

Pharmaceutical Innovation

*Incentives, Competition, and Cost-Benefit Analysis
in International Perspective*

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The Pharmaceutical Sector in Health Care

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I. Introduction

In 2004 total global pharmaceutical sales were reported to have been about \$550 billion in U.S.-dollar equivalents (IMS Intelligence 2005), only a tiny fraction of total global gross national product (GNP) of about \$35 trillion (FinFacts 2005).

Sales reported for 2004 in the United States, which spends more per capita and absolutely on pharmaceuticals than does any other country, amounted to only \$200 billion, which is about 1.7% of U.S. gross domestic product (GDP) in that year, or 11.1% of total U.S. health spending; Heffler et al. (2005). Assuming that drug manufacturers received about 75% of total retail sales and that their net after-tax profit margin was 16% on sales (*Fortune* 2005), their after-tax profits of about \$24 billion in 2004 amounted to only 0.20% of U.S. GDP in that year, and about 1.3% of total U.S. national health spending.

These statistics, which portray the pharmaceutical industry as only a minor player in health care and an almost trivial player in the economy as a whole, belie the importance of the industry in terms of value added and in terms of the heated policy debate it triggers all around the globe.

The value that pharmaceutical research and products add to human existence can be appreciated by anyone who has used pharmaceutical products to reduce pain, eliminate potentially lethal infections, or control high blood pressure or cholesterol, not even to speak of other popular life-style drugs. That value has been more formally explored in a recent compendium of essays written by highly distinguished economists (Murphy and Topel 2003b). Addressing the question "Are we getting our money's worth?" from health spending in general and medical research, including pharmaceutical research in particular, the consensus among the authors was "From an



economic perspective, the answer is a resounding 'yes': in fact, considering the extraordinary value of improvements in health, we may even be spending too little on medical research. . . . The average new drug approved by the FDA yields benefits worth many times its cost of development" (p. 2).

As the world looks anxiously at the possible impact of the bird flu virus on humans, that passage has added import: anxious policy makers do not look to surgeons or hospitals to solve this problem, but to the pharmaceutical industry.

Remarkably, while the pharmaceutical industry undoubtedly is one of the highest value-added industries in modern economies, that industry is not generally the focus of gratitude or affection. On the contrary, almost everywhere on the globe the industry is viewed with suspicion and often is the butt of vocal criticism and rancor. Relative to its size, it attracts a disproportionate share of attention from public policy makers and critical illumination from the media.

What can explain this seeming paradox — the evidently high value the industry adds to human life and the sharp criticism of which it so often is the focus?

Part of the apparent paradox stems from the industry's awkward position on the spectrum from publicly owned enterprise and pure private, investor-owned, and profit-driven enterprise. On the one hand, the pharmaceutical companies are structured as profit-seeking enterprises. Unlike many other profit-seeking industries, however, the research-based pharmaceutical industry cannot survive without government protection.

Another source of friction is the industry's widespread practice of price discrimination wherever government does not outlaw it outright. Price discrimination is a two-edged sword. On the one hand, it allows the industry to extract more revenue from society than a single-price policy would. On the other hand, however, it allows customers to be served who would be priced out of a single-priced market.

Yet other friction arises over the clash of national regulatory policies on drug pricing, on the one hand, and international attempts to place global trade more on free-market principles, on the other. This issue touches on the question of how the cost of pharmaceutical research and development (R&D) should be shared by nations. This debate has led in recent years to unwelcome attempts by the United States to engineer changes in the health systems of other countries through trade negotiations.

This chapter explores some of these issues in greater depth, at a general level that cuts across individual nations. It begins with a review of the various protections government extends to the industry. Next, the focus is

on the industry's cost structure and the controversial pricing practices that structure begets. Thereafter follows an exploration of what it would take to introduce a more economically efficient, evenly distributed balance of power into the market for pharmaceutical products.

II. Government Protection of the Pharmaceutical Industry

Every research-based pharmaceutical company has two major product lines: (1) scientific knowledge and (2) pills and other pharmaceutical products. Both thrive on protection by government and could not survive long without it.

Intellectual Property Rights

The research findings produced by the pharmaceutical industry are inherently in the nature of a *public good*, because a public good exhibits two distinct characteristics. First, its consumption by one person does not detract from another's consumption of that same good. Clean air is a classic example, as is national security or scientific knowledge, such as a basic theorem. Economists call this characteristic "nonrival," in the sense that there need not be rivalry over the use of the public good. Second, unless government explicitly excludes potential users of the good from using it, for example, through patent laws, it is technically impossible to exclude would-be-users from using it. Economists call this property "nonexclusivity."

Ideally, according to economic theory, the production of goods that are nonrival and nonexclusive should be *collectively* financed through government, so that thereafter the government owns the rights to the public good and then can make it freely available to potential users. Basic scientific knowledge clearly falls into this class of goods. That approach will then lead to an *efficient* use of the public good, in the sense that no one willing to pay the incremental cost of using it is excluded from it. In the case of scientific knowledge, that incremental cost is zero.

