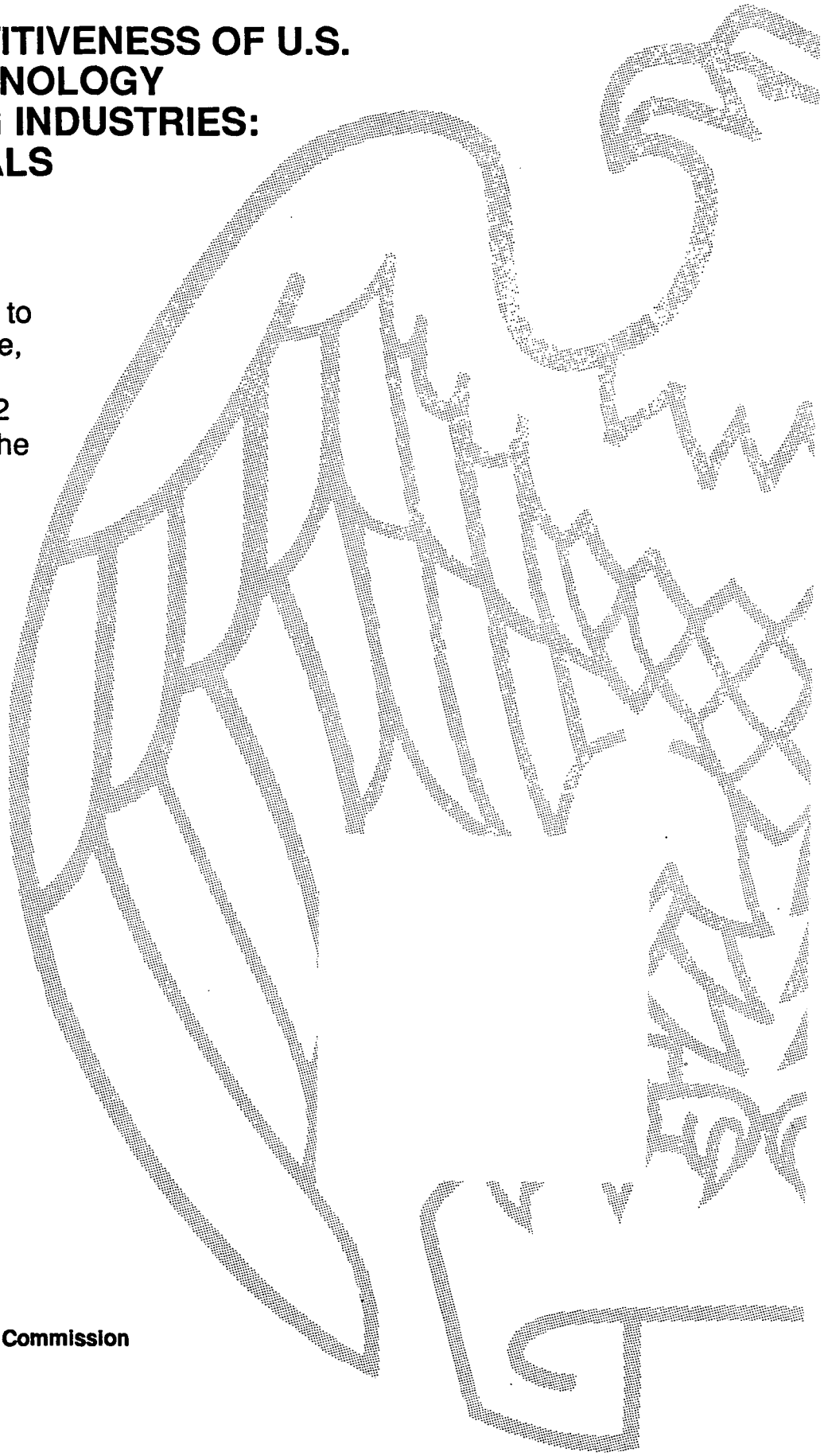
GLOBAL COMPETITIVENESS OF U.S. ADVANCED-TECHNOLOGY MANUFACTURING INDUSTRIES: PHARMACEUTICALS

A Summary of the Report to the Committee on Finance, United States Senate, on Investigation No. 332–302 Under Section 332(g) of the Tariff Act of 1930



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INTRODUCTION

The globalization of the pharmaceutical industry in recent years and ongoing concerns regarding the viability of the United States industrial base have led to an increasing focus on the activities of operations located in the United States and on the operations of U.S.-owned corporations in the international market. Although considered globally competitive by many, the U.S. pharmaceutical industry faces a number of pressures that cumulatively could have a significant adverse impact on its future competitiveness. These factors and their effects on the industry are the focus of the Commission report, inv. No. 332-302, entitled "Global Competitiveness of U.S. Advanced-Technology Manufacturing Industries: Pharmaceuticals" (henceforth referred to as "the report"). This publication summarizes the issues presented in that report.[1]

The report, prepared for the Senate Committee on Finance, identifies and analyzes the principal determinants of competitiveness associated with the U.S. pharmaceutical industry. The report addresses such factors of competitive performance as U.S. and foreign government policies, research and development (R&D) productivity, and structural change within the industry to provide an overall assessment of the performance of the U.S. industry during the past 5 to 10 years. The report also examines these factors in Western Europe and Japan.[2] The discussion of the impact of the potential implementation of policies such as price controls and cost-containment programs in the United States on the future competitiveness of the U.S. industry is drawn, in large part, from the current impact of similar policies enacted in Western Europe and Japan.

The global pharmaceutical industry transcends geographical barriers and distinctions of geographical boundaries have been further blurred by recent mergers in the industry that have created entities such as the "transnational" SmithKline Beecham.[3] Aggregate measures of the industry's performance can be constructed on the basis of either geographic location or ownership. Many data sources evaluate the industry in terms of geographic location (i.e., by including the activities of foreign subsidiaries producing in a given location). Evaluation in terms of ownership on the other hand, is reasonable in that profits may be repatriated to the home country.[4] Most of the industry-level information included in this report has been collected on the basis of geographic location, unless otherwise indicated.

In general, government policies affect all firms selling or producing in a particular country/region, regardless of parentage. It is important, however, to distinguish between policies that affect the competitiveness of the suppliers in any given geographical area and those that affect the profitability of the global industry. It should be noted that inasmuch as a given country's industry may derive much of its profits from its home market, policies implemented in that country, such as slower regulatory approval procedures, could have more of an impact on domestic firms than on foreign firms operating there. Considering these effects, this report attempts to assess the ability of the United States to maintain its preeminence in the pharmaceuticals sector, particularly its potential to retain its share of global sales and R&D productivity.

The data presented in the report were gathered from primary and secondary sources of information and by extensive interviews with industry, associations, and government officials in the United States, Western Europe, and Japan. Information was also obtained from the public hearing held at the Commission on January 17, 1991, in Washington, D.C.

Products

Pharmaceutical products[5] are used in the prevention, diagnosis, alleviation, treatment, or cure of disease in humans or animals.[6] Pharmaceutical products can be grouped in several classes, including ethical preparations,[7] generic (nonpatented) products, and proprietary products.[8] Ethical products accounted for about 80 percent of sales of pharmaceuticals worldwide during 1988-89.[9]

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[1] Many of the quotes and statements presented in this summary are drawn directly from the report. As such, the cites for these appear in various chapters of the report. The conclusions, and any inferences, herein are based on the analysis found in the report.

