted R&D expenditures away from self-originated NCEs and towards new delivery systems for existing products because FDA approval can be obtained if companies demonstrate that the potency of the new product is equal to or better than the potency of the existing product. Some of these firms have increased their licensing of NCEs from others and suggest that this increase indicates that basic research is being viewed with increased caution.

It is the thesis of the research-intensive firms that patent-term extension will raise the expected profitability of drug research. It will therefore offset current pressures on decision-makers to reduce the size of their research project portfolio and provide a positive incentive for undertaking research activities. These activities, in turn, would increase the rate of innovation.

The research-intensive companies welcome an analysis of patent-term extension from an overall health-care perspective. They point out that innovative drugs save lives, reduce pain and suffering, and provide substantial health-care savings. Examples cited include an $11 pneumococcal pneumonia vaccine that can prevent a *$3,300* treatment of the disease; a 22¢ per day glaucoma drug that saves *$590* in surgery costs as well as hospitalization costs; and a rubella vaccine that for *$25* million in costs has been estimated to provide a net savings to society of more than $1 billion. They believe that patent-term extension will provide drugs that offer better and less expensive health care, and that it will result in the introduction of more innovative drugs. They contend that the additional drugs will increase the competition among patented drugs and cause a downward price pressure on patented drugs with a resulting savings to the consumer .25

The production-intensive firms believe that patent-term extension will delay their entry into the market and that they will be economically penalized for each year that the extension prevents them from marketing a drug. They further contend that the market for some drugs may have declined to such a degree during the extension that their entry into the market will not be economically feasible. They point out that they play an important role in providing low-cost pharmaceuticals to consumers.

The concerns of the production-intensive companies are that patent-term extension will increase the ability of research-intensive firms to

[25]The research.intensive firms' positions have been gathered from private communications from the Pharmaceutical Manufacturers Association, May *1981* and July *1981:* private communication from Lewis Sarett, Vice President of Merck and Co., May 1981: testimony of L. Engman, President of the Pharmaceutical Manufacturer's Association before the House Subcommittee on Health and Environment of the Committee on Energy and Commerce, Apr. 1, 1981, and before the Senate Committee on the Judiciary, Apr. 30, 1981,

achieve overall effective patent terms that exceed 17 years if these firms secure more than one patent on a product. They are also concerned that nonpatent barriers to acceptance of their products will prevent them from successfully competing against products whose patents have expired. They believe that a national formulary that listed the generic and therapeutic equivalency of drugs would encourage use of their products. They also believe that if the FDA premarketing requirements for generic equivalents of drugs coming off patent were simplified, more generically equivalent drugs would be marketed. From the point of view of the generic firms, one of the greatest barriers to market acceptance of their products has been court decisions inhibiting their use of the size, shape, and color of drugs whose patents have expired.

The production-intensive firms see the need to provide an equitable, effective patent term to innovator firms in certain situations in which the combined period of protection from all patents on the drug during marketing is significantly less than 17 years due to excessive regulatory delay. They do not believe that it is desirable for the pharmaceutical industry to have longer patent terms than other industries. Nor do they believe that extensions should compensate for time spent on testing that would have been conducted by the innovator firm whether or not FDA premarket regulations existed. Furthermore, production-intensive firms believe that efforts should be directed toward making regulatory proceedings more efficient in order to increase effective patent terms. They believe that any legislation to extend patent terms should not weaken their market position and that such legislation should eliminate the nonpatent barriers that can prevent them from successfully competing against products whose patents have expired.[26]

Spokesmen for consumer interest groups believe that patent-term extension will result in higher drug prices without providing better health care. They point out that increased drug costs will fall disproportionately on the elderly and the chronically ill (whose incomes tend to be lower than average).

The spokesmen argue that the pharmaceutical industry is extremely profitable and needs no additional incentive to conduct research. These groups are concerned that the legislation proposed to date provides no guarantees that additional revenues derived from patent-term extensions will be invested in R&D activities. There is concern that patent-term extension may encourage less R&D because market exclusivity will be assured for a longer period of time.

Concerns are also expressed by spokesmen that expenditures made for R&D may not be directed toward research areas that provide the greatest benefit to society. A central concern is the degree to which patent-term extension will encourage minor innovations having only nominal therapeutic importance rather than major pharmaceutical advances.

Therefore, many consumer spokesmen oppose patent-term extension,[27]

[26] The production-intensive firms' positions have been gathered from private communications from Kenneth Larson, President of Zenith Laboratories, April 1981, and July 1981; Mr. William Haddad, member of the board of the Generic Pharmaceutical Industry Association, April 1981, June 1981, and July 1981; and Mr. James Flug, counsel for the Generic Pharmaceutical Association, July 1981, and the testimony of Larson and Haddad before the Senate Committee on the Judiciary, Apr. 30, 1981.

[27] The consumer interest groups' positions have been gathered from private communication from Fred Wegner, pharmaceutical specialist, National Retired Teachers Association and American Association of Retired Persons, June 1981; and Sidney Wolfe, Director, and Benjamin Gordon, Staff Economist, Public Citizen, Health Research Group, July 1981; the testimony of Wolfe and Gordon before the Senate Committee on the Judiciary, Apr. *30, 1981;* and statements by Marcia Greenberger, attorney, Center for Law and Social Policy, during the OTA workshop on patent-term restoration, Mar. *24, 1981,*

Chapter 3

Factors Affecting Innovation in the Pharmaceutical Industry

Chapter 3

Factors Affecting Innovation in the Pharmaceutical Industry

Innovation in the pharmaceutical industry is dependent on many factors including scientific knowledge, profit levels, research and development (R&D) expenditures, and expected returns to research investment. Clearly these factors are interactive and dependent on decisions made in the private sector. Government action can, however, affect these factors and thereby increase or decrease the likelihood that innovation will occur.

in this chapter, trends in both pharmaceutical innovation and the determinants of innovation are examined so that the effects of patent-term extension on innovation may be assessed in chapter 4.

DECISIONMAKING IN THE INDUSTRY

Before examining any of these trends, some characteristics of decisionmaking in the industry will be noted briefIy, for, no matter what the actual trends, it is how the trends are perceived in the decisionmaking process that determines R&D activities. If decisionmakers foresee declines in the returns to research investment, they will invest less and innovation levels may decline. The decline, however, would not be noticeable for several years because of the time that elapses between research discoveries and product marketing. Decisions made today, therefore, will affect the supply of drugs over the next 10 to **15** years.

The current decisionmaking environment for pharmaceutical innovation has been compared to the "gamblers ruin" problem, in which investment is made with an uncertain distribution of returns, and the objective of the investor is to win often enough to avoid experiencing severe cash-flow difficulties in the interim. No matter how high the return to investment, a firm that experiences a sufficient number of research failures in a row will not have adequate capital to hold out for the eventual "big win. " In an environment of increasingly uncertain returns to pharmaceutical research, only firms with R&D budgets that are large enough to fund several projects at a time can survive the periods of little return and achieve eventual success.[1]

Because of the nature of pharmaceutical research, the characteristics of the decisionmaking process can be very important. One study notes that scientists have less control over research activities than they did in the 1960's and that the decisionmaking process has become more financially oriented. [2]

As a result, research projects undertaken today may receive closer scrutiny than in the past, and assessments of the likelihood of financial and therapeutic success may become more important in corporate decisionmaking. However, the decisionmaker's expectations for different projects may vary, and different *firms will* perceive the market in different ways.

'Thomas R. Stauffer, "Discovery Risk, Profitability Performance, and Survival Risk in a Pharmaceutical Firm, " in *Regulation, Economies, and Pharmaceutical Innovation,* Joseph Cooper (cd.) (Washington, DC.: The American University, 1976), pp. 93-122.

'Steven N. Wiggens, "The Pharmaceutical Research and Development Decision Process, " *Drugs and Health (Washington,* D. C.: American Enterprise Institute for Public Policy Research, *1980).*

TRENDS IN PHARMACEUTICAL INNOVATION

Pharmaceutical innovation is usually measured by the number of new chemical entities (NCEs) introduced, Although this information can be obtained easily, it fails to reflect innovations resulting from new formulations, new combinations of active ingredients, or new uses for existing drugs. Of the 1,916 notices of claimed investigational exemption for a new drug (INDs) pending at the Food and Drug Administration (FDA) on October 1, 1980, only 43.4 percent were for NCEs. Of the 209 candidates judged by FDA to offer important therapeutic gains, 86 were not NCEs. Thus, NCE introductions provide an incomplete measure of innovation and one that gives no weight to differences in therapeutic value.

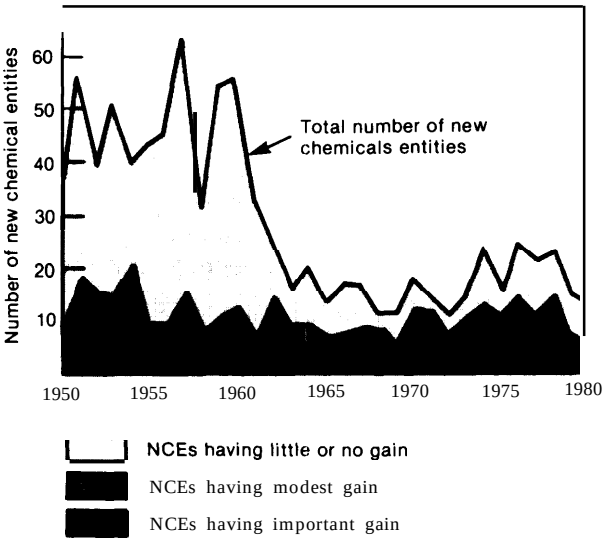
Figure 2 depicts the number of NCEs approved by FDA over the last 30 years, along with FDA's judgments on their therapeutic value. Although the criteria used for assessing the value of the innovations have been subjective and have varied over time, FDA's judgments can provide some perspective on the trends in NCE introductions.

Although the total number of NCEs approved by FDA has dropped significantly since 1950, the number of NCEs approved since 1963 has remained relatively constant. The bulk of the decline in FDA approvals occurred in the early 1960's and involved NCEs considered to offer little or no therapeutic gain. This decline may have been the result of the more stringent FDA drug approval process adopted in 1962. The FDA data indicate that approvals of NCEs offering important or modest therapeutic gain have remained relatively stable.

Trends in innovation have also been measured by NCE sales as a percentage of total ethical drug sales. By this measure, innovation is declining. NCE sales accounted for *20* percent of total sales in 1957 to 1961, 8.6 percent in 1962 to 1966, and 6.2 percent in *1972* to *1976*.[3] Actual sales of NCEs have, however, grown since 1962 because total sales have grown,

Thus, interpretations of trends in innovation depend on the measures used and the time period being measured, but, by most measures, innovation does not appear to be increasing.

Figure 2.—Annual Approvals of New Chemical Entities Reflecting FDA's Judgment of Therapeutic Potential



SOURCE: Testimony of J. Richard Crout before the Subcommittee on Health and the Environment of the House Committee on Energy and Commerce. April 1, 1981.

[3] Henry Grabowski and John Vernon, "Government Policy and Innovation in the Pharmaceutical Industry," draft report (Durham, N. C.: Duke University, 1980).

THE KNOWLEDGE BASE

New drugs will not be developed unless scientific progress is made. Advances in the understanding of drug therapy and the physiological interactions in the body, along with advances in molecular biology, have opened up important frontiers in pharmaceutical innovation. Technological advances have improved pharmaceutical research techniques for identifying the

types of chemicals that should be synthesized for biological testing, and screening tests have been developed to determine whether a chemical has a good probability of being safe and efficacious.

As the therapy provided by drugs continues to improve, new pharmaceuticals will, however, have to meet tougher standards. Furthermore, as testing procedures become more sophisticated, more drug candidates will be rejected earlier because problems will be detected sooner.

FACTORS AFFECTING RETURNS TO RESEARCH INVESTMENT

The anticipated rate of return is believed to play a major role in the pharmaceutical industry's decisions to invest in innovative activities.

Several studies have indicated that the rates of return to research investment have declined significantly over the last two decades.[4] The assumptions made in these studies about costs, product lives, and profit margins have, however, been questioned.[5] Because of the unavoidable uncertainties involved with assumptions which must be made to project rates of return, this report focuses on the underlying factors affecting returns to research investment.

The major determinants of returns to research investment are the costs involved in R&D activities, the levels of R&D expenditures, and the revenues and profits of the industry. These factors are not only interrelated but are also dependent on other influences. The costs of R&D are controlled by inflation, regulatory actions, and technological advance. R&D expenditures are influenced by current revenues of the firm, by rates of returns, and by the decisionmaker's expectations for the future. Revenues are determined by prices and the quantities sold which, in turn, are determined by market demand, patent protection, and the number and types of competitors.

In the following discussion, the conclusions drawn pertain to the industry as a whole; but the reader is reminded that R&D costs, prices, sales volume, and profits vary among pharmaceutical products. Most companies are dependent on a few high-income drugs for substantial portions of their revenues. Table 3 provides the sales of the three leading products of selected manufacturers as a percentage of the manufacturers total sales. The effect of the determinants on these high-income drugs may be of particular concern to the pharmaceutical industry.

Table 3.—Percentage of Corporate Pharmaceutical Sales Accounted for by Three Leading Products[a]

	1970	1975	1979
Abbot	36	33	28
American Home Products:			
Ayerst	64	74	84
Wyeth	37	44	43
Bristol-Meyers:			
Bristol	69	46	28
Mead-Johnson	40	38	37
Burroughs-Wellcome	NA	56	51
Ciba	47	NA	55
Lederle	48	31	32
Lilly	46	60	43
Merck	35	44	44
Pfizer	52	65	65
Robins	43	45	46
Roche	80	80	70
Searle	45	49	44
Shering	42	48	40
SmithKline	44	42	66
Squibb	28	31	23
Upjohn	47	50	56
Warner- Lambert:			
Warner	53	NA	NA
Parke-Davis	25	27	22

NA = not available
[a]U S sales

SOURCE: Charles River Associates, Inc, "The Effects of Patent-Term Restoration on the Pharmaceutical Industry, " a report to OTA, May 4, 1981.

[4]Charles River Associates, Inc., "The Effects of Patent Term Restoration on the Pharmaceutical Industry, " prepared for OTA, May 4, 1981, pp. 4-1 to 4-3.

[5]Ibid.

TRENDS IN REVENUES AND PROFITS

The revenues and profits of the industry have direct bearing on the amount of funds available for R&D activities. As seen in chapter 2, profits in the pharmaceutical industry have been relatively stable. As shown in table 4, the revenues of U.S.-based firms from the sales of ethical pharmaceuticals have grown significantly since *1965*, even on a constant-dollar basis. Real growth has occurred in both foreign and domestic sales.

As shown in table 5, the relationship between revenues and R&D expenditures in the U.S. pharmaceutical industry has also been stable. For the years 1965 through 1978, research expenditures ranged between 8.2 and 8.8 percent of total sales. The stability of this relationship suggests that trends in revenues may be a good indicator of trends in R&D expenditures.