Much, though not all, of the scientific knowledge produced around the globe has traditionally been handled in this fashion. One thinks here of the scientific research performed by government research facilities or of academic research funded either by government or by private donors who wish the product of that research to be shared, free of charges as widely as possible, on a global basis. One occasionally sees proposals to apply this approach also to pharmaceutical research. Various models could be used to that end.

For example, government could fund and conduct pharmaceutical R&D to the stage at which a product is ready for the market and then allow competing manufacturers to produce and market the products. Alternatively, government could contract with investor-owned research facilities to produce specified, targeted pharmaceutical R&D, just as it now does for military R&D, take ownership of successful R&D, and then make it freely available to competing manufacturers. Finally, government could simply stand ready to purchase from private R&D enterprises the property rights to successfully completed R&D and then make it available freely to competing manufacturers, leaving the private research facilities to decide what avenue of research to pursue.

One should expect these and similar proposals to emerge around the globe in the decades ahead, although it is not clear how easily they could be sold to public policy makers and to private industry. In the meantime, governments probably will continue to rely for pharmaceutical R&D on privately produced intellectual property whose right to private ownership will then be protected through patents. That approach by now has a proven track record of over a century, although it inevitably will remain an unending source of controversy, as the pharmaceutical industry and governments wrestle over the proper length of patent protection and over the disposition of intellectual property rights upon the expiration of patents, with a critical media reporting on the fight.

The central point to note, however, is that without patent protection the pharmaceutical industry as we know it could not long survive, because imitators could always quickly destroy its economic base. It would, of course, deprive the world of the highly valuable contribution that the research-based pharmaceutical industry makes to human well-being.

Protection of Quality

One could imagine a world in which pharmaceutical companies could develop, produce, and market their products without any government supervision whatsoever. If a particular product turned out to be unsafe in use, the market would quickly discover it and punish the producers economically. The coup de grace would be given by litigation that would punish the company's owners further. Some libertarian thinkers might imagine that such an arrangement would work. In a compendium, "Policy Medicine versus Policy Quackery: Economists against the FDA," for example, Daniel B. Klein (2005) quotes the libertarian Nobel laureate economist Milton Friedman as follows: "The FDA has already done enormous harm to the health of the

American public by greatly increasing the costs of pharmaceutical research, thereby reducing the supply of new and effective drugs, and by delaying the approval of such drugs as survive the tortuous FDA process." When asked "If you could do anything to improve health in America, what would you do?" Klein quotes Friedman as replying: "No more licensing of doctors. No more regulation of drugs. Not of any kind. Period."

In practice, no country follows that libertarian approach. Apparently reliance on private market forces and litigation as adequate safeguards in pharmaceutical therapy is viewed as much too risky. First, the protection of limited liability granted the owners of publicly traded companies severely limits the recourse injured parties would have to the personal wealth of the owners of pharmaceutical companies. The now universal principle of limited liability allows the owners of an enterprise to escape most of the financial consequences of even truly grievous mischief that a company may have visited on behalf of these owners on the rest of society, including grievous environmental hazard. Many corporate executives may not be aware that this protection actually is one of the earliest forms of social insurance. Second, no country is willing to countenance the human casualties that this approach to product safety would have. Although, using a human capital approach, economists probably could justify these casualties in many instances by the added lives saved, the general public and the politicians who represent them undoubtedly would not find the economists' collectivists calculus persuasive.¹

It may well be that the public authorities who do attempt to safeguard the quality of pharmaceutical therapy in each country, for example, the U.S. Food and Drug Administration (FDA) in the United States, typically may be more averse to risk, and hence more restrictive, than would be the majority of the patients being protected. Even so, on balance, both the general public and the pharmaceutical industry probably benefit greatly from the existence of these public authorities. Pharmaceutical companies benefit from having a powerful external stimulus for internal quality control. Furthermore, approval of a product by the authorities can serve as a helpful, if not decisive, shield in litigation over product safety. Few pharmaceutical companies around the globe would be likely to prefer a world without such public supervision.

A question that arises in an international context is whether the quality and safety standards one nation imposes on products sold within its own borders necessarily should be binding upon products sold from pharmaceutical companies within its own borders to other nations. One could imagine, for example, that citizens in high-income country A (e.g., the United States

know how to manage it well. Those who do not risk running afoul of both government and the general public.

As to the financial risk taken on by investors in publicly traded pharmaceutical companies, these are no larger than the risk one assumes in investing in a broad stock-market index, such as the Standard & Poor's 500 index, which reflects the risk and returns for some 500 publicly traded companies (Myers 1999), a point revisited below in the section on the economics of the industry.

III. The Industry's Cost Structure

The development of new pharmaceutical products, from basic research to approval for marketing, is a complex process everywhere and can span a decade or more. According to Pharmaceutical Research and Manufacturers of America, for example, "only one of every 10,000 potential compounds investigated by America's research-based pharmaceutical companies makes it through the research and development pipeline and is approved for patient use by the United States Food and Drug Administration," and "winning approval, on average, takes 15 years and research and development costs over \$800 million dollars" (2005, p. 1; see also Dickson and Gagnon 2004).