[2] For the purposes of this study, Western Europe is defined primarily as the EC and Switzerland. The Japanese industry, although historically not as innovative as those in the United States and Western Europe, is expected to become a strong competitor within the next 10-20 years primarily as a result of its efforts to expand globally.

[3] Although SmithKline Beecham is considered by many to be a "transnational" company, it should be noted that the firm's global headquarters are in London. SmithKline USA is based in Philadelphia, Pennsylvania.

[4] See Henry G. Grabowski, "Innovation and International Competitiveness in Pharmaceuticals," *Proceedings of the 2nd International Joseph Schumpeter Society Meetings* (Ann Arbor, MI: University of Michigan Press, 1990), pp. 167-168.

[5] In this report, the terms "pharmaceutical preparations," "pharmaceutical products," and "drugs" are generally used interchangeably to refer to pharmaceuticals in dosage form. Any exceptions are explained in context in the text. The term "new chemical entity," or NCE, is used as indicated in footnote 10.

[6] *Stedman's Medical Dictionary*, 23rd edition, 1976, p. 423.

[7] An "ethical" product is one that is available only through prescription. Ethical products can be either patented or nonpatented (i.e., generic).

[8] Proprietary products are nonprescription, over-the-counter (OTC) products. OTC products are not discussed in detail in the report.

[9] Pharmaceuticals are defined under the Standard Industrial Classification (SIC) code 283 "Drugs," which, in turn, includes SIC 2833 "Medicinal Chemicals and Botanical Products" and SIC 2834 "Pharmaceutical Preparations." The latter two categories have traditionally constituted the majority of shipments under SIC 283 (SIC 283 also includes two other categories: 2835 (In Vitro and In Vivo Diagnostic Substances) and 2836 (Biological

The report focuses primarily on innovative companies, including those companies that produce biopharmaceuticals.[10] Innovative companies are those which develop new chemical entities (NCEs)[11] through extensive R&D programs and market them as brand-name ethical preparations. Many also market generic products.[12] By 1995, the U.S. patents on approximately 200 products will expire, potentially expanding the generic market by approximately $6 billion.[13] To offset the increasing competition from generics, innovative firms are providing active ingredients to generic formulators, entering the over-the-counter (OTC) market with additional products (which, in some cases, were available only by prescription), and investigating novel drug-delivery systems.[14]

Global producers

In 1990, the world market for ethical pharmaceutical products was valued at about $147 billion.[15] The top three companies in that year, in terms of ethical drug sales, were Merck (United States), Glaxo Holdings (United Kingdom), and Bristol-Myers Squibb (United States).[16] The top 80 pharmaceutical firms worldwide accounted for about 90 percent of global sales in 1989. Of these 80 firms, U.S.-based companies accounted for approximately 40 percent of global sales of ethical pharmaceuticals (see Fig. 1-1). The European-based firms in this grouping also accounted for about 40 percent of world sales, the majority made by firms in the United Kingdom, West Germany, and Switzerland.

Of the top 20 firms in the global industry in 1990, 9 were based in the United States.[17] One reason for the U.S. industry's strong position in the world market is its level of innovation, which, in turn, is based on a number of factors including the domestic industry's continuing commitment to high R&D expenditures; the productive relationship between industry and university scientists in basic research; the size of the domestic market; the industry's expansion overseas; and, perhaps most important, the "relatively unencumbered" U.S. economy, in that it has not to date implemented price controls on pharmaceuticals and is considered by many to be the country with "the last of the free pricing." The U.S. industry was a leader in innovation during 1975-89, developing the majority of the globally successful products introduced during this time period. The industry routinely allocates approximately 17 percent of its sales of ethical pharmaceuticals to R&D, or approximately three times the level allocated by the remainder of the chemical and related-industries sector.[18] Companies must finance R&D activity internally through profits, through external financing, or both. In addition, the industry requires access to a highly developed research base to develop innovative pharmaceutical products and improve R&D productivity.

The U.S. market, largest in the world, was valued at about $43 billion in 1989, compared with about $31 billion for Japan, the second largest market. As an aggregate, Western European sales were valued at about $44 billion. The three largest markets in Western Europe in 1989 were Germany (23 percent), France (21 percent), and Italy (19 percent). In 1986, total assets of U.S. affiliates of European-based companies were estimated to be valued at approximately $9.7 billion, of which $8.9 billion, or 92 percent, was accounted for by firms of Western European heritage. Of the Western European firms, the largest share of the assets was attributed to firms with parents located in Switzerland (56 percent). Japanese-owned firms represented approximately 3 percent of the total.[19] In spite of the relatively recent entry of Japanese firms into the U.S. market on a majority-owned basis, about 18 Japanese companies with equity ownership of

[9]—*Continued*
Products, Except Diagnostics)). The two major manufacturing stages for pharmaceuticals are: (1) the production of pure pharmacologically active chemicals, or active ingredients, in bulk form either by conventional methods or through use of bioengineering procedures (SIC 2833) and (2) the formulation of these concentrated pharmacologically active components into dosage form, or pharmaceutical preparations (SIC 2834). Pharmaceutical preparations are typically the pure chemicals plus excipients such as diluents or extenders. Pharmaceutical preparations are available in several forms, including pills, capsules, tablets, creams, and lotions.

[10] Biopharmaceuticals are broadly defined as pharmaceutical products produced through the use of biotechnology.

[11] An NCE, as defined by the FDA, is a drug for which the active ingredient has not been previously marketed [approved] in the United States for use in a drug product. The term has often been used in the literature and by industry, however, to refer to products that have been approved either in the United States or elsewhere. For instance, a global NCE, as referred to later in this report, is defined as an NCE that has been approved/marketed in at least 7 countries, including the major pharmaceutical markets (see footnote 2 in Chapter 5). It should be noted that the term "NCE" does not in itself designate approval has been granted.

[12] "Generic" is defined as being nonproprietary and denoting a drug name that is not protected by a trademark and that is usually descriptive of the drug's chemical structure. A glossary that includes these and other terms is provided in the appendix.

[13] U.S. Department of Commerce, *U.S. Industrial Outlook 1990*, p. 50-3. It should be noted that some innovative firms also produce generic products.

[14] "Pharmaceuticals," *Financial World*, May 30, 1990, p. 54.

[15] Derived from the CountyNatWest Securities Ltd. rankings.