Table 4.–Sales of Pharmaceutical Products of U.S. Based Firms 1965-78

Year	Total domestic and foreign sales (millions)	Deflator	Deflated sales (millions)	Real growth in sales (percent)
1965	$ 3,939	103.2	$ 3,817	Base year
1966	4,340	102.6	4,230	10.8%
1967	4,744	100.0	4,744	12.2
1968	5,302	99.0	5,356	12.9
1969	5,837	99.5	5,866	9.5
1970	6,425	99.3	6,470	10.3
1971	7,009	99.0	7,080	9.4
1972	7,739	99.1	7,809	10.3
1973	8,722	99.9	8,731	11.8
1974	9,956	104.2	9,555	9.4
1975	11,554	113.2	10,207	6.8
1976	12,775	120.3	10,619	4.0
1977	13,838	125.4	11,035	3.9
1978	15,978	131.9	12,114	9.8

SOURCE: Derived from Pharmaceutical Manufacturers Association-OPA, April 1981, using BLS, producer price deflator for pharmaceuticals

Table 5.—Research and Development Expenditures and Sales Revenues of U.S. Ethical Drug Industry (1965-78)'

Year	Domestic sales total	Foreign sales (including exports) total	Domestic R&D current dollars (millions)	Foreign R&D current dollars (millions)	Ratio of R&D to sales in current dollars[b] (percent)
1965	$2,940	$ 999	$ 304.1	$ 24.5	8.30/o
1966	3,178	1,162	344.2	30.2	8.6
1967	3,393	1,351	377.9	34.5	8.7
1968	3,808	1,494	410.4	39.1	8.5
1969	4,135	1,702	464.1	41.7	8.7
1970	4,444	1,981	518.6	47.2	8.8
1971 , ...	4,796	2,213	576.5	52.3	8.6
1972	5,136	2,603	600.7	66.1	8.6
1973	5,644	3,078	643.8	108.7	8.6
1974	6,273	3,683	726.0	132.5	8.6
1975	7,086	4,468	828.6	144.9	8.4
1976	7,867	4,908	902.9	164.9	8.4
1977	8,434	5,404	984.1	197.7	8.5
1978	9,411	6,567	1,089.2	222.0	8.2

[a] Veterinary-use pharmaceutical research and development is excluded for the years 1965 through 1974.
[b] Globalpharmaceutical R&D and sates of U.S firms.

SOURCES Henry Grabowski and John Vernon, "Government Policy and Innovation in the Pharmaceutical Industry, " draft report, November 1980, and Pharmaceutical Manufacturers Association, "Annual Survey Report– 1979-80" (Washington, D C : PMA, 1980),

Prices of Drugs Sold

Revenues are determined by the prices and quantities of drugs sold. Pharmaceutical prices have risen very slowly since **1967,** but, because the quantity of drugs sold has increased there has been real growth in revenues (see table 4). The Firestone Report of August 1980 indicates that pharmaceutical producers' prices (wholesale) have risen **46.1** percent since **1967.** Prices of all industrial producers have risen, on average, **136.5** percent since **1967.** Table *6* indicates that producer price indexes for all industries have typically been considerably higher than producer price indexes for pharmaceuticals.

Producer prices vary among therapeutic classes. Table 7 shows the average change in producer prices by therapeutic category. From tables *6* and 7, it can be seen that the average growth in price across all therapeutic classes was **46.1** percent and that the average price change ranged from – **17.8** to + **187.0** percent.

According to a study of price statistics of all NCEs introduced into the United States between 1958 and 1975, prices also vary with the therapeutic value of the drug. Of the NCEs classified as important therapeutic gains, 44 percent had prices that were more than double the prices of the closest competitive products; of the NCEs providing modest, little, or no therapeutic gain, about **10** percent had prices more than double the prices of the closest competitors. Similarly, *30* percent of the former had prices that were less than *120* percent of the closest competitors' prices and about *72* percent of the latter had prices that were less than *120* percent of the closest competitors' prices. [b]This study also indicates that prices for NCEs vary widely: introductory prices ranged from about one-quarter of the price of the closest competitive product to 15 times the price of the closest competitive product.[7]

Table 6.—Producer Price Indexes for Selected Years
(1967 = 100)

Year	All industries	Pharmaceutical industry
1949	75.3	117.3
1969	106.0	100.1
1974	153.8	109.3
1975	171.5	116.2
1976	182.4	123.8
1977	195.1	131.7
1978	209.4	138.8
1979	236.5	146.1

SOURCE *The Firestone Report,* August 1980, p 4

Table 7.—Average Percentage Change in Producer's Prices by Therapeutic Category, 1969-79

Group	Percent
Contraceptives, oral	+187.0
Sedatives	108.6
Antiobesity	81.3
Cough and cold	72.6
Bronchial therapy	66.7
Hormones	63.2
Diabetic therapy	63.0
Antiarthritics	62.3
Antispasmodic	60.7
Cardiovascular	53.9
Vitamins	46.5
Dermatologicals	41.1
Analgesics	38.0
Diuretics	34.7
Psychotherapeutics	17.5
Anti-infectives	– 1.4
Broad and medium specialists	0.0
Penicillin	– 17.8
Sulfa and antibacterial	+ 24.6
All others	57.1
Total	46.0

SOURCE. *The Firestone Report,* August 1980, p 2

The prices and quantities of drugs sold are determined by several factors: market demand, patent protection, and the number and type of competitors. In chapter 2 demand was examined, in this chapter other determinants of revenues are examined.

Product Lives.—Product lives do not necessarily parallel patent lives. Irrespective of the patent, a drug will be prescribed and consumed as long as no other drug or therapy comes along that is better and as long as the disease or condition for which the drug is prescribed continues to be prevalent in the society.

Table 8 lists the 15 top selling drugs in the United States in 1980 and their new drug application (NDA) approval date. The table in-

[7]Duncan W. Reekie, "Price and Quality Competition in Drug Markets: Evidence From the United States and the Netherlands," *Drugs and Health* (Washington, D. C.: American Enterprise Institute for Public Policy Research, 1980), p. 132.
[b]Ibid., p. 134.

Table 8.—Top Selling Drugs by Volume in 1980 and Year of N DA Approval

Drug (trade name)	Year
Valium	1963
Inderal	1967
Dyazide (dyrenium)	1964
Lanoxin	(a)
Tylenol with codeine	(a)
Lasix	1966
Dimetapp	(a)
Motrin	1974
Tagamet	1977
Darvocet-N	1972
Dalmane	(a)
Aldomet	(a)
Ortho Novum	(a)
Actifed	(a)
Keflex	1971

[a]Approval priorto 1963

SOURCE. *American Druggist*, February 1981, for ranking; FDA, private communication, for NDA approval data forNCE(June 1981)

dicates that 9 of the 15 drugs have product lives of 17 years or more.

Product lives are shortened by competition from other drugs and nondrug therapies, but a widely accepted drug may be able to retain a significant market share when competition emerges.

Since the 1950's, the average product life of drugs has increased. Product lives, however, vary widely depending on the competition within the therapeutic class.

Patent Protection. —Patents protect against competition from other generically equivalent products. (For a discussion of patents, see ch. 5.) Patents do not protect against competition from nonequivalent drugs or nondrug therapies.

Effective patent terms for pharmaceuticals have been declining. The average effective patent life for patented NCEs receiving FDA approval has reportedly declined from 13.6 years for drugs approved in **1966** to *9.5* years for drugs approved in 1979.[8] Three factors have contributed to this decline: an increase in the duration of the clinical and regulatory period required for drug approval; a slight increase in the time between the filing of a patent application and clinical testing; and a decrease in the time between patent application filing and patent issuance. Sixty percent of the decrease in effective patent life has been attributed to the increased testing and regulatory period and 40 percent to the other two factors.

Effective patent lives vary widely among products. Table 9 indicates that the effective patent lives of the drugs with the highest revenues ranged from 11 to 17 years.

Some of the factors influencing effective patent terms are undergoing change. The duration of the FDA regulatory procedure may be stabilizing. The average time between the filing and issuance of a patent application is increasing slightly as a result of a backlog of patent applications in the Patent Office. Thus, there is reason to believe that the decline may not continue in the future. Furthermore FDA is now giving highest priority to the drugs that it believes will provide significant therapeutic advances, hence, these drugs may fare better than the average drug in the future.

Competition and Concentration.—Competition, whether it comes from generically equivalent drugs or nonequivalent drugs, affects both the prices of drugs and the quantities sold. One indication of the degree of competition in an industry is the extent to which sales are concentrated among the leading firms in the industry. The relationship between innovation and concentration is disputed. According to some, high levels of concentration favor innovation since the more highly concentrated the market structure, the greater the ability to obtain higher profits. The higher profits can serve as incentives for innovation and make additional revenues available for R&D.

According to others, concentration can have negative consequences for innovation. In a very competitive market, consumer demands interact with costs of production to determine what drugs firms will produce and what the prices of these drugs will be. In highly concentrated markets, some or much of that power shifts to the producers, and innovation may therefore be determined by corporate needs, rather than consumer needs. The producers may be able to maintain high levels of profitability without innovation. Innovation may also suffer because the factors leading to the more highly concen-

[8]M. Eisman and W. Warden, "The Decline in Effective Patent Life of New Drugs," *Research Management*, January 1981, p. 18-21.

Table 9.—Effective Patent Lives of 1980 Top Sellers by Revenues

Drug (trade name)	1980 U.S. sales (millions)	Patent approval	NDA approval (date)	Patent expiration	Effective patent (years)
Tagamet	$250	1976	1977	1993	16
Valium	230	1968	1963	1985	17
Inderal	200	1967	1967	1984	17
Motrin	150	1968	1974	1985	11
Aldomet	150	1964	(a)	1981	17
Dyazide (dyrenium)	145	1963	1964	1980	16
Keflex	140	1970	1971	1987	16
Clinoril	125	1972	1978	1989	11

[a]Approved prior to 1963

SOURCE For ranking and sales New *York Times*, Sunday, May 17, 1981, quoting Oppenheimer and Co For NDA approval date and patent information private communication from FDA

trated market can discourage the entry of new firms.

The measurement of concentration has been a subject of controversy. When market shares of firms are calculated as a percentage of total pharmaceutical sales, concentration is relatively low in the pharmaceutical industry. When market shares are measured as a percentage of sales in particular therapeutic categories, concentration in some categories is quite high. When one looks at market shares over time, one finds that the firms in the leadership positions change considerably.[9] Since the shift in market positions is attributed to new product introductions, some economists suggest that this measurement is the one most relevant to innovation.

Competition From Nonequivalent Drugs.—Competition from nonequivalent drugs was somewhat higher between 1972 and 1980 than between 1963 and 1971. Table 10 shows the number of firms receiving NCE approvals and the number of NCEs approved, by FDA category, for those two periods. By aggregating NCE approvals for two 8-year periods, it was found that both the number of firms and the number of NCEs have increased for all but one category of drugs. The table does not explore entries and exits, but considerable turnover has occurred in the firms producing NCE drugs. For example, of the **20** firms producing cardiorenal drugs in the **1972-80** period, 15 had not produced such drugs in the earlier period.

[9]Douglas Cocks, "Product Innovation and the Dynamic Elements of Competition in the Ethical Pharmaceutical Industry, " in *Drug Development and Marketing* (Washington, D. C.: American Enterprise Institute,]975).

Table 10.—Number of Firms Receiving FDA Approval and Number of Drugs Approved, by FDA Drug Category (1963-71 and 1972-80)

	1963-71		1972-80	
FDA division	Firms	NCEs	Firms	NCEs
Cardiorenal	10	13	20	23
Neuropharmacological	20	25	17	23
Metabolism and endocrine	11	14	13	19
Anti-infectives	34	47	36	49
Oncology and radiopharmaceutical	12	24	23	45
Surgical-dental	12	13	13	16

SOURCE Food and Drug Administration, private communication, June 1981

Competition From Generically Equivalent Drugs.—After a patent expires, competition may emerge from generically equivalent drugs. Such drugs are manufactured by production-intensive firms who market nonbranded drugs under generic names and by research-intensive firms who market branded drugs either under trade names or under generic names accompanied by firm names. The reputation of research-intensive companies may enable their products to command higher prices than products marketed under generic names alone.

The revenues of branded and nonbranded drugs which either had not been patented or had patents that expired were about $4.4 billion in 1979; some of those drugs, however, did not have competition from generically equivalent drugs. Only about 7 percent of the revenues for branded and nonbranded drugs were earned by production-intensive firms with the remainder earned by the research-intensive firms.[10]

[10]Interview with William Haddad, Generic Pharmaceutical Industry Association, Apr. 21, 1981.

Branded and nonbranded drugs compete among themselves, as well as with the originally patented products. For example, a pharmacist, to avoid a large inventory, may carry only one branded and one nonbranded product. Competitive factors including price influence his choice of products.[1]

The Federal Trade Commission estimated that between **42.1** percent and 74.3 percent of the wholesale price of branded drugs could be saved by the dispensing of nonbranded products instead of more expensive branded drugs. 1[2]

Counter-Competitive Forces.—An important influence on the level of competitive activity when patents expire is the ease of market entry for generically equivalent products. Barriers to market entry arise from the requirements for FDA approval of generically equivalent products and from nongovernmental factors.

As stated in chapter 2, FDA plans to reinstitute its paper NDA procedure. This practice should significantly lower the barriers to second entrants. However, many firms seeking approval will not be able to provide such data and the FDA requirements for them will continue to discourage entry. FDA has also announced that it plans to consider changing its regulations so that its abbreviated NDA procedure could apply to some post-1962 drugs .13

FDA bioavailability tests also can act as barriers to market entry. Bioavailability relates to the absorption of drugs into the body. Tests for bioavailability are required in cases where precise dosage is critical because of narrow margins separating ineffective, effective, and toxic doses. When such tests are required, they may be difficult and time-consuming, and therefore act as disincentives to second entrants.

Nonregulatory barriers to successful market entry also exist. A principal barrier is the third-party aspect of consumer drug selection. The physician, who prescribes a drug for his patient, frequently cannot keep informed about alternative versions of a particular drug and their relative prices, and may prefer branded products because he believes them to be safer. This preference for trademarked brand-name drugs tends to give strong marketing advantages to first-entrant drugs that are therapeutically effective. These advantages can endure over time, and latecomers may need to wage vigorous promotion campaigns or offer improved substitute products to overcome these advantages. With gradually increasing product selection by pharmacists, this timing-of-entry barrier may be weakening.

Pharmacist preference can, however, also act as an entrance barrier. Pharmacists may be reluctant to fill prescriptions for brand-name drugs with generic equivalents because they fear they may be liable if generic equivalents cause injury.

Although pharmacists and physicians play a key role in determining the market for drugs, they are frequently influenced by consumer opinion. Thus, consumer preference also acts as a barrier to entry. Many drugs, have a particular size, shape, and color which are claimed by the innovator firm to be proprietary. A generic product that looks different from the product that the consumer customarily uses may be rejected in favor of a familiar product.