Estimating the R&D Costs of Successful Products

Given the length and complexity of the R&D process, estimating the total R&D cost of a successful pharmaceutical product is a daunting methodological challenge that, therefore, has remained a source of controversy, even among economists.

For one, there is the question of what costs to impute to a particular, successful product. A research-based pharmaceutical company can be likened to an oil company that roams the world in search of oil deposits. Such a company will drill many holes that ultimately fail to yield oil. The cost of these dry holes then must be recouped from successful wells. Therefore, the costs of dry holes are routinely allocated to the cost of successful wells. It is so also with pharmaceutical companies. To the total R&D cost incurred directly for successful new products must be added the R&D costs of products that had to be abandoned somewhere along the lengthy R&D process. Making that cost imputation properly presents the first methodological challenge in estimating the R&D costs of new drugs.

A second methodological problem is how to convert monetary outlays for R&D that are made over the span of an entire decade or more into a single

or Taiwan) may be far more intolerant of side effects and be willing to pay a far higher price to eliminate them than might be citizens in poorer country B (e.g., a much poorer country in Latin America or Southeast Asia) who might be willing to countenance greater risk for the benefits expected from a drug at a lower cost. This issue is not much discussed in the literature, but is one worthy of debate. From the perspective of public image, of course, many pharmaceutical companies in risk-averse, high-income countries might be reluctant to observe different safety standards for lower-income countries.

Restrictions on the Resale of Pharmaceutical Products

Governments may prohibit the resale of pharmaceutical products between buyers for two reasons. First, and most frequently mentioned, is safety. If any buyer of a pharmaceutical product could resell it to anyone else, government would effectively lose its ability to assure citizens of the safety of drug therapy, and potentially dangerous counterfeit drugs would abound. Second, permitting unfettered reselling of pharmaceutical products between buyers inevitably would drive each product to a single price worldwide. As will be argued later under the rubric of "price discrimination," neither the pharmaceutical industry nor public policy makers should naturally aspire to a single-price policy for such products.

Ostensibly for the first reason, but also for the second, the open resale of pharmaceutical products between buyers is generally not permitted in countries with the ability effectively to prohibit such sales. Although mainly intended to protect the general public, it protects as well the revenues of pharmaceutical companies.

Quasi-Public, Quasi-Private Enterprises

Most pharmaceutical company executives probably view their enterprises as classic manifestations of free enterprise, in which private investors take enormous financial risks purely for the sake of private gain, but doing much good for humankind in the process. The reality is rather different. As the preceding discussion suggests, however, the industry is best thought of as a fragile little bird, sitting in the hand of government, which protects it from all manner of the market's dangerous economic buffeting, and, in return for that protection, is required from time to time to chirp songs that it would rather not sing. By the very nature of the protection granted the industry, it inevitably becomes the focus of the government's health and science policies. Pharmaceutical executives who understand this requirement usually

amount that is properly adjusted for both inflation and the time value of money. Even after adjustment for inflation, which is straightforward, \$1 million spent today represents much more value than \$1 million to be spent only a decade hence, because much less than \$1 million would have to be invested now to have in hand \$1 million a decade hence.

Monetary outlays spaced over time therefore are converted into one number with identical time value, either as of the beginning of the time-phased cash flow, the so-called *present* value of the cash flow, or at its end, the so-called *terminal* value of the cash flow. The conversion into present or terminal values is made with an interest rate that reflects the pharmaceutical firm's weighted average annual cost of debt and equity capital, the weights being the relative fractions of debt and equity used to raise outside financing. The interest rates used for that purpose reflect the outside investors' opportunity cost of investing their money in the firm rather than in some riskless asset, for example, a long-term government bond, plus a risk premium to compensate investors for the risk they assume by investing with this particular firm.

The fact that a given time-phased cash flow can be concerted either into its present or terminal value can easily confuse persons not familiar with economics or finance. To illustrate with a stylized example, suppose that the relevant R&D outlays for a product represent an even money flow of, say, \$50 million a year for 10 years. If the firm's weighted average cost of financing were, say, 10% per year, then this cash flow would have a present value of \$307 million as of the beginning of that money flow and a terminal value of \$797 million at its end point, presumably when the product is about to launch in the market. At a weighted average cost of financing of, say, 8%, the two values would be \$335 million and \$724 million, respectively. At a weighted cost of financing of 15%, they would be \$251 million and \$1,015 million, respectively. Yet all of these different figures represent an identical cash flow.