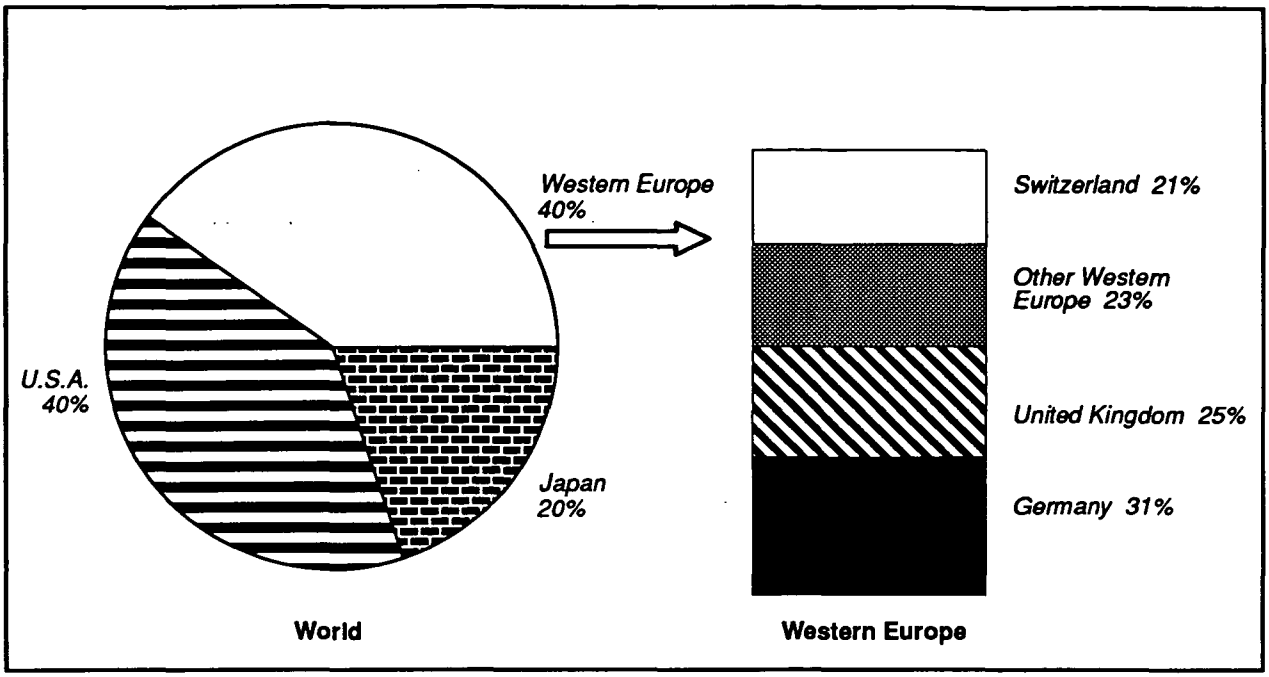
[16] The largest Japanese firm, Takeda Chemical Industries Ltd., ranked 20th in ethical drug sales.

[17] CountyNatWest Securities Co. ranking.

[18] "Changing Lineup Ahead for Global Drug Industry," *Chemical & Engineering News*, Dec. 17, 1990, p. 10. Of the 16 U.S. firms, 11 are included within the top 20 firms in the industry.

[19] Based on the countries indicated in U.S. Department of Commerce, *Foreign Direct Investment in the United States*.

Figure 1-1
Global sales of Top 80 firms, by corporate nationality



Source: SCRIP League Tables, 1989.

more than 50 percent were operating in the United States in 1989.[20]

Concentration on one's home market, however, is often not sufficient to build a strong industry capable of competing on a global basis, as indicated by the experiences of the industries in France and Japan. The industries in these countries have, until recently, focused primarily on their relatively large home markets. Consequently, these industries have not developed an R&D and marketing infrastructure that is comparable to that of stronger and more innovative industries such as those in the United States and some Western European countries.[21] Conversely, the strength of the industries in the United States, the United Kingdom, and Switzerland was established fairly early by their expansion beyond domestic borders.

The U.S. pharmaceutical industry has invested extensively throughout the world. Investment by the industry in developed countries accounted for the largest share of total such investment in 1986, or about 75 percent. Within this subgrouping, as shown in Figure 2, the majority of investment was in the EC (63 percent) and Japan (16 percent).[22] A recent study indicates that of the 20 or so U.S. firms operating in Japan, 13 had wholly owned subsidiaries and 8 had majority owned subsidiaries.[23]

United States, Western European, and Japanese firms have strong research programs, indicated by their having introduced over 90 percent of the new products that entered the world market in the past 50 years. During 1940-88, U.S. firms accounted for about 62 percent of the new drugs introduced, Western European firms about 27 percent, and Japanese firms about 2 percent.[24]

During 1976-90, the cost of developing a pharmaceutical product in the United States increased from $54 million to $231 million.[25] Approximately half of this cost is represented by direct, "out-of-pocket" costs, associated with bringing the drug through discovery, clinical testing, development, and

[20] *Data Book 1990*, p. 34. On an individual firm basis, this number of firms represented the largest share of Japanese investment overseas, or 23 percent. Taiwan was the next largest site, with about 16 majority-owned Japanese firms.

[21] It should be noted that the decline in strength of the French industry has been attributed primarily to the implementation of certain Government policies in that country.

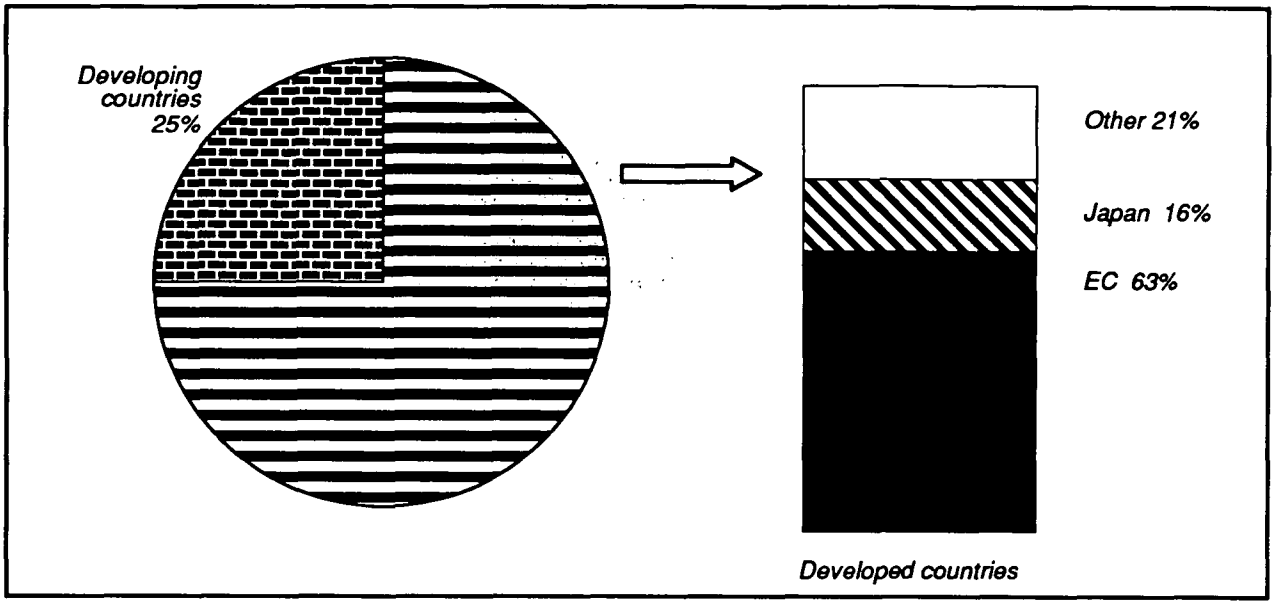
[22] This figure is defined as the "Total Assets of Affiliates, Industry of U.S. Parent by Country," U.S. Department of Commerce, *U.S. Direct Investment Abroad: Operations of U.S. Parent Companies and Their Foreign Affiliates* (Revised 1986 Estimates), July 1989.