Forces Favoring Competition.—As discussed in chapter 2, actions taken by the Federal and State governments over the past decade have facilitated the development of the low-cost generic market. More than 40 States have repealed laws which prevented pharmacists from substituting generic equivalents for prescribed brand-name drugs. Some of the State substitution laws, such as New York's, require pharmacists to fill prescriptions with the least expensive generic products available according to a State formulary. Other States permit substitutions only when physicians specifically note that substitutions can be made.

The Federal Government's Maximum Allowable Cost (MAC) program, which affects reimbursements to pharmacists under medicaid, also encourages competition, Under the MAC program, the lowest wholesale price of a generically equivalent, multisource drug is identified. The

[1] "Federal Trade Commission, "Drug Product Selection, " Washington, D. C., 1979 (staff report to FTC).
[2] Ibid.
[13] 46 Federal Register 24445, Apr. 30, 1981.

MAC regulations limit the reimbursement to the pharmacist to that lowest identified wholesale price plus a reasonable dispensing fee. Because a growing percentage of all prescriptions are paid by medicaid, MAC is expected to have a significant effect as more drugs fall within the MAC program. Because MAC encourages pharmacists to stock low-priced generic products, pharmacists may be more inclined to use these products when filling prescriptions of nonmedicaid patients.

Several other Federal actions also favor competition: the Government-wide Quality Assurance Program is designed to increase competition among drugs purchased by the Department of Defense, the Veterans Administration, and the Public Health Service; the Model State Prescription Drug Product Substitution Act is designed to assist States in developing laws that encourage the dispensing of generically equivalent drugs; and the FDA list of therapeutically equivalent drug products is designed to provide an authoritative statement regarding generic drug quality. The Supreme Court has also had an impact by voiding, as unconstitutional, laws which prohibited the retail advertising of drugs and drug prices.

The full impact of the repeal of the antisubstitution laws and the Federal Government actions may not yet have been felt. One study reported the market share of 12 selected patented drugs before and after patent expiration for drugstore and hospital markets through **1978.** After patent expiration, each of these drugs retained more than a 90-percent share of the drugstore market and more than an 80-percent share of the hospital market. Six of the drugs retained more than a 97-percent share of both markets in **1978.** The retail price, in constant dollars, of 4 of the 12 drugs declined; the greatest decline was about *35* percent .14 It is not clear if price declines were due to generic competition or other factors, such as competition from new patented drugs or the waning of product life.

Trends **in Generic Competition.** —The trends in generic competition activity levels after patents expire are uncertain. The full impact of recent actions by the Federal and State governments facilitating generic competition has not yet been felt. While these actions have thus far had relatively minimal effects, they could potentially have substantial effects *on* the revenues and profits of innovator firms. Barriers to subsequent entrants can provide a countervailing force to these Government actions. Over the next few years, as the patent terms end for many high-income drugs, the trends will become more obvious.

[14]Meir Statman, "The Effect of Patent Expiration on the Market Position of Drugs, " in *Drugs and Health,* Robert B. Helms (cd.) (Washington, D. C.: American Enterprise Institute for Public Policy Research, 1980), pp. 140-151.

THE COSTS OF RESEARCH AND DEVELOPMENT

Thus *far,* the factors that influence revenues have been discussed. The returns to R&D investment, however, also depend on R&D costs and expenditures.

The average absolute R&D costs for new chemical entities are difficult to ascertain. Several average R&D cost estimates have been made. One estimate projected the R&D cost for a self-originated NCE (one not licensed from another source) to be *$54* million (in **1976** dollars). This calculation included $21 million in opportunity costs of capital (the money that could have been earned by investing in an alternative venture at an 8-percent return for the number of years between the initial investment and the start of sales income) and the costs of failures (7 failures for each success at the clinical stage).[15]

[15]R. W. Hansen, "The Pharmaceutical Development Process: Estimates of Development Costs and Times and the Effects of Proposed Regulatory Changes, " in *issues in Pharmaceutical Economics,* Robert 1. Chien (cd.) (Lexington, Mass.: Lexington books, 1980).

Rather than relying on estimates of R&D costs, the factors influencing R&D costs to ascertain trends in R&D costs have been reveiwed in this report. The costs of R&D have increased. Part of the increase is due to inflation; facilities, equipment. and salaries are all subject to inflationary pressures. The Biomedical Research and Development Cost Index of the National Institutes of Health (NIH) has outpaced both the Consumer Price Index and the Bureau of Labor Statistics Producer Price Index for Pharmaceuticals. Many commentators expect such pressures to continue in the future.

Some of the increase in costs has been due to regulatory actions. Testing standards have become more stringent and have required longer amounts of time to conduct. FDA is, however, trying to expedite its approval of new drugs and the duration of the drug approval process may therefore stabilize. Table 11 shows the time required for FDA approval of NCEs between *1976* and *1980.* The average time and the median number of years needed to obtain approval dropped in **1980.**

Table 1 1.—Average and Median Number of Years Between IND Filing and NDA Approval for NCEs

Year	Average years	Median years
1976	5.8	5
1977	7.8	7
1978	5.2	5
1979	8.9	9
1980	8.2	7.5

SOURCE: Private communication from FDA, June 1981

Technological advances have helped to counter the upward trend in R&D costs. By all accounts, the sophistication of pharmaceutical R&D has increased. Some of these advances may provide more efficient (and therefore less costly) ways of conducting research. Although we have no data on this trend, technological advance can be expected to stem some portion of the rising costs in the future.

In an attempt to keep R&D costs down, U.S. firms are committing increasing amounts of research expenditures abroad where regulatory procedures often permit more rapid and less costly drug development.

Expenditures in Research and Development

Real growth has occurred in expenditures of funds for R&D. In table 12, the current foreign and domestic dollars spent on R&D have been deflated for the years 1965 through 1978, using the (NIH) biomedical R&D cost deflator (1967 = 100). R&D expenditures **have** apparently kept up with and surpassed the rate of inflation for biomedical research. This upward trend may be expected to continue in the near future. Many research-intensive firms have indicated that they are increasing R&D expenditures. For example, Merck & Co. expects to spend *$280* million on R&D in *1981, 20* percent more than in *1980.* [16]

[16] William Fallwell, "U.S. Drug Companies Held Up Well in Recession," *Chemical and Engineering News,* Mar. *9, 1981,* p. 8.

Table 12.—Trends in R&D Expenditures

Year	Total domestic and foreign R&D (millions current dollars)	Deflator	Deflated R&D (millions constant dollars)
1965	329	92.5	356
1966	374	95.8	390
1967	412	100.0	412
1968	449	104.7	429
1969	506	110.4	458
1970	566	117.5	483
1971	629	124.1	507
1972	667	130.3	512
1973	753	136.5	552
1974	859	145.2	592
1975	974	160.7	606
1976	1,068	172.7	618
1977	1,182	186.4	634
1978	1,311	200.3	655

SOURCE Table 5 and information obtained from the Pharmaceutical Manufacturers Association, April 1981,

Of concern is the allocation of funds between basic research and product development. Declining expenditures on basic research could result in a reduced number of new drug introductions in the future. Industry officials have indicated that a shift from basic research to product development is taking place. Lewis Sarett **(1981)** of Merck& Co. reported in congressional testimony that a recent survey of U.S. firms by the Organization for Economic Cooperation and Development indicated that pharmaceutical firms are reducing the research share of their R&D budgets. To avoid the risks of research, firms are increasingly licensing technology from other sources and are spending more on development.[17] Nevertheless, preliminary information provided in table 13 suggests relatively little change in emphasis.

Rising costs can also be expected to shift R&D program emphasis among therapeutic classes because some types of drugs can be developed less expensively than others. In periods of rising costs, firms can be expected to emphasize the less costly research areas. Table 14 shows the percentage of R&D expenditures for different therapeutic categories for the years 1975-79. Although some shifts in expenditures are evident, the shifts tend to be more toward areas in which significant therapeutic advances are occurring (e. g., cardiovascular) than toward areas which involve lower costs (e. g., anti-infectives).

These shifts in expenditures, however, may not indicate any shift in decisions about R&D spending. Expenditures vary depending on where the innovation is in the development process, and these shifts may therefore only reflect normal research progress.

[17] For another example, see: D. Schwartzman, "Innovation in Pharmaceutical Industry;" J. R. Virts and J. Fred Weston, "Expectations and Allocation of R&D Resources;" and Grabowski and Vernon, op. cit.

Table 13.—Relative Funding of Basic and Applied Research in the Pharmaceutical Industry
(millions **of dollars)**

Year	(1) Basic research	(2) Applied R&D	Column 2 as percent of total
1968	60	375	86.2
1969	67	417	86.2
1970	93	474	83.6
1971	77	535	87.4
1972	78	501	87.2
1973	90	605	87.1
1974	107	683	86.5
1975	112	783	87.5
1976	119	883	88.1
1977	131	959	88.0

NOTE: For the purpose of this table. the pharmaceutical industry IS defined as corporations primarily engaged in manufacturing biologicals, Inorganic and organic medicinal chemicals, pharmaceutical preparations, and grading, grind. ing, and milling of botanicals.

SOURCE. Derived from National Science Foundation, *National Patterns of Science and Technology Resources 1980,* tables *42* and *45*

Table 14.—Percentage of R&D Funds Spent by Therapeutic Class (1975-79)

Therapeutic class	Percent of total R&D spending[a] 1979	1978	1977	1976	1975
Anti-infectives	18.7	18.3	19.2	19.5	20.1
Central nervous system and sense organs	16.3	16.9	17.0	16.2	18.0
Cardiovascular	18.6	17.3	15.2	13.2	14.9
Neoplasms, endocrine system, and metabolic diseases	15.3	16.1	15.7	14.7	15.5
Gastrointestinal and genitourinary system	6.3	6.7	6.0	5.8	5.1
Respiratory	4.0	4.4	4.0	4.1	5.5
Biological	2.5	3.0	3.1	3.1	3.0
Dermatologicals	2.9	2.8	3.2	2.8	2.8
Vitamins	2.5	2.2	2.5	1.5	1.1
Diagnostic	0.5	0.6	0.8	1.2	1.2
Other human preparations	6.7	5.6	6.3	10.5	6.1
Veterinary preparations	5.3	5.7	6.6	7.2	6.5
Veterinary biological	0.4	0.4	0.4	0.2	0.2

[a] In the United States only

SOURCE" Pharmaceutical Manufacturers Association

SUMMARY OF FINDINGS

Research-intensive companies are committing increasing amounts of funds toward pharmaceutical R&D, and therefore, the potential exists for major pharmaceutical discoveries. Factors have been highlighted which, based on historical trends, will affect pharmaceutical innova-

tion. Below is a summary of these major trends. Following that is a summary of factors whose effects are uncertain.

Historical Trends That May Discourage Innovation

- The costs of research and development are increasing significantly.
- The price of drugs has generally not kept pace with the increase in R&D costs.
- Effective patent lives have declined, but may be stabilizing.
- A decline in the returns to R&D investment is widely perceived.

Historical Trends That May Contribute to Innovation

- The pharmaceutical industry continues to enjoy high and stable profitability in terms of return to stockholder's equity.
- Recent technological advances have improved research techniques and enhanced the efficiency of research activities. Researchers are no longer totally dependent on the expensive hit-or-miss method for screening new drugs.
- The competitive environment for innovation appears stable for most therapeutic classes, and there is no lessening of competitive pressure for innovation.
- Markets and sales of drugs are growing.

Uncertainties Affecting Innovation in the Future

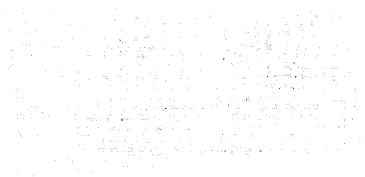
Historical trends do not reflect recent governmental actions that may affect the postpatent exclusivity of many drugs. These actions include the repeal of antisubstitution laws, adoption of FDA procedures that facilitate approval of generic equivalents of previously approved drugs, adoption of Government reimbursement programs favoring use of low-priced generic equivalents, and court rulings that allow advertising of drug prices.

Although these actions have, thus far, had only minimal effects on the rates of return to R&D investments and on the revenues and profits of research-intensive companies, they could have substantial impact in the future.

If the effects prove to be substantial, firms will probably be unable to maintain their current levels of research. The public, however, will not perceive a decline in innovation for many years. By the time such a decline is noted, the public will face a period of lagging innovation, since new research efforts will not bear fruits for at least a decade.

Chapter 4

The Implications of Patent-Term Extension for Pharmaceuticals



Chapter 4

The Implications of Patent-Term Extension for Pharmaceuticals

This chapter examines the possible impact of patent-term extension on the numerous factors that affect pharmaceutical innovation. The first portion of the chapter concentrates on whether patent-term extension will result in beneficial pharmaceutical innovation; the second explores the costs associated with patent-term extension and the implications of patent-term extension for the patent owner, the research- and production-intensive firm, and the consumer.

PATENT-TERM EXTENSION AND INNOVATION

A patent provides the right to exclude others from making, using, or selling an invention. The primary incentive provided by this right is the opportunity to derive economic benefits that result from an exclusive market position. By extending the patent term, Congress would extend the period in which these benefits could be derived, and thereby increase the incentives for research and development (R&D) activities.

Whether R&D activities actually increase as a result of these incentives will depend on decisions made in the private sector, and patent terms are but one consideration in these decisions. Patent-term extension will not provide a mechanism for reducing R&D costs, it will not enhance the likelihood of research breakthroughs, and it will not ensure that the results of innovative activity will meet with commercial success. Nor will it stem the trend of domestic companies conducting pharmaceutical R&D overseas.

To the extent that patent-term extension demonstrates Government support for R&D activities, it will provide psychological encouragement to decisionmakers; the effects of such encouragement might, however, be temporary. Since patent-term extension cannot provide firms with additional revenues before the extensions actually begin and the first extensions will not, under the proposed legislation, begin until the 1990's, the immediate incentive provided to the research-intensive firms by patent-term extension is the opportunity to obtain greater returns on R&D investment in the long term. Although an exclusive market position for a drug can exist beyond the expiration of the original patent term, patent-term extension provides a longer and more certain period in which exclusivity can be assured.

Whether firms will actually increase R&D expenditures on the basis of anticipated increases in returns is, however, highly speculative. On the one hand, the increased economic attractiveness of R&D investment could encourage firms to reallocate corporate funds or obtain external funds in order to increase R&D expenditures. On the other hand, the historic stability of the relationship between R&D expenditures and revenues would suggest that R&D expenditures would not increase unless revenues increased.

In the long term, firms obtaining additional revenues in the extended period will have additional funds available for R&D investment. If historic trends prevail, they will spend on average *8 or 9* percent of these additional revenues for R&D. A major portion of the additional revenues will be used for purposes other than R&D. Taxes will need to be paid, production costs allocated, and dividends distributed. The funds may be used for product promotion or diversification. In talking about additional revenues, it should be noted, however, that such revenues will never be able to be quantified since we can never know what revenues would have been generated if the patent term had not been extended.