One can think of the present value of the R&D stream as the sum of money the firm would have to have on deposit to finance the 10-year stream of R&D spending of \$50 million a year, if the balance in the account could earn the firm's weighted average cost of financing per year. Alternatively, the terminal value would represent the total amount of money the firm has invested in the R&D project on behalf of shareholders to the date of launch, including accumulated interest equal to the firm's weighted cost of financing, the return the firm presumably could have earned on alternative projects. Which of these numbers is the most appropriate depends on the use to which it is put. For practical purposes, the terminal value probably is the more intuitively appealing, because at the time of the launch of a

new pharmaceutical product, it is the amount that the present value of all future sales revenues from the product, minus production, marketing, and other future annual costs associated with the sale of the product, the firm must cover.

It was worth going into this methodological detail on the estimation of R&D costs because public estimates of those costs tend to be so controversial. DiMasi, Hansen, and Grabowski (2003) recently estimated the cost for U.S. pharmaceutical firms at between \$800 million and \$900 million. These estimates were promptly attacked as exaggerated by Light and Warburton (2005) in the same journal. Such arguments could arise over any or all of the following issues: (1) the estimates of the actual R&D outlays that should be properly attributed to a successful product, (2) the interest rate used to calculate the present or terminal value of that cash flow, and (3) whether, for policy purposes, the present or terminal value of that cash flow is the more appropriate figure. In the end, the only approach to settling such disputes would be to make the raw data used in making such estimates available to any researcher who would like to audit the calculations (Reinhardt 1997).

However those issues are settled, there can be no doubt that the upfront R&D costs incurred to launch a new pharmaceutical product is in the hundreds of millions of dollars, not only in the United States, but elsewhere as well.

The Risk of Investing in Pharmaceutical R&D

Because the R&D process leading to new pharmaceutical products is so long and may have to be abandoned at any time, investments in R&D may appear to be highly risky from a financial perspective. It is not so. Any sizeable research-based pharmaceutical firm invests simultaneously in many diverse R&D processes, many addressed to different illnesses, afflicting different parts of the human body. Many of these processes will fail to yield fruit; others will be successful to varying degrees. In a sense, then, a large pharmaceutical firm is not much different from a large mutual fund, except that the latter invests purely in diverse financial securities whereas a pharmaceutical company invests in the R&D for a diverse portfolio of new pharmaceutical products. From the viewpoint of an investor in the stock of a pharmaceutical company, the risk inherent in the overall flow of returns earned by a pharmaceutical company on its entire portfolio of R&D investments is not substantially different from the risk of an investment in a well-diversified mutual fund. That insight emerges from standard economic portfolio theory, but also from empirical research.

For example, Stewart Myers (1999) presented estimates of the financial risk and the associated weighted average cost of capital of large pharmaceutical firms. He found that the risk index of such firms, measured by the so-called beta coefficient, was close to the risk index of a broad market index, such as the Standard & Poor's 500, namely 1. The number suggests that, if the rate of return on the general market index rises or falls by, say, 10%, the rate of return of a large pharmaceutical company tends to rise or fall by about the same percentage. This risk index implies a corresponding weighted average cost of financing that is not purged of inflation of about 14% and an inflation-purged figure of about 10%. These are the interest rates one would use to convert time-phased R&D streams into their present or terminal values.

By contrast, Stewart estimated the beta coefficients for smaller biotech companies, organized around one or a few products, as anywhere from 1.5 to 2.3, suggesting that when the rate of return on the general market index changes up or down by 10%, the rate of return on biotech stocks tends to swing by between 15% and 23% up or down, which means that the stock certificates issued by biotech companies are much riskier from the perspective of investors and the associated weighted average costs of capital much higher.

Cost Structure and Pricing

Economists distinguish between annual *fixed* and *variable* costs. Fixed costs are those that do not vary with the volume of production and sales. Variable costs vary more or less directly with output volume. For purposes of analysis, it is convenient and generally realistic to assume that the variable costs per unit are constant over the empirically relevant range of output. What is a variable and a fixed cost, however, varies with the time frame. In the very short run, for example, a month or quarter, most costs are fixed. Over a year or more, costs that are fixed in the very short run become variable.

A distinguishing characteristic of the pharmaceutical industry is that its annual fixed costs (including an annual allocation of the cost of R&D) tend to be high relative to its variable costs in the sense that the variable or *incremental* cost of producing and packaging an additional batch of product tends to be quite small relative to the fully allocated average unit cost per unit of output, including the allocation of fixed costs.

A consequence of such a cost structure is that, in the short run, it will be profitable for the firm to sell output at prices that cover the lower *incremental* costs and yield some margin above those costs, but fall far short of *total*

average unit costs (fixed and variable costs per unit of output). That shortfall may be acceptable if not all output is sold at such low prices, but only some batches, leaving higher-priced batches to help recover all fixed costs -- in other words, if the firm can *price discriminate*. A controversial question is whether such price discrimination is in society's interest or whether it should be interdicted by public policy makers. That question is explored in the next section.