[23] "Competition Intensifies as Japanese Lift R&D Effort," *European Chemical News*, Apr. 1, 1991, p. 18.

[24] Pharmaceutical Manufacturers Association (PMA) *PMA Statistical Fact Book - Facts at a Glance*, December 1989, p. 19.

[25] The value presented for 1990 is in terms of 1987 dollars. It should be noted that the values for 1976 and 1990 in constant (1982) dollars are $86 million and $197 million, respectively.

Figure 2
Total assets of U.S. pharmaceutical affiliates, by country/region (percent)



Source: *U.S. Direct Investment Aboard.*

marketing approval. The remainder represents the cost of capital. The relatively high cost of developing a drug is based on factors such as (1) the uncertainty of success and the number of products that eventually fail during the development process; (2) the reported delays in receiving marketing approval from the FDA; and (3) the industry-wide trend towards development of products to treat chronic diseases. Estimates range from 1 of every 4,000 to 10,000 compounds discovered can be marketed commercially. If the product is developed overseas, PMA estimates that the direct costs would be comparable, but the cost of capital would be considerably less.[26]

The continued increase in the cost of R&D is considered to be one of the driving forces behind the industry's current trend towards consolidation. Consolidation allows firms to share the risks and the costs involved with bringing new products to market. It also allows firms, particularly those wishing to enter the U.S. market, to expand their geographical reach and balance product portfolios.

Continued innovation is one way for a company to overcome (1) the loss of market share for its innovative product that results from the entry of generic products after the expiration of the company's patent or (2) the launch of a strong competitive product. As such, a company facing gaps or dry spells in its drug development pipeline is likely to enter into an alliance with another firm, thereby gaining access to new products. Figure 3 illustrates the dynamic structure of the industry from 1970 to 1989 that resulted from the introduction of new products, expiration of the patent on others, and consolidation.

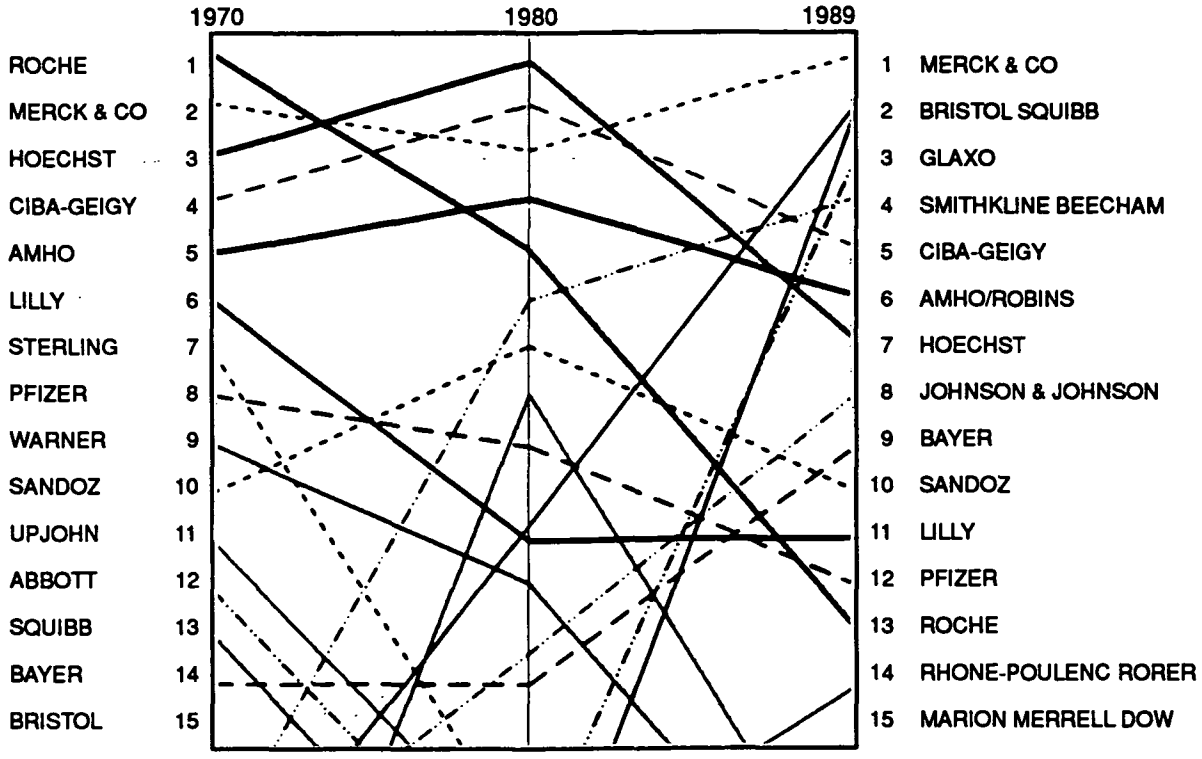
Industry consolidation takes many forms, ranging from mergers to strategic alliances. Strategic alliances, including licensing agreements and equity investments, can be quite varied in structure. In the past five years there have been a number of mergers in the industry and many strategic alliances, particularly in the biopharmaceutical sector.

Strategic alliances, once structured as a way to obtain financing to tide a company over until a product was launched on the market, are now entered into primarily to acquire advantages in several areas, including regulatory concerns and sales. Many industry representatives have stated that although they expect at least two more mergers in the industry involving medium-size U.S. firms and European firms, they believe that it is more likely that companies will enter into strategic alliances, given the actions of Merck, the industry leader. Merck has recently entered into alliances with DuPont and Johnson & Johnson. Merck's joint venture with DuPont is notable in that it is a research and marketing collaboration. Industry sources expect the trend to continue towards licensing products and establishing strategic alliances earlier in the development process.

Another sector of the pharmaceutical market, biopharmaceuticals, currently accounts for a relatively small share of the global pharmaceutical market.

[26] The differential in the cost of capital is attributed to "differences . . . in savings, in the relation of banks to industry, in tax policy, and in government responses to corporate distress." (*A Competitive Profile of the Drugs and Pharmaceuticals Industry*, (p. 28). The reasons for the differences cited are based on a comparison of the cost of capital in the United States, Japan, and Germany.)

Figure 3
Changes in world market rank of leading pharmaceutical companies, 1970-1989



Source: Reproduced with permission from Eli Lilly & Co.

Biopharmaceuticals, however, are expected to account for an increasing share of the market within the next decade.[27] The majority of the proliferation of small new companies exploiting discoveries in biotechnology has been concentrated mainly in the United States during the 1980s because of such factors as the ability of individual scientists to discover and produce new products using this technology and readily available U.S.-based venture capital looking for promising investment possibilities.[28] As the availability of venture capital declines in the United States, however, firms from other countries, particularly Japan, are entering through strategic alliances with U.S. producers.

The Japanese biotechnology industry is reportedly in a position to become a major competitor in the world market. Japan's biotechnology industry, whose strength lies primarily in process refinement, is actively seeking to obtain new biopharmaceuticals from innovative world drug firms through strategic alliances such as joint ventures and cross-licensing. As such, the Japanese, with their experience in process refinement, could obtain a larger share of the global market. However, for Japan to become a major world competitor in the industry, more emphasis must be placed on basic research to originate more global NCEs.