Despite the fact that revenues generated by the extension cannot be measured, firms with drugs whose patents are extended will probably derive additional revenues since they will have a longer period of exclusivity in which to market their products at premium prices. Therefore, both sales and prices should be greater than they would have been if no extension existed unless the supply of new drugs increases and exerts a downward pressure on prices. After extensions lapse, sales by research-intensive firms may continue to be higher than they would have been had competition entered the market when the original patent expired. In some cases, second entrants may consider the remaining product lives of drugs coming off extended patents insufficient to justify start-up costs and thus may not enter the market. Furthermore, by the time the extensions end, the patented products may be so firmly established in the market that generically equivalent products could not obtain as great a market share as they would have obtained if the extension had not occurred.

Thus, the revenues of research-intensive firms, particularly firms having high-income drugs, should receive a boost from patent-term extension. Nonetheless, pricing pressures are exerted by other patented drugs and nondrug therapies. Whether these pressures will override the research-intensive firms' ability to charge premium prices will depend on circumstances in the relevant therapeutic markets.

The distribution of additional revenues among firms can affect both the level of research activities that will be undertaken and the types of innovation that may result.

The bulk of additional revenues probably will be earned by high-income drugs. The possibility exists that the relatively few firms who develop those drugs will develop more sophisticated research techniques and more extensive research programs than other firms since they will have more funds available for research and development. Their successes may particularly encourage them to undertake additional R&D activities, some of which may be directed at therapeutic areas that go beyond their present expertise. Under these circumstances, innovation would be expected to increase.

On the other hand, other firms may be discouraged from conducting research in the areas pursued by these successful firms which have been able to increase their research dominance in these areas. In such cases some forms of innovation may suffer.

Furthermore, as a result of patent-term extension, specific types of innovation may be delayed. An originator of a drug may have little incentive to improve his product while it is benefiting from patent protection. Second entrants, when they engage in R&D activities, concentrate on manufacturing processes, drug formulations, combinations of active ingredients, or minor, unpatentable modifications of existing drugs. By delaying the entry of firms who engage in such activities, patent-term extension may delay the introduction of this type of innovation.

On balance, there is a reasonable likelihood that firms may undertake or increase pharmaceutical R&D activities because of the increased incentives provided by the longer effective patent term. If this occurs and drugs are developed more rapidly, a downward pressure might be exerted on the price of some drugs and the product lives of some drugs might decrease.

Although R&D expenditures are expected to increase, they will not increase evenly across all therapeutic areas. Since high-income drugs will derive the greatest benefits from patent-term extension, the tendency of firms to direct their research efforts torward developing drugs for large markets will be reinforced.

To the extent that patent-term extension affects the potential rate of return, drugs that might otherwise be economically marginal may become economically attractive. But this will occur only occasionally, particularly if opportunities exist for developing drugs with greater profit potential. For the many marginal drugs that do not have generic competition after their patents expire, patent-term extension will not generate additional revenues.

Patent-term extension could be a significant factor in encouraging certain types of pharmaceutical R&D. In some therapeutic areas, the loss of effective patent term due to the drug ap-

proval process can be great, and research-intensive firms may not initiate R&D activities in these areas. Patent-term extension may reduce or eliminate the discrepancy between the effective patent terms of drugs in these therapeutic areas and drugs in other areas.

Patent-term extension may also encourage second uses for existing drugs. Not infrequently an existing drug is discovered to have a therapeutic use other than the one approved by the Food and Drug Administration (FDA). FDA approval must be secured for the additional use before the drug can be sold for that use. Because of the period of exclusivity provided by the extended patent term, the development of the additional use of the drug may be financially attractive.

The balance between research spending and development spending is not likely to be significantly changed by patent-term extension. Generally, the results of research activities are less certain than the results of development activities, and patent-term extension will not alter the relative levels of uncertainty. However, if additional revenues are generated because of patent-term extension, the firms may be more willing to undertake the risk involved with research activities.

PATENT-TERM EXTENSION AND THE COST OF PHARMACEUTICALS

Drugs whose patents are extended are expected to command higher prices during the extension period than they would have, had their patents been allowed to expire. Despite these higher prices, the drugs may cost less than alternative therapies.

This section, however, does not evaluate the cost-benefit relationship of drug therapies, but is solely concerned with the additional costs of drugs during the extended period. The benefits of innovation that might result from patent-term extension are not taken into account in evaluations of cost. Furthermore this section does not take into account the fact that the prices of drugs with extensions can influence the prices of competitive drugs nor the fact that patent-term extension can affect the prices of drugs after extensions end.

There is a distinction between the additional costs to the consumer due to patent-term extension, and the additional revenues to the innovator firm. First, the additional costs to the consumer due to patent-term extension may not be directly comparable to the additional costs at the wholesale level. The drug is dispensed to the consumer by the pharmacist who assesses a prescription fee or a percentage markup. Nonetheless, substantial price benefits could be gained by the consumer from the purchase of generic drugs. Second, generic competition will have a greater effect on the additional revenues to the innovator firm than on the costs to consumers: when a consumer purchases a low-cost equivalent drug, he saves the difference between the cost of the generically equivalent drug and the cost of the branded drug; but the innovator firm, receives no revenues for the drug he might have sold.

The degree of difference between investment revenues to the innovator firm and increased costs to the consumer cannot be estimated and may vary widely, depending on the portion of the market that would have been captured by generic competition, and whether the innovator firm would have lowered its price in view of the competition. A portion of the revenues derived by the innovator firms can be viewed as the recovery of revenues that would have been generated had the historic postpatent periods of market exclusivity continued to exist.

Projections of the costs of patent-term extension based on historic trends alone overlook some important factors that may influence costs in the future. Some of the determinants of costs are currently undergoing changes, but the magnitude of these changes is not yet known. This

section discusses the uncertainties in the factors determining the costs of patent-term extension and the sensitivity of cost projections to variations in assumptions about the determinants.

Numerous uncertainties limit attempts to predict the increased costs to the public of pharmaceuticals under patent-term extension. The revenues that drugs would have generated without an extension and the revenues they will generate with an extension are not known. The number of drugs that have product lives sufficiently long to extend into the extension period and the average duration of the patent-term extension are not known. Revenues from patented drugs after original patent terms expire depend to some degree on whether competition enters the market. The length of the extension is another unknown factor. There are a number of proposals (discussed in ch. **6)** for limiting the duration of the extended patent term.

The general effect of variations in these uncertainties on the costs of patent-term extension can be derived from a sensitivity analysis with three variables: 1) the duration of the average extension; 2) the percentage of drugs, on a sales weighted average, having product lives continuing into the extension; and 3) the percentage by which total sales revenues would have been reduced because of generic competition if patent-term extension did not exist.

The following assumptions have been made to simplify this analysis: the innovator firm charges the same price for drugs during the extension that he charged before the extension; the number of units sold is constant throughout the extension period; the effective patent life for all drugs is 10 years; and the supply of new drugs is continuous, providing the same revenue each year. These assumptions are not intended to reflect actual conditions; the sensitivity analysis is, therefore, not a proper basis for projecting actual costs of patent-term extension to the consumer. However, recognizing this bias, some understanding can be developed from the sensitivity analysis of the effects of the uncertainties on the costs associated with patent-term extension.

For the sensitivity analysis, the values for the duration of the average extension are *3* years, which approximates the average time between the filing of a new drug application for a new chemical entity (NCE) and the FDA approval; 7 years, which approximates the loss of effective patent term now experienced by patented NCEs; and an intermediate value of 5 years. The values for the percentage of drugs, on a sales weighted average, having product lives continuing into the extension are *75* and **100** percent. This variable indirectly reflects the rate of innovation in that as more drugs are developed, product lives are expected to decline. The values for the reduction in total sales revenues that would exist because of generic competition if patent-term extension did not exist are **10, 30, 50,** and *70* percent. The *50* and *70* percent values are within the range of the maximum potential wholesale savings projected by the Federal Trade Commission if generic-named products were dispensed instead of more expensive branded drugs.

The results of the sensitivity analysis are provided in table 15. The results are provided per $1,000 of yearly wholesale sales of patented drugs during the original term of the patent. Thus, if it is assumed that: 1) the average extension will be 7 years, **2)** 100 percent of the patented drugs will be sold during the extension, and 3) the average total sales revenue would have been **70** percent less without patent-term extension; then the additional cost to consumers of patent-term extension will be *$490* per $1,000 of unextended, patented-drug sales or about 140 percent of the cost without patent-term extensions. If the average extension is 3 years, if only 75 percent of patented drugs are sold during the extension, and if the average revenue reduction is 10 percent; then the additional costs would be *$22.50* per $1,000 of unextended, patented drug sales, or less than 5 percent of the costs in the preceding example.

Evident from the sensitivity analysis is the fact that the additional cost to consumers due to patent-term extension will be highly dependent

on assumptions made about generic competition. Unless the total sales revenues for the drugs would have been significantly reduced without patent-term extension, the increased revenue to the innovator firms may be relatively insignificant on an aggregate basis.

Table 15.—Sensitivity of the Consumer Cost of Patent-Term Extension to Three Variables'

Variable 1: Average extension (years)	3		5		7	
Variable 2: Percentage of drugs that have product lives during the extension period (sales weighted average)	75	100	75	100	75	100
Annual sales revenues of drugs under patent extension (dollars).	225	300	375	500	525	700
Variable 3: Average total sales revenue reduction with competition, percent	Additional cost to consumers					
10	$ 22.5	$ 30	$37.5	$ 50	$ 52.5	$ 70
30	67.5	90	112.5	150	157.5	210
50	112.5	150	187.5	250	262.5	350
70	157.5	210	262.5	350	367.5	490

[a]The sensitivity analysis is based on an annual $1,000 worth of wholesale purchases of patented drugs during the original term of the patent The following assumptions are used in this table The innovator firm charges the same price for drugs during the extension as before, the number of units sold per year is constant throughout the extension period. the effective patent term for all drugs during the original patent period is 10 years, and the supply of new drugs is continuous, providing the same revenues each year

[b]It is assumed that $100 worth of new drugs were introduced annually to maintain $1,000 worth of revenues per year of drugs in their original patent term The amount of sales of drugs during patent extension would be ($100) x (the sales weighted average) x (the average extension)

[c](Sales of drug under patent extension) x (percentage reduction in revenue)

SOURCE Office of Technology Assessment

IMPLICATIONS OF PATENT-TERM EXTENSION FOR SOCIETY

The major groups in society that will be directly affected by patent-term extension are the patentee, the research-intensive firm, the production-intensive firm, and the consumer. Although in most cases the research-intensive firm is the patentee, in some instances the patentee is a separate entity who grants a license to the research-intensive firm to develop and produce the patented drug. In this section we define the consumer as the person for whom the drug is prescribed whether or not payment for the drug is made by a third party (e.g., insurance company or the Government).

The Patentee

Patent-term extension would benefit the patentee by providing a longer effective patent term. If the patentee develops and markets the drug, patent-term extension provides the patentee with the benefits of an exclusive market position during the extension period. If the patentee licenses the patent to another, the patentee can benefit from royalty revenues during the extension period.

Because decisions to develop or market drugs are often based on the length of time remaining in the patent term, the patentee may find that patent-term extension allows him more time to develop a drug or arrange with someone else to develop the drug. In this regard, patent-term extension may be particularly beneficial to universities, medical centers, research foundations, small firms, or foreign companies that may *not* be able to develop drug candidates in the United States. Therefore, they may arrange for licensees to develop and market the drug candidates. These organizations typically pursue drug candidates only to the preclinical phase; hence the innovator firm is faced with considerable expense and risk should it decide to develop the drug. Finding someone willing to develop the product and working out a licensing arrangement frequently requires up to 2 years. Without patent-term extension, the time spent

on licensing activities may reduce the expected patent term to such a degree that the candidate is no longer commercially attractive.

The Research-Intensive Firm

The research-intensive firm may be a patentee, in which case the effects described for the patentee apply. The primary benefit of patent-term extension will be additional revenue obtained due to the exclusive market position during the extension. Although the pharmaceutical industry traditionally has relied on internal funding for R&D activities, patent-term extension could be a favorable factor in securing external funding. This may be of particular advantage to the smaller company.

The costs of patent-term extension to the research-intensive firm are two-fold and appear to be nominal. First, many research-intensive firms market generic and branded-generic drugs. For firms which have not developed new drugs with regularity, these products can be a significant source of income. Patent-term extension may delay the entry of these firms into the generic and branded-generic markets. Second, if patent-term extension increases the rate of innovation, it is possible that the additional competition in innovative drugs could result in some downward pressure on prices and a reduction in the sales of the patented product.

The Production-Intensive Firm -

Patent-term extension offers benefits to production-intensive firms only if the rate of innovation is greater than it would have been without patent-term extension and product lives continue beyond the extension period. Production-intensive firms have conflicting interests with respect to patent-term extension. On the one hand, these firms must rely on research-intensive firms as sources of new products. A favorable environment for R&D could benefit them. On the other hand, patent-term extension delays their entry into the market.

The effect of the delay on the production-intensive firm will be particularly acute when the effects of patent-term extension first take hold and the supply of drugs coming off patent protection dwindles. Later, when extended patent terms expire, production-intensive firms may find that the number of drugs with sufficient markets to justify investment has decreased. For those drugs worth marketing, sales potentials will have been reduced, since, in most cases, their remaining product lives will have been shortened. Furthermore, the longer period of exclusive marketing provided by patent-term extension may increase the strength of nonpatent barriers such as brand loyalty and thus reduce the ability of the production-intensive firms to establish their drugs in the market. Thus patent-term extension may have a negative psychological impact on the production-intensive firms.

The Consumer

The consumer will benefit from patent-term extension if more and better drugs are commercialized with patent-term extension than would have been commercialized in its absence. If this happens, the consumer will get better therapy earlier. However, an increase in drug innovation does not necessarily result in improved drug therapies.

An increased supply of new medicines could exert downward pressure on the price of existing drugs. But during the extension, consumers will pay more for most drugs whose patents are extended. Thus, the net effect of patent extension on consumer expenditures is unclear. Furthermore, some groups of consumers, the elderly and chronically ill, will be disproportionately affected, and these groups may be less capable than the population as a whole of bearing the increased costs.

Besides the obvious cost to the consumer of the delayed entry of lower priced generic drugs, patent-term extension may also provide two more subtle costs. The magnitude of these ancillary costs are difficult to ascertain, and they may occur only in isolated cases. First, in some instances, production-intensive firms develop new formulations or compounds which are therapeutically advantageous. These developments may be delayed. Second, to the extent that the

innovator firm is reluctant to market improvements of the patented drug until the patent is about to expire, the consumer will have longer to wait for these improvements.

SUMMARY OF FINDINGS

Patent-term extension will enhance the incentives provided by patents for pharmaceutical research and development. Although patent-term extension lacks a mechanism that would assure increases in R&D activities, the incentives it provides may be sufficient to encourage additional R&D expenditures.

