Chapter 2

The Issue in Brief

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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.

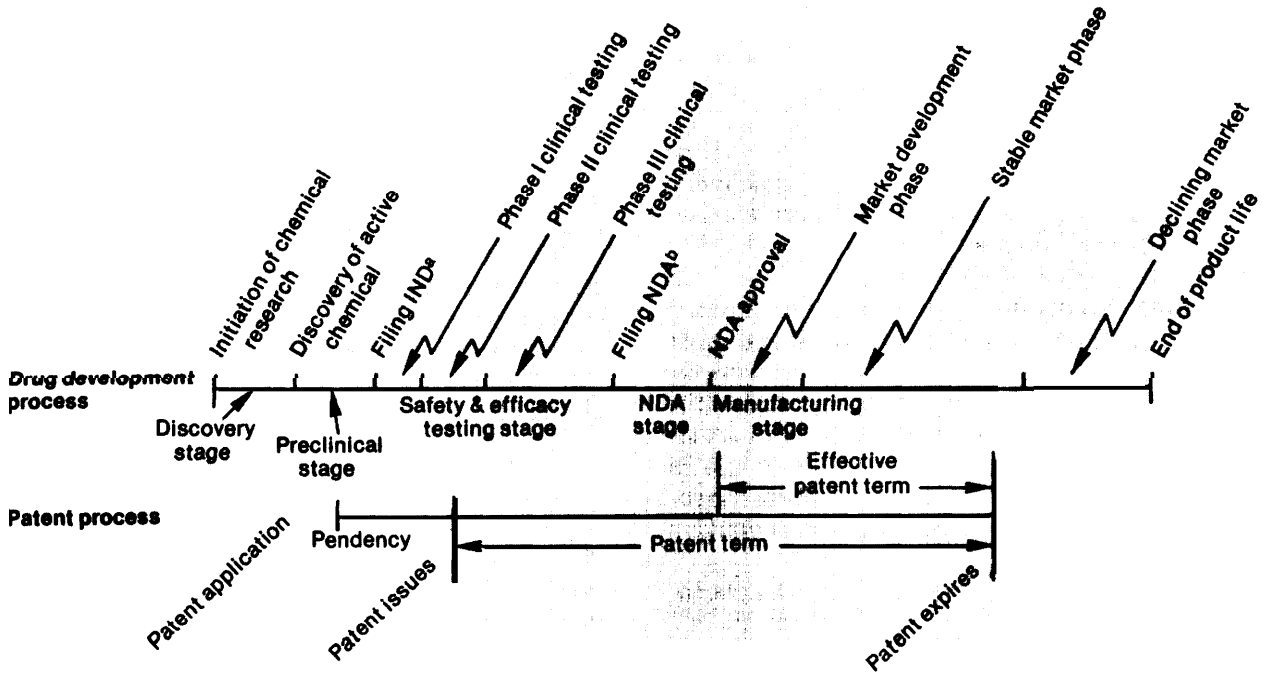
[1] William M. Wardell, "The History of Drug Discovery, Development and Regulation, " in *issues in Pharmaceutical Economics,* Robert I. Chien (cd.) (Lexington, Mass.: Lexington Books, 1979).

[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,*