IV. Price Discrimination in the Market for Pharmaceuticals

Price discrimination refers to the practice of selling identical products to different sets of customers at different prices. Expressed another way, different customers pay different markups over the identical incremental cost of producing an identical product. Price discrimination is widely practiced in the hotel and airline industries, by universities in the United States that can vary their tuition through scholarships, by electric power companies, and in the health care industry. Hospitals in the United States, for example, routinely charge different payers different prices for the same services. In the U.S. pharmaceutical market, different prices are charged to different insurance carriers and to self-paying patients. Worldwide, the same pharmaceutical firms sell the identical product to different countries at different prices.

Industries that engage in price discrimination have three common features. First, their incremental production costs at any moment in time are low relative to fixed costs, which means that, in the short run, a price-discriminating firm with ample capacity can earn a positive contribution margin to overhead and profits by selling product at prices below fully allocated costs (fixed and incremental costs per unit), as long as price exceeds incremental costs. Low incremental costs can imply very low prices for some customers. Second, the practice of price discrimination presupposes that customers can be segregated into distinct groups, each with a different price sensitivity or degree of bargaining power. Third, for either technical or legal reasons, customers cannot resell purchased products to one another.

The Potential Benefits of Price Discrimination

Suppose a pharmaceutical firm had been granted a patent for a new product and, thus, enjoyed a degree of monopolistic power in its product market. Suppose that initially the firm were free to set the price of the product so as

to maximize its profits, but had to charge all customers the same price. This arrangement would price out many customers willing to pay prices in excess of the incremental cost of producing the product but not a price as high as the single, profit-maximizing price. These customers would benefit if they could buy the product at a lower price, and the pharmaceutical company would gladly do so as long as that lower price exceeded its incremental production cost and did not oblige it to lower its price to customers willing to pay the higher, profit-maximizing price. This two-price policy would be a classic example of price discrimination. It would yield added profits to the manufacturer, but it would also benefit additional customers.

The two-part pricing strategy could be extended to a multiple-price strategy by selling successive batches of output at successively lower prices, as long as those prices exceeded incremental costs and as long as customers receiving the product at a lower price could not resell it to customers willing and able to pay a higher price. Each additional batch would enhance the firm's profits, but it would also benefit yet another group of customers.

At the limit, there might be one batch of output sold at a price equal to incremental cost. While the firm would not profit from selling that batch, it would serve customers (e.g., in a very low-income country) willing to pay only that very low price. The firm might willingly do so, especially if this enhanced its reputation as a good world citizen. Economists would call this outcome "efficient" in the sense that no customer willing to pay a price equal to at least the incremental cost of producing the product would be left unserved by the pharmaceutical firm.

The preceding analysis can be modified to include as a starting point not a profit-maximizing single price, but a single price constrained by government to a level that merely allows the pharmaceutical producer a regulated rate of return, as is the case, for example, in the United Kingdom. Given the cost structure described earlier, such a rate-of-return-regulated single price, still would be likely to price out certain customers, especially those in lower-income countries, who would be willing to pay prices greater than or equal to incremental costs, but not the higher regulated single price.

Why Price Discrimination Might Be Criticized

The previous exposition, of course, has been carefully styled to lead to what appears to be a benign policy. It accepts as the baseline a single price determined either under profit maximization or under price controls, and then asks whether, relative to that baseline single price, allowing price discrimination would be in society's interest.

It should be clear to anyone, however, that a pharmaceutical manufacturer could extend backwards as well, that is, that the firm could earn even higher profits by segregating the first set of customers charged the highest price into distinct smaller groups with different degrees of price tolerance and all but one of them paying prices higher than the baseline single price assumed above. At the limit, at least in theory, the firm could so segregate its customers that every one of them pays the maximum bid price that the customer would have been willing to pay for the product. The firm then would have extracted from its customers the maximum amount of money that could have been extracted from them, which is apt to elicit criticism from the general public and policy makers alike. However, every customer willing to bid a price at least equal to the incremental cost of producing the product would be served, which would make the strategy efficient in that sense.

V. Price Discrimination in the International Market

In most modern economies, large fractions of the sales of pharmaceuticals are covered by public or private third-party payers, rather than patients themselves. These third-party payers act as bulk buyers. If those bulk buyers represent entire countries that can set prices through government price controls, the market muscle can be enormous. Only buyers with little or no market power, either small insurance carriers or uninsured patients paying fully out of pocket, can successfully be charged the highest retail prices for a given product. It is the situation, for example, that obtains in the United States today. There, millions of low-income Americans are without any health insurance and, therefore, without any market power at all in the market for prescription drugs, routinely paying far higher prices than do patients in relatively wealthy countries with more market power exercised through government price controls.

Few citizens of high-price countries complain when pharmaceutical products are sold to very low-income countries at prices approximating incremental production costs, as is now widely done. But citizens in high-price countries, especially the United States, which has the highest prices for pharmaceutical products, regard it as unfair that citizens in other economically developed, relatively high-income countries can purchase the identical drug at much lower prices, especially for drugs that were developed in the high-price country (e.g., in the United States).