Chief among these incentives are the increased revenues that will occur when extensions begin to run. However, the first extensions will not begin for at least a decade. Thus, in the immediate future, patent-term extension will have no effect on revenues. Although historic trends indicate that R&D expenditures are closely related to revenues, research expenditures could increase before extensions begin if decisionmakers base their funding decisions on anticipated rates of return.

The extension will be most beneficial to firms selling high-income drugs and will therefore encourage research on drugs with potentially large markets. However, it will not increase the economic attractiveness of research on drugs with small markets. More research efforts may be directed toward second uses for existing drugs and towards drugs subject to extensive testing requirements as a result of patent-term extensions.

The bulk of revenues generated by patent-term extension will go to a relatively small number of firms who have a history of success in particular research areas. The successes could increase their dominance in these areas and discourage other firms from conducting similar types of research.

Competition from generically equivalent drugs will be delayed by patent-term extension. In some instances, the remaining product lives on drugs whose patents are expiring may not be sufficient to attract competition from generically equivalent drugs.

The prices of drugs whose patents are extended will be higher during the extension period. The magnitude of the increased costs of these drugs to consumers will depend on the extent to which generic competition would have existed had patent terms not been extended. Generic competition will have a greater effect on the revenues of innovator firms than on consumer costs.

Patent-term extension will benefit the research-intensive firm and the patent owner. However, to the extent that research-intensive firms rely on branded generics for revenues, the benefit will be diminished.

Production-intensive firms have the most to lose as a result of the extension. Although they cannot expand their lines of products if innovation does not occur, patent-term extension will delay their entry into markets and reduce their revenues. In the case of some drugs, production-intensive firms will not enter the market since the remaining product lives after the extensions expire will be insufficient to justify startup costs.

The consumer will benefit if new and better products are developed; however, some drugs will cost more, and the costs will fall disproportionately on the elderly and the chronically ill.

Chapter 5

The Fundamentals of the Patent System

Chapter 5

The Fundamentals of the Patent System

INTRODUCTION

This chapter provides background information on the patent system that will facilitate understanding of the implications of the various proposals for patent-term extension that are discussed in chapter *6.*

A patent is the grant by the Government of a right for a limited period of time to exclude others from making, using, *or* selling an invention.

Patents promote the progress of science and the useful arts in several ways:

- they encourage research since they can provide a mechanism for protecting research results from commercial use by others;
- they encourage the development of products since they can provide an exclusive market position or competitive advantage that enables the patent holder to earn a greater profit and recover his research investment costs;
- they provide a mechanism for the transfer of technology to others who may put the invention to practical use; and
- they enhance the rate at which technology grows by requiring that the invention be promptly disclosed to the public in return for the grant of the patent.

The effectiveness of patents in promoting innovation may vary depending on the other factors influencing the invention and innovation processes. This chapter discusses the patent system in the context of the pharmaceutical industry and examines the role of patents in promoting pharmaceutical innovation. It also provides a brief history of patent law in the United States and examines the practices of those administering and using the patent system.

THE ROLE OF PATENTS IN PHARMACEUTICAL INNOVATION

As stated earlier, once a drug has been discovered, developed, and marketed by a firm, other firms can produce and sell the drug at a price that is considerably lower than that of the innovator since their price need not include the cost of research and development (R&D) or the cost of creating a market. Thus, if there are no restrictions on market entry, later entrants may have a significant competitive advantage.

In view of these facts, research-intensive pharmaceutical firms consider patent protection as a prerequisite to innovation. From the perspective of these firms, patents are valued most highly because they provide a means for restricting the entry of competitors. But patents are also important to pharmaceutical innovation because they allow for the transfer of technology in a valuable form to those capable of putting the technology to practical use.

Historically, a substantial portion of pharmaceutical innovations have been marketed by firms that did not make the original discoveries but instead obtained licenses (i.e., the rights given by patentees to permit others to practice the inventions) to commercialize the inventions. For example, more than one-third of the new chemical entity drugs are commercialized by firms that hold a license for the new technology but do not hold the patent.]

The value of a pharmaceutical technology in the business world is significantly influenced by the risk-to-reward ratio and the certainty of the reward. Patents, because of the exclusivity which they provide, may, therefore, be critical factors in corporate decisions to license patents and then complete development of new pharmaceutical technologies.

'Private communication from W. Warden, University of Rochester, July 1, *1981.*

A HISTORY OF U.S. PATENT LAW

From the power vested in it by the U.S. Constitution, Congress has enacted the patent law, which establishes the following general principles:

- an invention, to be patentable, must be useful and must be a process, machine, manufacture, or composition of matter (statutory classes);
- a patent can be granted only for an invention that is novel and not obvious (patentability y requirements);
- a patent gives the owner the right to exclude others from making, using, or selling the invention in the United States; however, if the invention is made or used by or for the U. S. Government, the patentee cannot prevent the infringement but can only seek reasonable compensation; and
- a patent term shall run for 17 years.

In the Act of *1790,* Congress established a 14-year patent term. The selection of the term was somewhat arbitrary and was said to be equivalent to the length of two apprenticeships. The Patent Act of **1836** permitted the Commissioner of Patents, in certain instances, to extend the 14-year term by 7 years. In the Patent Act of 1861, however, Congress repealed the extension provision and established the 17-year patent term, which stands today. From accounts of the history of the Act, it appears that the term of 17 years was a compromise between the House bill, which provided for a 14-year term with a possible extension of 7 years, and the Senate amendment, which provided for a 14-year term with no extension.

Since *1861,* numerous bills have been introduced to change the patent term: proposed terms have ranged from 5 years to 34 years (17 years with a possible 17-year extension). The first proposal for changing the 17-year patent term was made in 1881 and authorized the Commissioner of Patents to extend patents for which no reasonable compensation had been received; under this proposal, licensing was compulsory and royalties were limited by law. Most of the other proposals for patent extensions provided for a 17-year term which would be extended for 17 years if the patentee, through no fault of his own, had received an insufficient financial return. The determination of the adequacy of the financial return resided, depending on the specific bill, either with the Commissioner of Patents or with the Court of Claims.

Despite these proposals, patent-term extensions had not received serious congressional attention until the patent-term restoration bills S. **255** and HR. **1937** were introduced in the first session of the 97th Congress.

THE PHARMACEUTICAL PATENT

The cornerstone of the patent system is the patent document. By law, the patent document must provide a teaching of the invention such that others can make and use the invention and contain claims that define the boundary of the invention. To be patentable, the invention defined by these claims can be neither known nor obvious to others.

The portion of the patent application that teaches the invention is commonly termed the specification. The specification serves several functions. First, it describes the invention. Second, it discloses the utility of the invention since patents are only granted for useful inventions. Third, it describes how to make and use the invention since, in part, the purpose of the patent is to secure a disclosure of the invention from the inventor in exchange for the patent right. Fourth, it discloses the best mode of practicing the invention, insofar as it is known to the patent applicant at the time the application is filed. The specification concludes with one or more claims defining the boundary of the patent rights.

The claims serve much the same purpose as a deed to a piece of land. When a patentee at-

tempts to enforce a patent, the claim is compared with the product or process against which the enforcement action is directed to determine whether an infringement exists.

On the other hand, if other parties can show that the claim encompasses subject matter which was known or was obvious prior to the invention, the claim is invalid in its entirety and no part of the claim can be enforced.

Consequently, patent applications frequently contain a plurality of claims that vary in scope. Some claims may be very broad and encompass many possible products or processes. However, the broader the scope of a claim, the greater the likelihood that the claim will encompass subject matter which was known or obvious prior to the invention. Thus as the scope of a claim increases, so does its chances of being declared invalid. Claims of narrower scope may be adequate to protect the particular aspect of an invention that will be commercialized and may be less vulnerable to attacks on validity.

Claims in pharmaceutical patents may be directed to a product, a method for using the product, or a process for making the product, Product claims may be directed to invented chemicals (chemical claims) or to compositions, i.e., mixtures of chemicals. Claims directed at all of these categories could be made for a single pharmaceutical. To illustrate this fact, an example of each type of claim is provided:

- *A chemical claim.* —A compound having the structural formula C_2H_5O-  $NHC(O)R$ wherein R is $-CH_3$ or $-C_2H_5$.
- *A composition claim.* —A composition useful for treating headaches when administered orally to a human suffering from a headache in a unit dosage form consisting essentially of 5 to 95 weight percent of phenacetin and 5 to 95 weight percent of aspirin.
- *A process claim.* —A process for making phenacetin comprising reacting a compound of the formula C_2H_5O-  $-NH_2$ with glacial acetic acid at a temperature of **50°** to **80°** C in the presence of an effective amount of dehydrating catalyst.
- *A method-for-use claim,* —A method for treating headaches comprising orally administering to a human suffering from a headache a therapeutically effective amount of phenacetin.

A headache drug containing *40* weight percent phenacetin and **60** weight percent aspirin is covered by each of these claims. Although these claims might be contained within one patent, it is possible that each of the claims might involve a separate invention and therefore a separate patent. Consider the following hypothetical example:

> Inventor A discovered a group of compounds expressed in the chemical claim (when R is $-CH_3$, the compound is phenacetin). In A's specification a method was disclosed for making the compounds and a use (as antioxidants to preserve rubber).
>
> Later Inventor B discovered an improved process for making the compound invented by A. B received a patent claiming the improved process (represented by the process claim).
>
> Inventor C subsequently discovered that one of the compounds (phenacetin) invented by A was useful in treating headaches and received a patent claiming the method for use (represented by the method-for-use claim).
>
> After C's invention, Inventor D found that the mixture of phenacetin and aspirin provided a better treatment for headaches than phenacetin or aspirin alone. Inventor D could obtain a method-for-use patent (claim not illustrated) and a composition patent (represented by the composition claim) for his discovery.

Each of the four patents can affect what the other patentees can do with their inventions. Table **16** is provided to assist in illustrating the activities which each of the patentees can undertake. It is assumed that the patents to A, B, C, and D were issued, and will therefore expire, in chronological order. While all four patents are

Table 16.—Activities Permitted Before and After Patent Expiration

Activity	Before expiration of any of the patents	After expiration			
		A's patent	A&B's patents	A,B,&C's patents	A, B, C,&D's patents
Make, use, or sell phenacetin.	A	anyone	anyone	anyone	anyone
Use B's process to make phenacetin . . .	no one	B	anyone	anyone	anyone
Use phenacetin to treat headaches.	no one	c	c	anyone	anyone
Make, use or sell combination of phenacetin and aspirin to treat headaches.	no one	no one	no one	D	anyone

SOURCE: Off Ice of Technology Assessment

in effect, only A can make, use, and sell phenacetin; no one including A, B, C, or D can use B's improved process or C's method-for-use, and no one can make, use, or sell D's composition. B, C, and D cannot practice their inventions since the practice would infringe A's patent on phenacetin, i.e., B, C, and D would be making or selling phenacetin.

When A's patent expires, anyone (including B, C, and D) can make, use, and sell phenacetin. Since B's patent is still in effect, only B can use the improved process, but B cannot use C's method for use nor make, use, or sell D's composition. C, however, can use phenacetin to treat 'headaches, but he cannot use B's improved process, or make, use, or sell, D's composition. No one, including D, can make, use, or sell D's composition since that would infringe C's patent because phenacetin, albeit in combination with aspirin, would still be used to treat headaches.

When the patents to A and B expire, anyone can practice A's and B's inventions. C's method-for-use patent prevents others from using C's invention and C's patent also prevents use of D's invention. When the patents to A, B, and C expire, D can practice his invention, and exclude all others from practicing his invention. Anyone can practice the inventions of A, B, and C,

Not all types of patents have equal value. Infringements on chemical and composition patents generally are easier to detect than infringements on other types of patents. Infringements on chemical and composition patents occur when manufacturers or distributors make or sell the drugs, and can be readily detected, because neither sales nor distribution can be kept secret. Infringements on process patents take place in relative privacy and may be impossible to discover.

Additionally, a product made abroad using the patented process can be imported into the United States without providing an actionable infringement of the patent. The patentee, however, does have recourse against the infringer through the International Trade Commission but must prove that the importation of the product results in substantial economic harm to a domestic industry and that the process practiced in the foreign country infringes the patent. Proving either of these points can be quite difficult.

The enforcement of method-for-use patents provides unique difficulties. First, the direct infringer is the ultimate user and not the manufacturer. For the manufacturer to be found liable for infringement, the patentee must prove that the manufacturer induced the user to infringe the patent. Second, except in instances in which the drug has no other use, the owner of a method-for-use patent cannot stop the manufacturer from making and selling the drug. For example, if the method-for-use patent were for the discovery that aspirin could be used as a contraceptive, the patentee could not stop existing manufacturers from making and selling aspirin. Because of the vast number of individuals who may use aspirin for its contraceptive activity, and because enforcement of the patent would involve a suit against each user, the enforcement of the patent would not be financially feasible.

Because of their potential for enforcement, chemical and composition patents are generally preferred by the inventor, but method-of-use and process patents could, on occasion, be sufficient to ensure an innovator an exclusive market position.

SECURING A PATENT

The progress from an invention to an issued patent is characterized by three stages: the preliminary evaluation stage, the patent application drafting stage, and the patent examination stage.

Preliminary Evaluation

In the preliminary evaluation stage, the inventor attempts to determine the importance of his invention. For example, once an inventor has discovered a new chemical, he must attempt to discover its utility and determine its potential economic value. The length of the preliminary evaluation stage may range from 1 week to 5 or more years, depending on the perceived importance of the invention and the ability of the inventor to develop the invention to a point that he can sufficiently fulfill the requirements for patenting.

Drafting of the Patent Application

The patent application drafting stage usually takes between **6** months to **2** years, but this stage can vary greatly. During this stage, the breadth of the invention is investigated. For example, is the invention one chemical or a group of related chemicals? The potential patentability of the invention is also considered. Is the invention novel? Is it obvious? The patent application is prepared according to statutory requirements and the legal, regulatory, and procedural requirements of the Patent Office.

If the invention appears to be of economic significance, substantial incentives exist for pursuing the invention diligently and filing a patent application at an early date. The primary incentive is to reduce the potential of losing the patent right to another who has made the same invention. In the United States, if two or more inventors independently discover a patentable invention, a proceeding termed an "interference" is declared to determine which of the inventors was the first to conceive the invention. If, however, the inventor has not diligently pursued the invention, he may be precluded from using his date of conception for determining who was the first to invent. Moreover, procedural advantages are provided to the inventor who files the first patent application. The advantage of an early filing is even more important if foreign patents are sought since almost all foreign countries award the patent to the inventor who files the first patent application. By treaty with many countries, if certain requirements are met, the U.S. filing date serves as the critical filing date for this determination in those countries.

A second incentive for speedy filing of a patent application is to enable the technology to be disclosed to others without the loss of proprietary rights to the invention. In most foreign countries, if the invention is disclosed prior to the filing of a patent application, a patent is barred. In the United States, a l-year grace period exists in which a patent application can be filed after the invention has been disclosed to the public. This secondary incentive is usually most important in the university environment where pressure is placed on the researcher to publish.