The competitive stature of an industry depends on the industry's level of commitment to R&D and the productivity of its R&D programs. Thus, it is probably not surprising that the economic analysis developed in the report found that a competitive pharmaceutical industry is likely to be located in a country (or region) that fosters innovative activity and attracts new products. The estimations indicate that a higher level of R&D commitment in a country is consistent with the origination of more global NCEs. The results of the empirical analysis indicate that pharmaceutical firms must make a considerable commitment to research and development, both in terms of the size of their R&D budget and R&D staff to remain competitive.

[27] Government policies are likely to have a significant effect on the continued development of the industry, particularly in such areas as patent and environmental protection.

[28] Unpublished USITC staff working paper on biotechnology, 1990.

The economic analysis in the report also examined the determinants of two important measures of competitiveness in the pharmaceutical industry, global market share and R&D productivity, at a firm level. With respect to global market share, the analysis found that higher levels of R&D spending, larger numbers of R&D employees, and a large salesforce are associated with higher market shares. With respect to R&D productivity, the analysis found that increases in expenditures per R&D employee and increases in the number of R&D employees lead to greater R&D output. Furthermore, the estimations reveal that the effect of additional R&D spending is subject to diminishing returns. Finally, the productivity estimations suggest that there are positive spillovers to firm level productivity from national government research efforts.[29]

COMMISSION RESEARCH FRAMEWORK

Measures of Competitiveness for the U.S. Pharmaceutical Industry

An important measure of international competitiveness for any industry is the degree to which it can achieve profitability and growth relative to its foreign rivals. These goals require the ability to sustain and increase market share, either by lowering costs and prices through continuous improvements in factor utilization or by improving the quality of product. Measures of competitiveness therefore usually include market share, profits, and productivity. A firm (or industry) that is more productive is likely to increase its market share relative to its competitors. Although productivity is clearly a determinant of competitiveness, it can be used also as a measure of future potential competitiveness.

For the pharmaceutical industry, maintaining profitability requires the ability to develop innovative drugs which, because of their unique therapeutic value, can capture a significant share of the global market. Thus, one measure of competitiveness for the U.S. industry is the number of "global" ethical pharmaceutical products that it develops in comparison to its foreign counterparts.[30] However, this measure may not necessarily reflect the current productivity of the industry.

Productivity can be measured in terms of output per worker. The pharmaceutical industry's reliance on R&D to produce and market NCEs suggests another productivity indicator that may be more accurate in terms of measuring international competitiveness: R&D productivity. R&D productivity in the pharmaceutical industry can be measured by the number of R&D compounds developed or R&D compounds developed per R&D employee.

Determinants of International Competitiveness

A number of factors related to demand and supply conditions contribute to the ability of the pharmaceutical industry to develop, produce, and market innovative ethical drugs. Figure 4 illustrates the major determinants of competitiveness discussed in the economic literature and indicated by industry officials during staff interviews.

The demand for ethical pharmaceuticals is determined by demographic and socioeconomic factors. For example, factors such as the composition of the population in terms of age as well as socioeconomic factors such as diet or access to health care can affect the demand for drugs in a particular region or country. Government policies and programs such as cost-containment, degree of health-care financing, and support for health-related education may also affect the demand for drugs, directly or indirectly.

An important factor affecting the supply of ethical pharmaceuticals is the level and productivity of R&D spending. Such activity requires sufficiently high profits, the ability to secure external financing, or both. Government actions ranging from macroeconomic policies, treatment of product liability, tax policy, and regulatory controls exert indirect and direct effects (positive and negative) on the ability of firms and the industry as a whole to produce pharmaceuticals.[31]

Because the U.S. industry operates worldwide, government policies in other countries may have an impact on the activities of U.S. pharmaceutical firms. Research has been hampered by the lack of available international data on the effects of foreign government policies on the U.S. industry. Nonetheless, industry officials have identified issues such as the protection of intellectual property rights, tax policy, and pricing policies as being of major concern to the U.S. industry.

MAJOR COMPETITIVE FACTORS AND DETERMINANTS

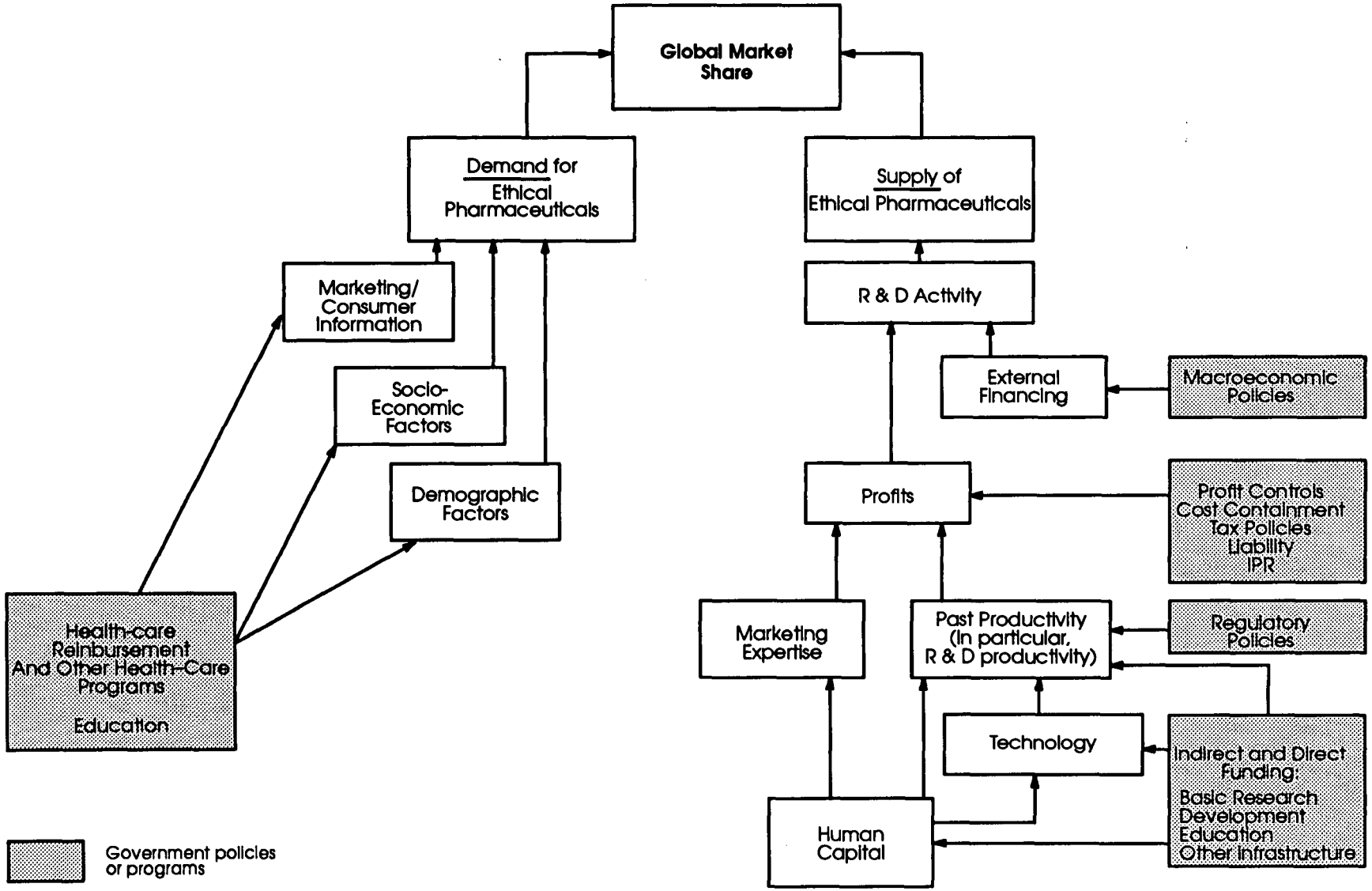
The competitive factors examined in the report range from those that are quantifiable to those that are

[29] The economic results should be interpreted with care due to potential inconsistencies in the data from different countries. See ch. 5 and app. E of the pharmaceutical report for more information on the data used in the economic analysis.