The research-based pharmaceutical industry, although having practiced this form of price discrimination for decades, resents this practice when it is effectively imposed on the industry through price controls by foreign

governments. First, the industry fears that, with the help of clever entrepreneurs and sometimes even local government officials, such as state governors in the United States, citizens in the high-price countries will be able to reimport pharmaceutical products from lower-price countries and, thus, drive the world toward a single price substantially dictated by foreign governments practicing price controls. Second, the industry fears what it calls "external reference pricing," that is, the practice by some foreign governments of tying the prices they allow to the lowest price paid by any other country. Third, the industry argues that, absent these price controls abroad, its members could earn higher revenues even if freer-market regimes abroad would continue to entail some degree of differential pricing for the same product. Implied in that argument is the tacit suggestion that most of any added revenues from the removal of foreign price controls would flow into added R&D. Finally, the industry typically suggests that the removal of price controls in low-price countries would enable it to lower prices in the high-price countries, although it is not clear what market mechanism would bring about that effect.

Unconvincing Critics of Cross-National Price Discrimination

Media pundits, think tanks, and consultants who are ideologically sympathetic to the pharmaceutical industry, or are economically beholden to it, have echoed and amplified the pharmaceutical industry's concerns over cross-national price discrimination in sometimes hysterical tones. It may be well to review briefly the merits and demerits of these critics' sometimes vehement arguments, because their voices often are highly influential in government circles.

In a commentary posted on the Web site *USANext*, for example, Steve Forbes (2005), owner and publisher of the internationally known magazine *Forbes*, former presidential candidate in the United States, and a friend of many foreign heads of states, accuses Europe, Canada, and Japan of "mooching" off the U.S. pharmaceutical industry, which he considers nothing less than a "costly form of piracy." Why he includes Japan as a "moocher" is not clear. After all, that country is known among the experts to pay prices closer to American levels and sometimes even higher (Danzon and Furukawa 2003).

James K. Glassman (2005), a highly popular media pundit in some circles, including government, has sternly lectured European and Canadian policy makers thus on his own Web site *Tech Central Station*. He writes

that "price controls kill. . . . Europe kills its citizens and makes them sicker because it restricts access to drugs it considers too expensive. . . . Europeans, Australians and Canadians are doing something immoral."

Glassman cited a study of drug price controls by the consulting firm Bain & Company (2005). In that study Bain also focused on the effects drug price controls have for the countries imposing them. The authors estimated that if Europe's pharmaceutical spending per capita had matched the level of the United States, Europe would have spent an additional \$160 billion in 2002 and \$840 billion cumulative over the preceding decade. Using Germany as an illustration, they argued that Germany saved \$19 billion from price controls in 2002, but this policy imposed \$22 billion of added costs on Germany in the form of foregone benefits. Only about \$5 billion of that alleged cost, however, consisted of costs attributable to better outcomes for patients. The rest was money that would have been spent on added inputs used by the pharmaceutical and related industries.

While this kind of benefit-cost calculus may have intuitive appeal among business consultants and even among some policy makers, it would not be accepted from a first-year student by any reputable economics department. As a general rule, economists measure the benefits produced by an economic activity by the value that the *output* from that activity produces, and not by the value of the *inputs* it consumes.

In any event, it is not clear that policy makers in these other countries, notably Germany, will be persuaded by these shrill exhortations or by the dubious benefit-cost calculus offered by management consultants Bain & Company. After all, Glassman's moral sermon emanates from a nation in which some 45 million individuals find themselves without any health insurance whatsoever at any point in time and a larger percentage yet finds itself without coverage for prescription drugs. As a highly accomplished panel of scientists concluded in a study published by the Institute of Medicine of the U.S. National Academy of Sciences (2003), some 18,000 Americans die prematurely every year because of this lack of health insurance, not even to speak of the avoidable suffering of those chronically ill uninsured who survive, among them many elderly Americans.

Furthermore, health policy makers in Europe and Canada can point to widely respected statistics gathered annually by the Organization for Economic Cooperation and Development, according to which the United States ranks remarkably low in the OECD on many standard health status indicators, such as the infant mortality rate, life expectancy at birth and at age 60, and "potential years of life lost per 100,000 population," that is, life

years that ought not to have been lost if timely and appropriate health care had been given (Anderson and Hussey 2001). Accusing policy makers in other nations of "killing people" through price controls from the perch of the United States therefore requires a certain temerity. Although probably meant to be helpful to the U.S. pharmaceutical industry, one may wonder whether it is.

Finally, policy makers in these other countries can properly wonder how much of any additional dollar or Euro that they might allow to be spent in their countries on prescription drugs actually would be allocated to R&D by the pharmaceutical industry. These policy makers can point to income statements of the U.S. pharmaceutical companies, according to which only about 13–14% of total revenue flows into R&D, while over a third of total revenue flows into marketing and general administration. The question can legitimately be raised by policy makers in other countries whether, from the viewpoint of society at large, some of these funds now going to marketing and general administration might not be more productively spent on R&D. Figure 2.1 exhibits the relevant financial statement data for the 1990s. More recent data, provided in 2003 by Bank of America Securities Equity Research, corroborate the earlier data. In 2002, for example, 13 large research-based U.S. pharmaceutical companies jointly spent about 32.8% of total revenue on SG&A, 25.3% on cost of goods sold, and 14% on R&D.