Examination of the Application

Once the third stage is reached, the rate at which the application proceeds is no longer solely dependent on the inventor and his patent attorney but also on the Patent Office.

The patent examination stage is initiated with the filing of a patent application in the Patent Office. The patent application, containing the specifications and claims that the applicant seeks to have patented, is examined by a patent examiner who must determine whether each of the claims defines an invention that is novel and not obvious, and whether the patent application has met other statutory requirements and the regulatory and procedural requirements of the Patent Office. In his examination, the examiner conducts a search of relevant publications and patents. He reports the findings of his examination to the patent applicant. The time between the filing of the patent application and the first report, or "action, " from the examiner ranges from 3 to **18** months.

The examiner often finds a publication or patent that brings into question the patentability of one or more claims. Thus, the first action by the examiner may be a. rejection of the questionable claims. The applicant is given 3 months (which can be extended by an additional 3 months) to respond to the action. The applicant may modify the claims to overcome the rejection or may show that the rejection was unsound and should be withdrawn.

Approximately 2 months after the applicant responds, the examiner must act on the application and either allow the patent application or issue what is called a final rejection of the questionable claims. The patent applicant then has 3 months to respond: he may delete or amend claims to overcome the rejection; he may argue that the rejection be withdrawn; or he may appeal directly to the Board of Appeals in the Patent Office. If the applicant responds without filing an appeal the examiner can entirely withdraw the rejection or notify the applicant that the rejection, in its entirety or in modified form, still stands. The applicant must thereafter appeal to the Board of Appeals or abandon the patent application.

Because of the heavy workload on the Board of Appeals, 2 years may pass between the filing of an appeal and a resolution of the appeal. If the applicant is unsuccessful at the Board of Appeals, he may then appeal either to the Court of Customs and Patent Appeals or to the District Court of the District of Columbia, in which case the judicial appeal process applies. Another 12 to **18** months maybe consumed.

At any point in the examination period, the patent application may be judged allowable. The Patent Office then requires the payment of a fee by the applicant. After this payment has been made, the patent document is printed and issued. A period of 5 to 12 months may elapse between the allowance of the patent and its issuance.

The period between the filing of a patent application and the patent issuance generally ranges from **18** months to 3 or more years. The average patent-pending period is currently a little more than 2 years. In the mid-1970's, it was about **18** months, and in the 1950's, it was well over 3 years.

During the patent examination stage, an applicant may file more than one application. For example, after the initial patent application was filed, the applicant may have discovered additional information regarding the invention and may wish to supplement the original application. To do so, he must file a second patent application containing the information in the first application (old matter) and the supplemental information (new matter). This second application is termed a continuation-in-part application and maintains the benefit of the filing date of the first patent application with respect to the old matter and the filing date of the second patent application with respect to the new matter. The identical patent application may also be refiled (a continuation application), perhaps to obtain a reconsideration by the examiner. If a patent application claims more than one invention, the Patent Office can require that applications be filed for each of the inventions (divisional applications). The divisional applications need only be filed before the first application is abandoned or is issued as a patent. There is no statutory limit on the number of times that an application may be refiled as continuing applications.

While sound reasons exist, in most instances, for a patent applicant to file continuing or divisional applications, there is a potential for abuse. So long as no competitor has entered the market, the delays in the issuance of a patent work to the advantage of the patent applicant since the patent expiration is also delayed.

Interference Proceedings

Interference proceedings are time consuming. Approximately *2.5* percent of all patent applications are involved in interferences, and the figure for important inventions is higher. Interference proceedings can last 20 or more years and most interference proceedings are not completed in less than 4 years. The subject of the interference proceedings might be two or more patent applications or it might be a patent and one or more patent applications.

The time consumed during the interference proceeding will delay the issuance of a patent from an involved patent application and thus delay the expiration of the patent.

These proceedings have, on occasion, lasted so long that pharmaceutical patents have been issued ‘years after FDA premarket approval was obtained.

FOREIGN PATENTS

A U.S. patent provides the right to exclude only in the United States and its territories. Patent rights must be sought in each country in which a patent right is desired.

Although many differences exist between foreign patents and U.S. patents, only three aspects will be discussed: the duration of the patent, the types of inventions that can be patented, and the compulsory licensing of patents.

Duration of the Patent

Virtually all foreign countries have patent terms that begin on the patent application date. The patent term in most industrialized foreign countries is *20* years. The period in which a patentee can exclude others from making, using, or selling his invention is, however, considerably less than **20** years since a portion of the patent term is spent in obtaining the patent. Moreover, in countries in which the grant of a patent can be opposed by the public (opposition procedures), the patent term, may be further eroded. After the patent is granted, however, the patent owner may be able to recover damages for any patent infringement that occurred while the patent application was pending if the infringer knew or could have known of the patent application.

Extensions of patents in foreign countries generally have not been permitted in recent history except to compensate for the patent term lost as a result of war. Some of the British Commonwealth countries do, however, permit extensions (usually up to 5 years) if the patent owner has not been adequately remunerated for his invention. Prior to *1978,* Britain had a **16-**year patent term that could be extended in cases of inadequate remuneration, but her patent law now conforms with the laws in other European countries: the patent term runs 20 years from the date of the patent application and no extensions are permitted.

Patentable Inventions

The types of inventions that can be patented in foreign countries are in a state of flux. Many countries do not permit chemical claims, and some that allow chemical claims have specifically excluded such claims for pharmaceuticals. Of the approximately **120** countries that have patent systems, nearly one half do not allow claims to pharmaceuticals. Recently, many of the more industrialized countries have begun to permit chemical claims and to permit claims to pharmaceuticals, but the lesser developed countries are not following suit. In some of the lesser developed countries that do permit pharmaceutical patents, the local courts may not find the patent enforceable because it relates to pharmaceuticals. Method-for-use claims for pharmaceuticals are permitted in less than **20** percent of the foreign countries with patent systems. Some countries (Egypt and India) provide shorter patent terms for pharmaceuticals than for other chemicals.

Compulsory Licensing

Most foreign countries (including most industrialized nations) have compulsory licensing laws, which allow members of the public to demand that the patent be licensed for a *reason*able royalty. The purposes behind compulsory licensing may be twofold: to provide incentives for putting inventions to practical use, and to encourage industrial development in the country. In most foreign countries a compulsory license can be demanded if the patentee is not “working” the patented invention in the country within a certain time after the issuance of the patent. The term “working” varies in definition

from country to country. In some countries, marketing the patented invention in the country is all that is required. In other countries, the product must be manufactured in the country. In still other countries, an attempt to secure a licensee for the patent is sufficient.

Several countries also require compulsory licensing if the patent owner is not meeting national demand for the product, and several countries require licensing if such licensing is in the public interest.

Chapter 6

The Mechanics of Patent-Term Extension

Chapter 6

The Mechanics of Patent-Term Extension

INTRODUCTION

Throughout this report, patent-term extension has been discussed as a concept, but the specifics of its form have not been reviewed. The effects of patent-term extension will, however, vary depending on the technical details of the extension.

By extending the period in which a patentee may exclude others from making, using, or selling his invention, patent-term extension provides potential rewards to the patentee. However, it also delays use of the innovative technology by others. Thus, to assess the effects of patent-term extension on innovation, *one* must compare the value of the extended protection for the patentee with the reduced use of the technology by others after the original patent term expires. This comparison can only be made in terms of the type of extension that is granted.

The effects will vary depending on whether the entire patent right is extended or whether the focus of the extension is narrowed to a portion of the invention claimed in the patent. For example, a chemical patent may claim several new chemicals, only one of which is marketed as a drug. If the full patent right were provided during the extension, the patentee could exclude others from making, using, or selling any of the patented chemicals for any purpose. Under this circumstance, those aspects of the patented technology that were not subjected to the Food and Drug Administration's (FDA) premarketing review would have patent protection for more than 17 years. The rights protected during the extension could be modified in a fashion that would still provide meaningful incentives for the patentee but yet allow others to use the patented technology for some purposes during the extension.

As seen in chapter 5, claims can be made for chemicals, compositions of known chemicals, processes, or methods-for-use but not all classes of patents are considered to have equal value. The relative value of each of the classes can be further affected by modifications of the patent rights during the extension. These modifications and their implications *on* the classes of claims are discussed in the following sections.

Modifications could be directed at the scope of claims during the extension, the products, processes, and uses against which the patent could be enforced during the extension, and the remedies available to the patentee for infringement of the patent during the extension.

Two other aspects of patent-term extension will significantly influence its effects: the duration of the extension, and the obligations of the patentee during the extension.

LIMITATIONS IN SCOPE AND ENFORCEMENT

The most important factors affecting the balance between the degree of protection provided to the patentee and the extent to which the patented technology can be used by others during the extension are those relating to limitations in scope and limitations in enforcement. Although these factors are described separately, they are interactive.

Scope: A patent claim defines the breadth of the invention for which the patent rights are sought. The claim may contain many possible embodiments of the invention, and the full scope of the claim would include all of the embodiments. A limitation in the scope of the claim would result in the claim being narrowed during the extension. For example, a chemical

claim is directed to chemicals A, B, and C in its full scope. If the scope were limited during the extension to only chemical A, the making, using, or selling of chemicals B and C for any purpose would fall outside the narrowed scope of the claim and would not be an infringement.

Enforceability: A patent is enforceable against an infringement of the invention defined by the claim. In the above example, during the original term of the chemical patent, the patentee can enforce the patent against anyone in the United States who makes, uses, or sells any of chemicals A, B, or C, regardless of how the chemical is made or used. During the extension, the enforceability of the claim might be limited by conditions not expressed in the claim. For example, the patentee might only be permitted to enforce the patent against anyone who used or sold the chemical for a particular purpose. Thus, if the enforceability of the claim were limited to chemicals A, B, and C, as used for treating headaches, the claim would not be enforceable against someone who made or sold any of the chemicals for gasoline additives.

Limitations in Scope

If the full scope of the claim could be enforced during the extension, the effects of the extension on the patentee's rights and the availability of the technology for use by others would be those described in chapter 5. If, however, the scope were limited during the extension, the effects would vary depending on the way in which the scope was limited and the type of claim involved.

The scope of claim could be limited in three ways:

- Method S.1—The extension might be provided only for those aspects of the patent claims that involve the specific active chemical approved by FDA.
- Method S.2—The focus of the claim might be narrowed during the extension by restricting the parameters (e.g., temperature range, dosage amount, or type of chemical) recited in the claim to the specific value existing in the FDA approved product, process, or method-for-use.
- Method S.3—The extension might be provided only for the specific chemical (in the case of chemical claims), composition (in the case of composition claims), the specific process (in the case of process claims), or method-for-use (in the case of method-for-use claims) approved by FDA regardless of whether a parameter for each product, process, or method-for-use condition is recited in the claims.

Examples of these methods are provided in the discussion of the various types of claims. These examples are provided to help explain both the concepts involved in these methods and the distinctions between them. As will be seen in the following sections, meaningful patent protection could result if the full scope of the claim is enforceable during the extension or if the scope is restricted, according to method S.1, to the active chemical approved by FDA. Methods S.2 and S.3, however, provide little protection for composition, process, and method-for-use claims.

Chemical Claims: For chemical claims, there is no difference in the amount of protection provided by any of these methods. Since the aspect of the claimed invention involved in the specific FDA approval is a chemical, all of the methods would restrict the claim during the extensions to the specific chemical contained in the FDA approved product.

During the extension any other chemical claimed in the patent could be freely made, used, or sold by others. For example, even a minor modification of the chemical would create a different chemical and take it outside the scope of the extended patent. During the extended period, therefore, the patentee could face direct competition from chemicals covered by his claims during the original patent term. However, the competitor would have to undergo the expense of conducting safety and efficacy tests for FDA approval of the modified chemical. Moreover, the modified chemical would not be chemically and therapeutically equivalent to the existing drug and could not be generically substitututed for the patented drug. The developer of the modified product would, therefore, have to establish a market for the drug.

Because of the nonpatent barriers that supplement the patent protection, these methods provide the patentee with moderate protection.

Although it is possible that the modified chemical might have enhanced therapeutic value, the therapeutic value in most cases would be similar to that of the patented drug. Thus, considerable effort would be spent by competitors to secure FDA approval but few social benefits would accrue. The innovator could attempt to broaden the scope by securing FDA approval (and patent-term extensions) for other chemicals within the original scope of the claim, but, such efforts, while blocking competition, would be costly and would provide few benefits to society.

Composition Claims: For composition claims, the three different methods would have different effects on the amount of protection provided to the patentee and the availability of the technology for use by others.

Assume that a composition claim recites: "A therapeutic composition for treating headaches in humans comprising a unit dosage amount of chemical A or B in an inert carrier" and that the product approved by FDA consists of **0.4** milligrams of chemical A and 3 grams of sodium stearate as a binder.

If method S.1 were used to limit the scope to chemicals approved by FDA, the claim would apply to compositions containing chemical A and any carrier. Thus, the scope of the claim would be limited more by chemical than by composition, and the claim would cover many compositions for which FDA approval was not sought. The scope of the claim would still be broad and the value of the claim to the patentee would be similar to the value of a chemical claim.

If method S.2 were used, to restrict the scope to the specific values for the recited parameters present in the FDA approved composition, the claim would be limited to compositions containing chemical A and sodium stearate. The claim would still cover many compositions for which FDA approval was not sought. The value of the claim would be limited to the patentee since many possible inert carriers exist; by selecting a different, but equivalent carrier, the claim could be avoided. The modifications to avoid infringement would, however, necessitate FDA approval.

If method S.3 were used and claims were restricted to the precise embodiment approved by FDA, the claim would, in our example, be limited to compositions containing **0.4** milligrams of chemical A and 3 grams of sodium stearate. Because the claim covers only one composition it could be easily circumvented.

Process Claims: FDA, in approving a drug, also approves the processes by which it is made. The aspects of the claimed invention involved in the specific FDA approval are, therefore, the process conditions.

For example, the process claim recites: "A process for making chemical A or A' by admixing chemical X or X' and chemical Y and heating the mixture to between500 and800 *C* in the presence of a dehydrating catalyst. " The process used to make chemical A, which was approved by FDA, involves very specific conditions including amounts of reactants and purification procedures.

If extensions were based on method S.1 and the scope of claims were limited to chemicals approved by FDA, in our example the claim would be limited to a process for making chemical A using the specified reactants, a reaction temperature between *500* and **80°** C, and any dehydrating catalyst. The process could be used by anyone to make chemical A'. Many processes for making chemical A other than the one specifically involved in the FDA approval would be covered by the claim.

If method S.2 were used and the scope of claims during the extension were narrowed to the specific values of parameters in the FDA approved invention, the claim would be limited to processes for making chemical A using the specified reactants, a specific temperature, and a specific catalyst. If method S.3 were used, the claim would be limited to the precise process involved in the FDA approval including process limitations not specifically recited in the claim, e.g., the amounts of the reactants and the procedure for purifying chemical A.

Under methods S.2 and S.3, the patent could be easily avoided by minor and insignificant process modifications and the patentee would have disclosed specific process information to the public so that the scope of the claim would be known. Methods S.2 and S.3 would not provide meaningful patent protection.