[30] An alternative measure is the total number of new chemical entities (NCEs) developed by the industry. This measure is flawed because it is not always a good proxy for global market share. Many NCEs do not capture a significant share of the market outside of the country in which they are developed.

[31] Figure 2-2 presents a simplified view of the various factors that may influence the development and sale of pharmaceutical compounds. R&D activity, as shown in the figure, includes the level and productivity of current R&D. Just as past R&D productivity is influenced by a number of government policies and programs, so also is current R&D activity.

Figure 4
Determinants of global market share



best discussed in anecdotal terms. Table 1 lists, by country, a number of the factors and determinants presented in this report.[32]

Government Policies

The results of the economic analysis developed in this report suggest that major industrialized countries are likely to maintain their strong demand for medicinal products, which, in turn, will continue to provide pharmaceutical firms with the revenues necessary to continue to develop innovative products. Future levels of revenues and innovation, are likely to be strongly affected by government policies. A number of domestic and foreign government policies are examined in this report, including policies on regulatory issues, product liability, intellectual property rights, taxation, the Drug Export Act, and the implementation of pricing controls and cost-containment programs. Each of these government policies has a significant effect on members of the global industry. However, they do not operate in isolation. The multinational pharmaceutical industry must confront a combination of many of these policies, which compounds the total impact.

Regulatory Issues

Optimal regulatory policy for pharmaceuticals is difficult to enact in that it requires a balance between the time necessary to prove a product safe and efficacious, the time needed by companies to recoup their R&D expenditures, and the time needed to launch new products on the market for patients who need them. Delays in regulatory procedures can delay a product's entry onto the market and shorten its effective patent life by a number of years. Although regulatory delays generally affect all companies operating in a given geographical area, it is possible to argue that the domestic industry bears a large share of the impact inasmuch as the domestic industry often incurs a major portion of its revenues from its home market.[33]

In 1960, the drug approval process in the United States took about 3 years. After the Kefauver-Harris amendments in 1962, total testing and FDA review time increased, on the average, to 10 years, given the increased emphasis on safety and efficacy. The average FDA review time for the 20 new drugs approved in the United States in 1988 was about 31 months, compared with approximately 15 months for those of the 20 that were first approved in foreign markets.[34] Industry sources state that this differential in approval times prompts many companies to seek market approvals overseas first. According to a recent study, the average break-even point for new products in the United States can be reduced by about 3-4 years for each year regulatory delays are reduced. In the EC, delays in the registration process under the current system cost the industry an estimated 0.5 to 1.0 percent of EC industry costs.

Delays at the FDA have been attributed to a number of factors, ranging from personnel shortages to the increasing amount of data required to demonstrate the safety of the product under consideration. Suggestions on improving the efficiency of the FDA approval process range from the implementation of user fees on new drug applications (NDAs) to the better preparation of applications on the part of industry. Reaction to the idea of user fees is mixed, both in industry and in Congress. User fees are perceived by many to be a tax on innovation. Others question the administration of user fees. Still others believe, however, that users fees could provide needed resources for the FDA, presuming that the fees would go directly to that agency and not to the U.S. Department of the Treasury.[35]

In addition to allowing for the extension of a product's period of market exclusivity based on delays in the regulatory process, the 1984 Waxman-Hatch Act authorized accelerated approval procedures (ANDAs) for generic products in the United States, allowing them to enter the market faster after the patent expired on innovative products. The entry of generic products now results in upwards of a 50-percent loss in market share for the innovative products within two years. Since the recent FDA generic drug problem, however, it is possible that generics will also be required to undergo more testing to prove safety and efficacy, thereby prolonging their approval process. This could increase the prices on many generic products over time, possibly resulting in the closure or sale of a large number of domestic generics manufacturers.

Intellectual Property Rights

Intellectual property rights (IPR) have a significant effect on the development of pharmaceuticals; most importantly, they allow firms a period of market exclusivity in which they can partially recoup R&D expenditures. Two basic IPR considerations are (1) the extension of patent terms on pharmaceuticals to allow for regulatory delays and (2) the implementation of adequate patent legislation in a number of countries. Companies generally patent products as soon as they show signs of pharmacological activity. Given that patents are applied for fairly early in the discovery process, however, any delays in regulatory approval can shorten the period of market exclusivity for a given product.

The period of market exclusivity for innovative products has become considerably shorter in the United

[32] Please note that the time frames presented for the data are not consistent across all fields in the table.

[33] For example, according to a representative of PMA, U.S. pharmaceutical sales accounted for 55-57 percent of total pharmaceutical sales of U.S.-based innovative companies in 1989.

[34] It should be noted that comparison of approval times in the United States and overseas can be difficult in that 1) time periods vary depending on when in the process the "clock was started" and 2) foreign approval times do not necessarily include the time used for pre-clinical testing in the United States.

[35] "Should Drugmakers Pay FDA Bills," *Business Week*, Feb. 19, 1990, p. 108.

Table 1
Some of the factors/determinants of competitiveness considered in this report

Issue	*United States*	*Western Europe*	*Japan*
Estimated global market share, 1989 (percent)[1]	39	41	20
Industry R&D expenditures, 1989 ($ billions)	[2]7.3	[3]8.4	[4]3.3
Number of "global" NCEs discovered during 1975-89[5]	47	44	5
Number of "global" NCEs discovered during 1985-89[5]	14	5	0
Percent of GDP spent on healthcare, 1987[6]	12	4-12	7
Percent of healthcare expenditures on pharmaceuticals[6]	7	10-17	22
Pricing policies implemented?	No	[7]Yes	Yes
Cost-containment programs implemented?	[8]	[7]Yes	Yes
National health insurance programs	No	Yes	Yes
National patent restoration programs?	Yes	[9]No	Yes

[1] Derived from the market shares held by the top 80 companies worldwide.
[2] PMA.
[3] Derived from data provided by EFPIA.
[4] Derived from data provided by JPMA.
[5] P. E. Barral, *Fifteen Years of Pharmaceutical Research Results Throughout the World (1975-1988).*
[6] Derived from data compiled by Eli Lilly & Co. (Data for the United States and Japan cited from a 1989 reference.)
[7] In some member states.
[8] Implemented on a limited scale in the United States under the Omnibus Budget Reconciliation Act of 1990.
[9] Legislation to allow for extensions of market exclusivity based on delays in the approval process is pending under the EC92 program.