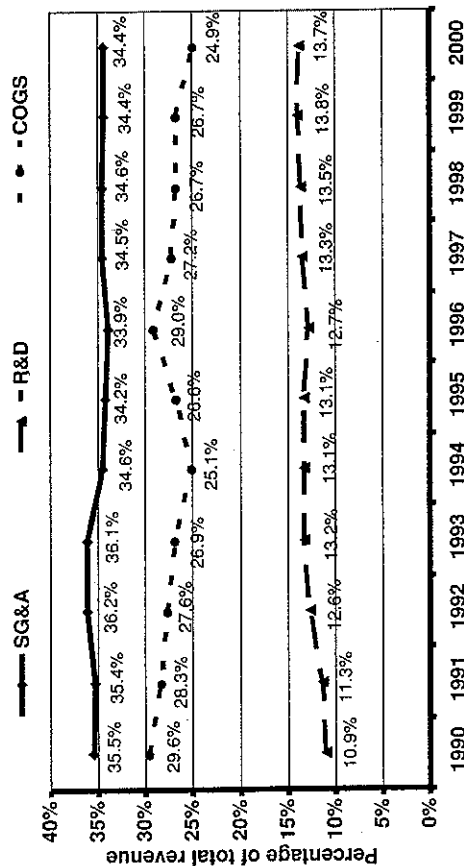


Figure 2.1. Trends in the financial statements of major pharmaceutical manufacturers, top 10 firms, 1990–2000. Source: Kaiser Family Foundation (2001), Exhibit 31, p. 45.

The Location of Pharmaceutical R&D

Running through virtually all of the criticism leveled at drug price controls in Europe, Canada, and Asia is the theme that these controls drive pharmaceutical R&D from the countries with price controls to those countries with fewer or no government controls on drug prices, for example, the United States. Petulance among the executives of the research-based pharmaceutical industry might trigger such a response, but not among cool-headed executives who sincerely wish to serve their shareholders. Because pharmaceutical products can be sold worldwide, regardless of where the underlying R&D was performed, and because even clinical trials can be conducted on a worldwide basis, the location of pharmaceutical R&D should not be substantially driven by the presence or absence of government controls on product prices at various alternative locations. Elementary economic theory suggests that these locational decisions should be driven instead by the availability and cost of scientific research personnel and by government regulations directly affecting the R&D enterprise.

It is entirely conceivable, for example, that, over the next several decades, more and more pharmaceutical research will shift from Europe and the United States to Asia, especially to China, where there will likely be an abundance of highly trained and relatively low-cost scientific personnel to conduct the research. Even the more economically developed Asian nations, such as Korea, Singapore, and Taiwan, are likely to benefit from this migration, as long as they strive to have a comparative advantage in scientific research vis-à-vis the United States and Europe.

The "Free Trade" Argument

Probably more compelling in the political realm than the critiques of foreign drug price controls reviewed thus far is the argument that these controls simply are "unfair" and violate tenets of free international trade.

That argument was first famously raised by the then U.S. FDA Commissioner Mark McClellan before the First International Colloquium on Generic Medicine in Cancun, Mexico (September 25, 2003). It was raised again by the Republican Policy Committee of the United States Senate (2005). Its policy statement, "Pharmaceutical Price Controls Abroad: An Unfair Trade Policy," cited the 2002 U.S. Trade Promotion Authority Act, which acknowledged that "price controls" and "reference pricing" for pharmaceutical products (to be discussed below) are "trade-distorting

barriers" and "disguised trade barriers." Indeed, the Republican Policy Committee went so far as to decry even conventional economic evaluations (referred to as "cost-utility evaluation") as a trade barrier, singling out "Australia, Canada, the Netherlands, Portugal and the United Kingdom" as practitioners of such analyses (p. 5). That a committee of the U.S. Senate would declare standard economic evaluation of new medical technology to be a trade barrier speaks volumes about what American policy makers had in mind concerning the relationship between free international trade and national health policies.

The 2002 U.S. Trade Promotion Authority Act gives the U.S. president the authority to "strive to eliminate unfair trade practices" in international trade negotiations. That authority was subsequently exercised in the Australian-U.S. Free Trade Agreement negotiated in 2004 (Becker 2003; Outterson 2004), drawing international attention to the linkage now made by the U.S. government between the domestic health policies of nations and international trade policy. Exercise of the authority is bound to surface again and again on the agendas of future bilateral or multilateral international trade negotiations. This intrusion by the United States into the domestic health policy of other nations is apt to become a source of friction in international relations.