Method-for-Use Claims: The method used for extending patent terms can have a significant effect on the value of method-for-use claims.

Assume that a method-for-use claim recites: "A method for relieving pain in a human comprising internally administering a therapeutically effective amount of chemical A or B" and that the FDA approval is for orally administering **10** to **20** milligrams of chemical A three times a day to relieve the pain of headaches in adults.

Under method S1, the claim would be limited to any internal administration of chemical A to relieve pain. The patentee could exercise his rights against another who used or sold chemical A for the treatment of any pain, e.g., arthritis, even though the FDA approval was only for the treatment of headaches.

Under method S.2, the claim would be limited to any oral administration of 10 to *20* milligrams of chemical A to relieve the pain of headaches. Under method S.3, the claim would be limited to the specific use of orally administering 10 to *20* milligrams of chemical A three times a day to relieve the pain of headaches in adults.

Under methods S.2 and S.3, others could use chemical A for relieving the pain of arthritis. Both of these methods present problems of enforcement since doctors could prescribe and consumers use chemical A (produced by another as an arthritis pain reliever) for treating headaches; the only remedy available to the patentee would be to sue each of the infringers individually.

Limitations in Enforcement

If no limitations were placed on enforcement, the patent could be enforced against any product, process, or use that falls within the scope of the claim regardless of the purposes for which it would be used. Thus the public would have no right to use any of the patented technology during the extension. There are, however, methods for limiting enforcement of actions during the extensions:

- Method El: During the extension the patent could be enforced only against a pharmaceutical product, process, or use that requires FDA premarketing approval.
- Method E.2: During the extension the patent could be enforced only against one who uses the claimed invention for the same therapy that was specified in the patentee's drug application and for the therapy (termed "specific therapy approved") for which FDA approval was granted.

These methods are illustrated in relation to the following example: the patentee has a chemical claim on chemical A and obtains FDA approval for treating headaches with chemical A.

Under method El, the patent could be enforced against anyone making, using, or selling chemical A as a drug, (e.g., sale of the drug for treating high blood pressure would be prohibited) but not against anyone making, using, or selling chemical A for a nondrug use, even though the nondrug use might be regulated. Thus, one could sell the chemical as an herbicide. Method E.1 therefore enables the public to use the patented technology during the extension for other than drug uses. Such use would not result in competition for the innovator's drug.

Under method E.2, the patent could only be enforced against anyone making, using, or selling chemical A for treating headaches. Method E.2 could significantly affect the patentee's incentives but could provide the public with a greater right to use the patented technology during the extension,

From the standpoint of the patentee, method E.2 presents a disadvantage since the patent would be enforceable only when the drug is used for the specific therapy approved. A competitor could obtain FDA approval and manufacture and sell the identical drug for a different therapy; yet the doctor could prescribe or the con-

sumer could use the competitor's drug for the specific therapy approved. As with method-for-use patents discussed in chapter 5, the patentee may not have an effective mechanism to enforce his patent. His only remedy would be to sue each of the prescribers or users for patent infringement.

From the standpoint of promoting pharmaceutical innovation, method E.2 (limiting enforcement to the specific therapy approved) could be beneficial for developing new therapies for existing drugs. A competitor would have an incentive to develop another pharmaceutical use for the drug so that he could market it. The patentee would also have an incentive to develop other pharmaceutical uses so that those uses would be covered during the extension. While some uses developed may provide significant improvements in health care, others may not.

Interaction Between Limitations of Scope and Limitations of Enforcement

By combining scope limitations with enforcement limitations, one can achieve a desirable balance between meaningful patent protection for the patentee and public use of the patented technology during the extension. Three combinations of the methods discussed appear to be most attractive from the standpoint of balancing these sometimes conflicting objectives. Each combination strikes a different balance.

Combination A:

- Limitation in scope: Method S. I—Claims restricted to the chemical approved by FDA.
- Limitation in enforcement: Method E.l — Enforcement only against FDA approved product, process, or method-for-use.

In combination A the scope of the claim would be limited to the chemical approved by FDA, and the patent could be enforced only against products, processes, or methods-for-use which were subject to FDA approval. Of the three combinations, this one would provide the most protection to the patentee.

Combination A would have the following effects:

- the patented technology could be used for all but pharmaceutical purposes;
- others could produce minor variations of the chemical and use the technology for drugs;
- others could not develop the approved chemical for new FDA uses; and
- the patentee could enforce the patent against anyone who marketed an identical drug regardless of the drug therapy for which it was prescribed or used.

Combination B:

Ž No Imitation in scope.
- Limitation in enforcement: Method E.2—Enforcement limited to specific therapy approved.

With combination B, the claim would be interpreted to its full scope; however, the patent could only be enforced against anyone who made, sold, or used the patented product, process, or method-for-use for the specific therapy approved. This combination differs from combination A in that the claim would be broader with respect to the active chemicals covered, but the patented technology could be used for other drug therapies.

Combination B would have the following effects:

- the patented technology could be developed for all uses other than the specific therapy approved by FDA; and
- enforcement would not be practicable against an identical drug developed for a different therapy but prescribed or used for the patentee's therapy.

Combination C:

- Limitation in scope: Method S.1—Claims restricted to chemical approved by FDA.
- Limitation in enforcement: Method E.2—Enforcement limited to specific therapy approved.

Under combination C, the scope of the claim would be linked to the chemical or chemical and use approved by FDA, and the patent could only be enforced against the sale or use of the patented product, process, or method-for-use

for the specific therapy approved. Of the three combinations, this combination would provide the least protection to the patentee.

Combination C would have the following effects:

- others could make, use, and sell minor variations of the chemical for uses identical to the specific therapy approved;
- others could develop the patented technology for all uses other than the specific therapy approved; and
- enforcement would not be practicable against an identical drug developed for a different therapy but prescribed or used for the patentee's therapy.

LIMITATIONS IN REMEDIES

In the original patent term a patentee can secure an injunction against an infringer and obtain damages for the infringement. Proposals have been made to limit the remedies available to the patentee during the extension period. The most restrictive proposal would not permit the patentee to exclude others from making, using, or selling the patented drug but would require him to license the invention for a reasonable fee (compulsory licensing).

If the objective of extending the patent term is to increase the potential for returns to the innovating firm, compulsory licensing would probably not accomplish that objective. The benefits of a reasonable royalty are likely to be less than the benefits received by the patentee through the sales of products. Moreover, the determination of a reasonable royalty can be difficult, expensive, and time-consuming. Burdens would be placed on both the administrators of the law and on the firms contesting the royalty. Most significantly, compulsory licensing would create an uncertainty which would not be resolved until a request for a license was made and granted. For these reasons, compulsory licensing could detract from any incentive for pharmaceutical innovation provided by patent-term extension.

There are, however, intermediate grounds. For example, compulsory licensing could be required only if the firm were not satisfying the needs of the public or if the licensing were essential for national security (e.g., to assure more than one source of supply in the event of a catastrophe). Such intermediate grounds presently exist to protect national interests. Title 28, section **1498** of the U.S. Code, provides that the United States can use or manufacture, or have used and have manufactured for it, a patented invention without the patentee's permission. The patentee however, is entitled to reasonable compensation for such use and manufacture.

THE DURATION OF THE EXTENSION

Several proposals have been made for establishing the duration of the extension.

- the duration could be a period which enables the innovator to obtain adequate remuneration for the invention, and would be decided on a case-by-case basis (proposal D.l);
- the duration could be a predetermined and uniform period (proposal D.2);
- the duration could be the period between the date on which the innovator was prepared to commercialize the invention and the date on which marketing approval was obtained (proposal D.3); or
- the duration could be a period corresponding to at least a part of the time consumed in the regulatory review process (proposal D.4).

Each of these proposals could be modified in such a way that the extension would be terminated if the drug were not being sold by the innovator firm or if the patented technology (e.g., in the instance of a patented process) were no longer being used for the drug.

Proposal D.1: Adequate remuneration.

This method would pose significant administrative problems but because very few new drugs are marketed (between 40 and 100 new drug applications (NDAs) are approved per year), the problems would be small in number. More significantly, the determination of adequate remuneration would be subject to controversy. The extension is most meaningful to the research-intensive companies as it applies to drugs that have been most profitable during the original patent term. Unless the extension included these drugs, the economic benefits from pharmaceutical innovation provided by patent-term extension would be significantly reduced.

Because this method would not provide the public with notice that the patent was being extended until the expiration date of the original patent term was approaching, potential competitors might not initiate steps for manufacturing and marketing the drug until they knew that no extension would be granted. Thus, if the administrative proceedings were lengthy, a de facto extension might result.

Proposal D.2: Predetermined and uniform period.

Extending the patent term for a predetermined period, e.g., 7 years, might result in inequities, with some drugs being protected for more than 17 years. There would be no direct correlation between the regulatory approval time and the patent life. This method, however, would be easy to administer.

Proposal D.3: Marketing delay compensation.

Determining the delay between the time when a firm was ready to market a product and the time the product was approved by FDA would be difficult and the determination would be subject to dispute. Making these determinations would be an administrative burden. Moreover, firms would be encouraged to prematurely proceed with manufacturing plans in order to increase the extension which could be obtained. If the firm timed its manufacturing plans according to the progress of the drug through FDA, the measured delay might be unduly brief.

Proposal D.4: Time consumed in the regulatory review process.

This proposal, which makes the duration of the extension dependent on the time consumed by the regulatory proceedings, overcomes some of the difficulties and inequities of the other three proposals. Because the dates that premarketing approval procedures begin and end are known, this method would not impose a great administrative burden.

Basing the period of extension on the regulatory review period could compensate the patentee for time he would have spent developing and testing the drug even if FDA did not exist. The likelihood of this occurring would depend on when the period eligible for compensation begins. If the objective of patent-term extension is to encourage pharmaceutical innovation, the issue of whether the patentee receives excess compensation may not be of prime importance.

If proposal D.4 were adopted, the innovators might delay the testing needed to secure premarketing approval. But, such dilatory tactics would also delay the marketing and would therefore be disadvantageous to innovators. If, however, the new drug would compete with an existing drug of the innovator firm, dilatory tactics might be used. But such tactics are discouraged by the courts. If a patentee has purposefully delayed steps needed for FDA approval, the court may refuse to enforce the patent, but proving purposeful delay can be quite expensive and time-consuming.

The effects of this proposal would depend on when the period eligible for compensation begins. In general, the earlier in the regulatory process that the clock starts ticking for determining the duration of the extension, the longer and more economically meaningful the patent-term extension will be. There are a number of dates at which the clock could start.

The period could begin on the date that the NDA was filed with FDA. The period between NDA filing and final approval is frequently about 2 to 3 years, This amount of time might be insufficient to provide significant additional incentives for pharmaceutical innovation, A predetermined period of time could, however, be added to the extension. In some instances, adding a predetermined time would more than compensate for time lost in the regulatory review process.

The period eligible for compensation might instead begin on the date that the first clinical trials in the United States were initiated. The time between the initiation of clinical trials and the approval of the NDA for new chemical entities is frequently **5** to **8** years. Beginning the clock at the first clinical trials could result in significantly extended patent terms.

Alternatively, the period eligible for compensation could begin on the date on which the investigational new drug (IND) application is filed with FDA. The filing date of an IND is easy to determine and the filing of an IND is a precondition to the initiation of clinical trials in the United States. The IND could be filed long before clinical trials began.

Another proposal would begin the eligibility period when substantial preclinical animal tests (e.g., tests of longer than **6** months) were started. These tests are frequently initiated prior to the filing of an IND.

Maximum Extension Period

A maximum period of extension has been proposed to eliminate extensions of long duration and to discourage innovator firms from delaying the premarketing approval process to obtain later expiration dates on extensions.

The effects of the extension will depend on the length of the extension. If the maximum period is too short, the potential for incentives for pharmaceutical innovation may be too small to be meaningful. If the maximum period is too long, the social costs of innovation may outweigh its benefits.

The maximum extension could simply be a specific number of years with no qualifications. Proposals have been made, however, that would prevent the extension from going beyond a fixed time from the filing of the first patent application.

This constraint could act as a disincentive for delaying proceedings in the Patent Office. If the date of the filing of the first patent application were selected as the starting point, the patentee would receive no benefit from filing continuation or divisional applications to delay the issuance of the patent application.

OTHER CONSIDERATIONS

There are several other aspects of patent-term extension that must be addressed. Should extensions be granted to marketed drugs that are ordered off the market for further testing? Should patent extensions be granted in cases involving alternative uses of drugs, since alternative uses also must be approved by FDA?

With respect to the first question, extending a patent to compensate for the period when the product is ordered off the market could pose difficulties. If an extension were granted only when a Federal regulatory agency ordered a withdrawal, the innovator firm might be reluctant to voluntarily withdraw the product until such an order was issued. In any event, drugs are withdrawn from the market infrequently.

With respect to the second question, drugs frequently possess efficacy in more than one therapeutic area. The ability to extend the enforceability of the patent to other therapeutic uses that the patentee has developed might promote innovation. If the enforceability of the patent were limited during the extension to the specific therapy approved, the additional extension would not have any effect on the length of the extension for the first use. If the enforceability were not so limited, providing an extension for another therapy would also extend the patent

for the first therapy, and the patentee could therefore increase the effective patent term for the first therapeutic use.

The Number of Patents Extended per Drug

It is possible that more than one patent may provide protection to a drug. The issue dates of the patents may differ, thereby allowing the patent protection provided by a later-issued patent to extend beyond the expiration of the first patent. Patent-term extension could be restricted to only one patent per drug or could apply to each patent covering the drug. Depending on the method used for determining the length of the extension, permitting more than one patent to be extended could result in extensions that expired at different times. If the method for determining the extension corresponded to the effective patent term lost due to premarketing review, no patent could have its term extended beyond 17 years.

The Obligations Incurred by the Patentee

In the normal operation of the patent system, a patent is granted and, in return, the public receives a disclosure of the invention and a description of its best mode. The patentee incurs no further obligations (other than maintenance fees) during the patent term.

Proposals have been made to impose additional obligations on the patentee in return for the extended patent period:

1. after the extension the patentee could be required to provide potential competitors with available data (results from clinical and toxicity testing) needed for securing FDA approval for generically equivalent drugs;
2. after the extension the patentee could be required to relinquish all rights to the trade name;
3. after the extension the patentee could be required to allow others to use the size, color, and shape of the drug that is coming off patent;
4. during the extension maximum prices for the drug could be mandated; and
5. patentees could be required to use a portion of the revenues derived during the extension for research and development.

Appendix

Appendix

Patent-Term Extension for Other Industries

The Medical Devices Industry

The medical devices industry manufactures products that are used in the diagnosis, treatment, or prevention of diseases or conditions. The benefits of these products reside in their ability to affect the structure or function of the human body through means other than chemical action. [1]The definition includes simple products, such as surgical instruments and orthopedic shoes, and vastly complex products, like cardiac pacemakers and diagnostic equipment. The Food and Drug Administration (FDA) regulates this industry, and only in certain instances is premarket approval required.