States, Western Europe, and Japan during the past decade, given the increase in the time needed to bring a pharmaceutical product to market. The average length of the effective patent life of a pharmaceutical in the United States has declined to 10 years and 10 months, compared with 15 years in the early 1960s.[36] Innovative products also face competition from the speedier entry of generic products per the provisions of the Waxman-Hatch Act.

Erosion of the product's period of market exclusivity can reduce a company's ability to recoup some of its R&D expenditures. It is estimated that in the United States the average NCE recovers its R&D investment in 19 years.[37]

Patent restoration programs, however, offset regulatory delays to some extent. In 1984 and 1988, the United States and Japan, respectively, implemented patent-restoration provisions that were intended to mitigate the impact of delays in the regulatory procedure. Although the two systems vary in terms of actual procedures, the basic effect is to allow a maximum of 5 years additional market exclusivity for pharmaceutical products. The average length of time for extensions granted in Japan since enactment in 1988 was 3 years and 11 months. As of April 1990, although 85 innovative products had their patents extended in the United States, no products were able as yet to take advantage of the full 5-year extension permissible under the Waxman-Hatch Act.

The EC Commission recently issued a regulation on patent restoration that allows for the creation of a supplementary protection certificate for medicinal products. The certificate is seen by many as a device to confer an additional period of market exclusivity rather than an extension of the patent term itself.

In regard to Japan, industry sources have indicated that although the Japanese Government has generally been responsive to the needs of foreign firms in the area of IPR, there are still some areas of concern.[38] The prehearing submission of the IBA specifically referred to two problems with the Japanese patent system as it relates to biopharmaceuticals. First, delays in the granting of patents during which time Japanese companies can sell these pharmaceuticals domestically, and second, the narrowness in scope of many of the patents granted. The latter provision can result in more cross-licensing, reducing profits for the firm that originated the product.

Industry representatives have stated that the Canadian patent system remains the weakest of any industrialized country and some developing countries[39] and, therefore, the U.S. pharmaceutical industry seeks to eliminate all compulsory licensing laws in Canada.[40]

Compulsory licensing for bulk active ingredients used in the preparation or production of a medicine has

[36] It should be noted that innovative companies generally patent a product fairly early in the discovery process. Therefore, any delays in bringing the product to market shorten the product's effective patent life.
[37] Questions have arisen in the post-World War II period as to what level of return on a pharmaceutical product is appropriate and what period of time is needed to achieve this return.
[38] USITC staff field interviews in Japan with representatives of U.S.-based multinational firms and representatives of industry associations during April 1991.
[39] Testimony of Gerald J. Mossinghoff, President, Pharmaceutical Manufacturers Association, before the U.S. International Trade Commission on January 17, 1991.
[40] Concern exists about patent systems in a number of developing countries, as well as in developed countries such as Canada. The Canadian patent system is said to be the weakest of that in any industrialized country.

been in effect in Canada since 1923.[41] In 1969, the Canadian Patent Act was amended to include bulk active ingredients that were imported, rather than produced in Canada,[42] resulting in an increase in the compulsory licensing of patented medicines[43] and a reduction in the annual growth rate for pharmaceutical research in Canada.[44] Many pharmaceutical companies reportedly closed or moved their Canadian research facilities to the United States as a result of the 1969 amendments [45] because of concerns that their patented products would be licensed, thereby earning, at most, a 4 percent royalty.[46] In addition, many of the Canadian firms became increasingly dependent on obtaining compulsory licenses to other firms' products rather than developing their own products through innovation.

The Patent Act was amended again in 1987 by legislation frequently referred to as C-22.[47] The amendments, which somewhat tempered, but by no means eliminated, the compulsory licensing provision, were reportedly made in an attempt to foster a stronger Canadian industry. C-22 allowed for a deferral of the use of a compulsory license granted to a company intending to make its own brand of the product.[48] In return for this extended period of market exclusivity, innovative companies operating in Canada agreed to increase their ratio of R&D expenditures to sales in Canada to 10 percent by 1996.[49] The Patented Medicine Prices Review Board (PMPRB), an independent quasi-judicial agency intended to protect consumer interests by "ensuring that the prices of patented medicines are not excessive" was also created under C-22. Industry representatives are also concerned about differentiations in the terms of market exclusivity for products researched and developed in Canada compared with those discovered elsewhere.

[41] Patented Medicine Prices Review Board, *Third Annual Report*, June 1991, p. 5.

[42] Ibid.

[43] Ibid.

[44] According to one source, compulsory licenses were granted almost routinely. Generic manufacturers simply applied for the license.

[45] John W. Rogers, III, "The Revised Canadian Patent Act, the Free Trade Agreement, and Pharmaceutical Patents: An Overview of Pharmaceutical Compulsory Licensing in Canada," *EIPR*, 1990, p. 351.

[46] Compulsory licensing affected the innovation of these companies in that it reduced their revenues, thereby potentially reducing their R&D expenditures.

[47] "The Revised Canadian Patent Act, the Free Trade Agreement, and Pharmaceutical Patents," p. 351. The amendments to the patent system were applicable only to the pharmaceutical industry. The article states that Bill C-22 was of the 33d Parliament, 2nd session, 35-36 Eliz. II (1986 to 1987). "Royal assent to Bill C-22 was given on 19 November 1987, and most sections thereof have been proclaimed."

[48] Although the companies seeking the compulsory licenses are called "generic" companies, compulsory licenses are applicable to products that are still patented (i.e., non-generic products).

[49] Patented Medicine Prices Review Board, *Third Annual Report*, p. 19.

Under the provisions of the 1984 Trade Act, the U.S. Government has been able to negotiate improved patent protection in a number of countries/regions, including Argentina, Chile, Mexico, Korea, and, most recently, Eastern Europe. However, a number of countries are still believed to have inadequate patent systems. It was estimated that worldwide IPR infringement in 1986 cost the U.S. industry approximately $6 billion, possibly reducing R&D investment by $720-900 million.[50]

Cost containment and Price Controls

The enactment of cost-containment programs, price controls, or both, on a national level often results in decreased levels of R&D spending in that these programs reduce revenues that can be reinvested in R&D programs. Several countries that have implemented such programs have seen their pharmaceutical industries weaken or shift outside their borders.

Cost containment

The United States has historically had a "relatively unencumbered" economy, with, according to industry sources, the most market-oriented pricing system in the world. In 1989, the Federal Government implemented a cost-containment program. Under the Omnibus Budget Reconciliation Act of 1990 pharmaceutical companies are required to provide rebates to the Medicaid program to have their prescription drugs reimbursed by the Government. This legislation is perceived by representatives of the pharmaceutical industry as one of the first stages of cost-containment efforts in the United States.[51] The level of rebate directly affects a company's profits. The industry is concerned that (1) such rebates, although currently limited to the Medicaid program, could be adopted by other insurance programs in the United States and (2) additional cost-containment legislation could be implemented.

A number of countries in Western Europe have implemented cost-containment programs for health-care expenditures. Among other things, these programs are intended to lower the portion of health-care expenditures accounted for by pharmaceuticals. Germany, for example, one of the

[50] *Health Care Innovation*, p. 21.