The medical devices industry emerged after World War II as a result of technological developments. In the last two decades, the industry has experienced substantial growth in sales: between 1974 and 1980 sales increased by more than 100 percent, with **1980** sales estimated at about $11.5 billion. [2]The industry is comprised of several thousand firms, many of whom are quite small.[3]Several relatively large firms in the industry appear to play a dominant role in the market. [4] According to one source, the larger firms constitute the stable portion of the industry; but the turnover rate for smaller firms is high. This difference does not derive from differences in the types of devices produced. Since a company need not have a large minimum plant size to produce medical devices, it appears that medical devices in general are not characterized by great economies of scale. [5]Thus, entry is not dependent on large amounts of capital.

Sales in the industry are made through a large independent distributor network. Recently, there has been a shift in the character of this network from small local/regional dealers to major national suppliers. [6] Under these circumstances, larger manufacturers have a distinct advantage because they are capable of delivering the quantity a national distributor would require. Insofar as the larger medical-device manufacturer may tend to be a multiproduct concern, its reputation in one line will influence a distributor's decision to carry another of its product lines. Thus, the development of a national distribution network may act as an entry barrier for the smaller medical device company.

For several reasons, the patent system is not as important in this industry as it is in the pharmaceutical industry. First, there are generally many more substitutes available for any one medical device than there are substitutes for drugs. Second, there is a very high turnover in technological achievements in the industry and products are often outmoded before their patents expire. Third, devices are generally simpler to invent around than drugs and the patent, therefore, may provide little protection from imitators. Fourth, premium prices commanded by patented medical devices may not be as great as premium prices in the pharmaceutical industry because some downward price pressure is exerted through an informed and price-conscious market (hospitals, laboratories, and independent distributors, etc.). Thus, while the patent may be viewed by the industry as one of several avenues for the minimization of risk, it is typically not the overriding incentive for innovative activity.

The growth in sales and in the number of firms in the industry seems to indicate a reasonable degree of competition and therefore an environment conducive to innovation. However, insufficient information exists for a reliable evaluation of the industry's competitiveness. First, we have not studied how concentrated any particular device area may be within the industry (e. g., we do not know if one firm or a thousand produces X-ray equipment). Second, regulation of the industry began recently (1976) and its effects may not yet be evident.

FDA began its present scope of regulation of medical devices in 1976 with the passage of the medical device amendments to the Food, Drug, and Cosmetic Act. Prior to 1976, some devices such as soft contact lenses, IUDS, hemostats and others, fell under the purview of FDA because the agency had these devices classified as "drugs. " As well, prior to

1 Health Industry Manufacturers Association, Summary Report, ' (Washington, D C HIMA, October 1978), p. 8.

2Predicasts Inc Value of Shipment, (SIC code 2831 3841-43, 3693) 1980

3Health Industry Manufacturers Association Summary Report,' reported over 1,000 members in 1978 with 72 percent having sales less than $10 million Thus 280 companies had $73 billion of the 1978 $8 billion sales figure.

4Manufacturers of Medical Devices Join the Choruses of Regulatory Critics *The National Journal* (Sept 20, 1980) p 1566, reported more than **5,000 manufacturers** in 1980

5Office of Planning and Evaluation, Economics Staff Study 53, Food and **Drug** Administration (Washington, D C FDA, 1980)

6Ibid

7SRI International **Structure** of the **U S** Medical Supply Equipment and Dev 1Icc\Indu\t ry (Stanford, Calif. SRI In ternationa 1 Print ing, 1979)

1976, FDA had postmarked surveillance regulatory powers for devices. That is, FDA could remove a device from the market if it was not safe and had power to ensure that the product's label was not misleading. Thus, while regulation of the industry is not as recent a phenomenon as it might appear, the scope of the regulation has widened considerably since **1976.** Currently, the thousands of medical device products are divided among three groups. Class I devices are noncritical items such as bedpans and are subject to generally the same standards of regulation as all devices were prior to **1976,** that is postmarked surveillance techniques. Class II devices include items thought to require something more than Class I regulation to ensure safety but not as much control as a premarket approval. Regulation of Class II devices takes the form of setting performance standards. Class III devices (those previously classified as "drugs" as well as others whose use can be similarly dangerous) require premarket approval. The process for obtaining Class III premarket approval is quite similar to that required for drug approval.

Devices can short-cut the regulatory procedures by being judged "substantially equivalent" to pre-1976 devices. In the 4 years since the medical devices amendment was enacted, about 98 percent of premarket notifications were declared "substantially equivalent."[7] Notifications are required 90 days prior to the marketing of a device to ensure that it will not be a member of Class III and require extensive testing.

The full effect of these regulations on the competition and innovation in the industry has not yet been felt. The uncertain}' about future regulations may change the weight of the patent as a factor in the innovative process. However, some general tendencies can be noted. The performance standards for Class II devices may dampen innovative activity, as the standards need only be met, not exceeded, to obtain approval.

In addition, FDA has been exploring the concept of voluntary standards for Class II devices. Larger device companies, by virtue of their larger voices, would appear to be able to have their products' standards emerge quickly and effectively as the accepted measure of voluntary standards, To the extent that smaller companies' voluntary standards are different from those of large companies, competition and innovation may become more difficult for smaller device manufacturers.

FDA regulations concerning "substantially equivalent" devices may hold the potential for dampening competition simply by encouraging manufacturers to produce devices that are based on minor changes in old products. However, such products may not be able to obtain patents. If manufacturers claim substantial equivalency at FDA, they may injure their chances to get a patent approved, i.e., an old device may be considered prior art for patent purposes. On the other hand, the issuance of a patent may be considered proof that a device is not substantially equivalent because patents are supposed to be granted for new and unobvious inventions. Thus, the patent may become much less important than it currently is for devices similar to existing products. By the same token, patents may become more important to first entrants with wholly new products.

Two other trends that may affect the industry's competitiveness should be noted. First, while medical devices are more price sensitive than pharmaceuticals, this industry is becoming more subject to price insulation from third-party reimbursement. [a]Compared to most industries, the medical device industry is considered price insensitive, however, hospital cost containment programs often look toward medical devices for areas of savings. Future competition may increasingly be based on other considerations in addition to price and, to the extent that this leads to higher profits, entry may be encouraged. It has been reported that the larger device manufacturers have generally been generating far more cash than they are able to reinvest profitably and thus can be expected gradually to lose their current market shares unless reinvestment alternatives emerge.[9]

In summary, the medical devices industry is likely to continue to be reasonably competitive and innovative in many product lines and patent-term extensions may, therefore, be unnecessary. However, for Class I and II devices, the level of innovation may depend on the balance struck between the attractiveness of obtaining a patent and the desirability of receiving rapid approval for "substantially equivalent devices." In this regard, patent-term extensions could have a limited, but perhaps important, positive effect by shifting the balance toward innovation.

Finally, regulation of this industry is in the early stages. As more devices become available for uses with potentially hazardous side effects, more aggressive regulatory measures may be seen in the future; that is, technological sophistication may lead to a larger portion of devices being classified as Class III (those requiring premarket approval).

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[7]"New Device Introductions on the Rise," in *Devices and Diagnostics Letter vol. 1,* Aug. 12, 1980.

[a]Arthur Young & Co., "A Profile of the Medical Technology Industry and Governmental Policies," draft final report (Washington, D. C.: Arthur Young & Co. Printing, Mar. 31, 1981), pp. IX-7.

[9]Mitch and Martinelli, "An Analysis of Business Performance in the Health Care Industries," *Business Economics,* March 1980.

The Pesticide Industry

Because the pesticide industry and the pharmaceutical industry are subject to similar regulations, the effects of patent-term extension will be similar for the two industries.

Companies selling the most pesticides are often very large and diversified; pesticide sales frequently account for 20 percent or less of company sales.[10] The pesticide industry manufactures herbicides, insecticides, and fungicides, all of which are subject to premarket regulatory approval by the Environmental Protection Agency (EPA). The products are regulated under the Federal Insecticide Fungicide and Rodenticide Act which was amended in 1972 and now requires a demonstration of human safety. As in the pharmaceutical industry, the more stringent requirements have increased the costs and times associated with research and development. The regulatory process in 1975 required about 7 years to complete in contrast with a little less than **3** years in 1960.

The measures of innovation available in the pesticide industry indicate that innovation has, thus far, been virtually unaffected by the increased costs and times required for regulatory approval. Table A-1 below illustrates a steady rate of new pesticide chemicals being registered per year in the United States between 1967 and 1979. It should be noted that fluctuations in pesticide registration are primarily a function of legal and administrative measures at the EPA and are not necessarily a sound measure of innovation in the industry.

Figure A-1 illustrates the growth in research and development (R&D) expenditures in both constant (1967) and current dollars. As can be seen, real growth in R&D expenditures has occurred, with particularly evident spurts taking place after 1975, when one would have expected the effects of the 1972 amendments to be felt.

In table A-2 below, we see similar constant growth in sales (at least for 1970-76).

No measure of the qualitative value of pesticides was available to this study. One can reasonably assume that regulatory requirements for efficacy did not produce a decline in the value of pesticides marketed since 1972.

The research companies appear to be continuing to increase R&D expenditures at the present time, regardless of the trends in patent life. Uncertainty exists as to whether R&D expenditures would increase more rapidly with patent-term extension or whether, without the extension, R&D expenditures would continue to increase if effective patent lives decline.

One important characteristic of the pesticide industry that is dissimilar from the pharmaceutical industry is the role of the Federal Government in pesticide research and development. The Conservation Foundation reports that the Department of Agri-

[10]The Conservation Foundation, "Product Regulation and Chemical Innovation," March 1980, p II-8

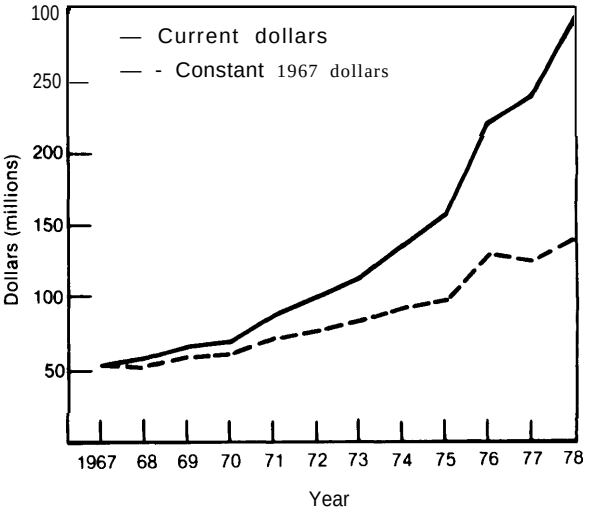
Table A-1.— New Pesticide Chemicals Registered in the United States, 1967-79

Year	Total number[a]
1967	16
1968	18
1969	14
1970	10
1971	4
1972	17
1973	13
1974	21
1975	34
1976	12
1977	4
1978	5
1979	17

[a]Herbicides, insecticides, fungicides, and others

SOURCES Organization for Economic Cooperation and Development, "Regulation and Innovation in the Chemical industry—A Preliminary Assessment of the Impact of Recent Chemicals Legislation," p 28; and The Conservation Foundation, *Production Regulation arrd Chemical Innovation,* March 1980, p III-14

Figure A-1.—Pesticide R&D Expenditures, Domestic Manufacturers Reporting to NACA, 1967-78



SOURCE: National Agricultural Chemicals Association, Industry Profile Surveys.

Table A-2.--U.S. Pesticide Sales in 1970 Constant Dollars

Year	Total sales (millions of dollars)
1970	$ 70
1971	81
1972	91
1973	91
1974	93
1975	107
1976	118

SOURCE Organization for Economic Cooperation and Development, "Regulation and Innovation in the Chemical Industry—A Preliminary Assessmentoftheimpact of the Present Chemical Legislation," p.29,

culture and the State experiment stations spent $332.6 million on research and implementation of pest control and pest management programs in 1978.[11] Several other Government agencies contribute to pest control research as well. While Government agencies also contribute to pharmaceutical research, the proportion of those funds as a percentage of the total is smaller. In cases where the funds support industry research which, in turn, produces an industry-owned patent, patent-term extension may entail double rewards.

Some of the similarities between the pesticide and pharmaceutical industries are also worth highlighting here in order to provide additional understanding of the possible effects of patent-term extension. First, while some 80 companies actually produce pesticides, another 5,300 are pesticide formulators, or companies involved in the combining and packaging of pesticide products for specific uses. As with the production-intensive pharmaceutical firms, the patented innovations made by formulators will not benefit from extensions of the patent term.

Finally, the pesticide industry has an analogous situation to the "orphan drug" research problem in the pharmaceutical industry. Minor crops do not present enough potential market for a pesticide company to invest in research for that crop. Here patent-term extensions also cannot be expected to induce firms to increase expenditures for minor crop research.

The Chemical Industry

The title of this industry is somewhat misleading; although pharmaceuticals and pesticides are chemicals, they are not meant to be included in this discussion. The chemicals considered here are basic industrial chemicals that are used to make other chemicals or products. Also included are dyes, pigments, paints, plastics, synthetic rubber, and synthetic fibers. The vast majority of the industry's sales are of intermediate goods; that is, they are used to make other products which are then used by consumers.

Chemical products, other than pharmaceuticals, pesticides, food additives, and cosmetics are regulated under the 1976 Toxic Substances Control Act (TSCA), which is administered by EPA. TSCA, in contrast to the laws regulating pharmaceuticals and pesticides, does not require Government approval before a product can be marketed. It requires only that the manufacturer submit a notice to EPA 90 days before he intends to begin manufacture. The notice must contain information about the use of the chemical, the anticipated volume of production, and the expected exposure of workers and others to the chemical, but EPA cannot require manufacturers to submit specific tests with the notice. If the notice does not contain enough information for EPA to evaluate the risks which may be posed by a chemical and if there is reason to believe that the chemical may pose a risk, the agency can delay manufacture of the chemical until adequate information is submitted. If the agency finds that a chemical for which a notice has been submitted will pose an unreasonable risk, it can impose any of a wide variety of restrictions, including a prohibition on manufacturing the chemical.

Because EPA is given only 90 days to review a chemical notice (the 90-day period can be extended up to 180 days), patent-term extension will not be applicable to the great majority of chemical products. Some new chemicals will fall into categories of chemicals which are required to be tested under section 4 of the Act, and for such chemicals a patent extension for the period it takes to conduct the required tests is meaningful. Manufacture of a chemical can also be delayed if the manufacturer submits inadequate information (TSCA sec. 5(e)) or if EPA finds that the chemical will pose an unreasonable risk to health and the environment (TSCA sec. 5(f)). Patent-term extension for chemicals delayed under section 5(e) or 5(f) might reduce the incentives for firms to conduct adequate testing or provide adequate information, since there would be no patent penalty for not doing so. Patent-term extension could be abused by premature filing of a notification without previously conducting adequate testing or withholding pertinent information.

[11] Ibid., p 11-10.

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