[51] Industry representatives, although recognizing the need to control expenditures on health care, are concerned that proponents of cost-containment proposals in the United States look only at drug prices and not at the companies' costs of developing and marketing the products, or at the offsets that pharmaceuticals provide in other areas of health care, such as reduced hospital stays. A recent study has found that over the next 25 years, the estimated savings in health-care expenditures from the use of pharmaceuticals will be valued at almost $500 billion. It also should be noted that pharmaceutical products, which represented about 7 percent of total health-care costs in 1989, declined from over 11 percent in 1983.

countries that has traditionally practiced free pricing, recently enacted the Health Reform Act (HRA). The HRA fixes reimbursement levels for products that are offpatent and have a relatively high volume at a level between the generic price and the original manufacturer's price (reportedly closer to the former than the latter). In addition to reducing revenues of the firms operating in Germany, the HRA has also increased the market share held by generics. Currently, one of the largest pharmaceuticals producers in Germany is a generic manufacturer.

In Japan, domestic companies are now said to be facing pressure to enter foreign markets as a result of national policies to curb expenditures on pharmaceuticals. Japan's pharmaceutical market, second only to that of the United States, has traditionally been large enough to generally disincline Japanese pharmaceutical manufacturers from attempting any large scale moves toward internationalization. However, because of cost-containment efforts on the part of the Japanese Government and increased international competition in the Japanese market, Japanese pharmaceutical producers have become aware of the necessity to increase R&D activity and investment and have been formulating globalization strategies to compete with the successful U.S. and Western European multinationals. Japan's globalization strategies for the pharmaceutical industry include merger, acquisition, and licensing activities abroad, and the construction of wholly owned subsidiary plants and research facilities in major market areas such as the United States and Western Europe.

Price controls

The United States has not yet implemented price controls on pharmaceuticals. In Japan, however, the prices for pharmaceutical products are set by the government and decline on a biennial basis. Pricing controls also have been enacted by almost all of the member states in the EC. The United Kingdom, for example, uses the Pharmaceutical Price Regulation Scheme (PPRS), a profit-control system. The voluntary program is intended to maintain price levels that allow for a "reasonable return on capital," to ensure that prices of pharmaceutical products are not raised arbitrarily, and to limit the cost of drugs to the National Health Service (NHS).[52] The majority of the pharmaceuticals consumed in the United Kingdom are provided through the NHS. The PPRS only addresses those brand-name ethical pharmaceutical products that are sold to the Department of Health and does not apply to generic or OTC products. The PPRS also calls for a cap on promotional spending by companies. This latter provision is said to have more of an impact on small- and medium-sized companies because of the higher ratio of promotional spending to sales generally incurred by these firms, as compared to that of larger firms.

It is unlikely that, under the EC92 program, a national price-control and/or cost-containment program will be implemented within the next 20 years. But many in the industry and in the EC Commission are watching the implementation of such programs in individual countries across the EC and weighing their merits. Industry sources have stated that, if it is necessary to have price controls and/or cost-containment programs, the PPRS is probably one of the best, particularly if compared with the reference pricing system implemented under the HRA in Germany.[53] The PPRS is credited with having increased investment in the British pharmaceutical industry.[54] The implementation of the HRA, which utilizes the concept of therapeutic clustering, has reportedly resulted in a 25-40 percent decrease in pharmaceutical prices in Germany. This decrease in revenues is expected to have a significant impact on future innovation in Germany. Therapeutic clustering, or the grouping of drug products for similar indications for reimbursement at similar price levels by either health insurance plans or national health systems, regardless of whether the products are patent protected, is expected to exacerbate the impact of cost-containment programs. One industry representative indicated that such efforts also undercut domestic IPR protection in that they decrease or eliminate the market exclusivity conferred by such protection.

The implementation of price controls in the EC has resulted in price differentiation in the individual Western European countries, which has, in turn, resulted in increased parallel trade (particularly from the southern countries), trade barriers, or both. According to EFPIA and PMA, the undercutting in price that results from parallel trade results in a decrease in revenue, which could potentially have a negative impact on R&D. Price controls are also believed, in some cases, to favor the domestic industry. France, for example, is said to foster its domestic industry by giving indirect R&D incentives to local firms or foreign-based firms with significant investment levels in France by allowing for better domestic prices, more rapid product approval, and reimbursement for exports. The French industry was reportedly weakened considerably by the implementation of price and promotion controls.

Product liability

Product liability law, under which an injured consumer can sue the manufacturer of a defective

[52] Shearson Lehman Hutton, *A Controversial Vision of the Future: Challenges Posed by Pharmaceutical Deregulation*, February 1989, p. 51.

[53] USITC staff field interviews in Western Europe with representatives of EC-based and U.S.-based multinational firms and representatives of industry associations during April 1991.

[54] One source argues, however, that despite the fact that the U.K. industry "has a good record of investment and innovation, . . . it is likely that it could have been still more successful if it had not been for the curtailment of profits through the PPRS."

product, is well developed in the United States, particularly in the area of pharmaceuticals. Aspects such as strict liability, contingency fees, jury trials, and extensive discovery have reportedly led to a system in which lawsuits are frequent, awards are high, and insurance is in retreat. According to industry sources, product liability has led to a decline in the ability of the U.S. pharmaceutical industry to compete with its overseas counterparts. The threat of extensive litigation and large awards to plaintiffs has stunted the willingness of industry to innovate and to market needed drugs, especially in the fields of contraceptives and vaccines.

In the European Community, a new product-liability directive is replacing traditional liability that required proof of negligence with a strict liability standard similar to the U.S. model. Switzerland still operates under the older negligence-based system. Product liability law in Japan in not as developed as in the United States, partly because of a preference for the negotiated settlement of disputes rather than litigation. The Japanese government has established a fund, to which pharmaceutical manufacturers and the government contribute, for the relief of persons injured by drug side-effects.

Taxation

In regard to taxation, industry concerns focus on the U.S. tax system. Industry groups identified three actions in the field of taxation that would strengthen the pharmaceutical industry: (1) restructuring the R&E credit and making it permanent; (2) reducing the cost of capital by reducing the tax on capital gains and encouraging long-term savings and investment; (3) resolving issues raised by section 861 by permanently setting a percentage of R&D expenditures for allocation against U.S. income.

U.S. Drug Export Act

U.S. firms are increasingly seeking marketing approval overseas prior to or during application for such approval in the United States. The 1986 Drug Export Act allows companies to export unapproved pharmaceuticals to countries with effective drug-approval regimes under certain conditions. The industry is, however, concerned about certain aspects of the law, citing that (1) a number of important markets have been omitted from the law; (2) a company cannot export a product that, although approved for marketing overseas, would not be approved in the United States; and (3) the process to obtain FDA authorization to export products under this Act is considered cumbersome. Without this law, it is likely that many firms would have had to relocate current facilities or site future facilities overseas in order to best access foreign markets. Negative aspects of the law, however, are believed to place domestic firms at a disadvantage with firms in foreign industries who do not operate under such laws.

Duty Suspensions in the EC

The primary tariff barrier identified as affecting the U.S. industry is the recent changes in the EC's procedure for granting duty suspensions. The new duty suspension guidelines may effectively limit the availability of duty suspensions for pharmaceutical products. The increased difficulty in obtaining duty suspensions in Europe may increase the possibility that U.S. firms will move production facilities to Europe.