The central tenets running through this foreign-trade argument are (1) that current levels of pharmaceutical R&D spending worldwide are sub-optimal in the sense that more R&D spending could easily be justified on the basis of future patient health benefits (e.g., Murphy and Topel 2003b), (2) that the R&D costs per successful new pharmaceutical or biotech products will continue to rise apace, and (3) that this growing burden should somehow be more fairly shared among nations on the basis of their ability to pay. There is the added assumption that a more "equitable" sharing of the fiscal burden of pharmaceutical R&D would automatically lead to lower drug prices in the currently high-price countries, notably in the United States. Although this line of reasoning has considerable intuitive appeal, and can be backed up by the awesome economic power the United States can bring to bear on foreign policy, it triggers in one's mind a number of questions.

First, in spite of annual compound growth of close to 13% in U.S. R&D spending during the past decade and a half, the numbers of both new drug applications and new drug approvals have not grown commensurately. On the contrary, both have leveled off in recent years. It appears that traditional approaches to chemical-based pharmaceutical R&D have run into strongly diminishing marginal returns, and a more pronounced shift to alternative approaches should be made, especially for biological products.

Second, the idea that the removal of price controls in other countries will lead to a lowering of drug prices in currently high-priced countries, notably in the United States, may have appeal at first glance, but the proponents of that idea are never clear about just what mechanism would produce these price declines. Presumably the sellers of pharmaceutical products in the U.S. market would continue to extract from it the maximum prices that U.S. consumers are willing to pay. Any future reduction of drug prices in the United States therefore hinges mainly on the relative market power of the buyer side in the U.S. market, rather than on what other nations pay for drugs. Elementary economic theory suggests that if other nations allowed drug prices to rise, but the buyer side of the U.S. pharmaceutical markets was to weaken for some reason, drug prices in the United States almost surely would rise accordingly, independently of the higher drug prices abroad. To argue otherwise stretches credulity.

Third, there is the question of how "unfair" current price differentials in the global pharmaceutical market actually are. The authors of the previously cited Bain study proposed that Europeans should "pay prices proportional to their GDP per capita" (Bain Company 2005, p. 5). That idea has been echoed by most critics of the current, allegedly "free rider" system. There is evidence that, by and large, this criterion is actually being met.

Differential Drug Prices and Ability to Pay

Danzon and Furukawa (2003) compared average price levels for pharmaceuticals in eight countries – Canada, Chile, France, Germany, Italy, Japan, Mexico, and the United Kingdom – relative to those in the United States. The authors used as their unit of analysis the "molecule-indication" for drugs, defined by active ingredient and therapeutic class. A country's price per dose was the volume-weighted average price per dose, averaged over all package sizes, in a molecule-indication, using U.S. volume weights for the cross-national comparisons. The manufacturers' prices were used instead of retail prices to purge the price data of cross-national differences in wholesale, retail markups, and taxes.

Using 1999 foreign exchange rates to convert all prices to U.S.-dollar equivalents, the authors found that Japan's average drug prices per molecule-indication in that year were the highest in the nine-country cohort, U.S. prices were the next highest, and Canada's the lowest, at 33% below U.S. prices. Prices in France were 30% lower than U.S. prices, and prices in the other countries about 15% lower (Danzon and Furukawa 2003, Exhibit 3).

When cross-national price comparisons are made using prevailing market exchange rates, the observed price differentials naturally fluctuate simply with fluctuations in exchange rates, which are heavily influenced by fluctuations in capital flows. To avoid this extraneous source of variance in the data, Danzon and Furukawa used two alternative exchange rates to convert prices in foreign currencies into U.S.-dollar equivalent prices: (1) gross domestic product-purchasing power parity (PPP) exchange rates, and (2) health care-PPP exchange rates. The GDP-PPP exchange rates equalize the purchasing power of different currencies in terms of a GDP-based basket of goods and services, while the health care-PPP equalizes the purchasing power of different currencies in terms of a basket of health care goods and services.

Using the GDP-PPP conversion, the authors found that Canada's average drug prices were only 14% below comparable U.S. prices in 1999, rather than the 33% suggested at market exchange rates. With GDP-PPPs, Japan's average drug prices were slightly below the comparable U.S. prices, although France's prices were about 40% below U.S. prices, rather than the 30% at market exchange rates. Germany's average drug prices were 25% below U.S. prices at GDP-PPP exchange rates, rather than about 15% at market exchange rates. Finally, at the health care-PPP conversion rates, all eight countries in the study had *higher* drug prices than comparable U.S. prices. This was so because the prices of health care goods and services other than prescription drugs in these countries were even lower than comparable prices in the United States.

The final adjustment made by Danzon and Furukawa to cross-national differentials in drug prices was to relate them to cross-national differences in GDP per capita, a reasonably good indicator of ability to pay. The authors found that, after this final adjustment, drug price differentials between countries roughly reflected income differences (except for Chile and Mexico). If one treats global R&D costs as a "global joint cost" to be recouped through efficient and equitable global pricing strategies, as the authors suggested, then the prevailing price differentials were reasonably, if not perfectly, consistent with both efficiency and equity.

From the perspective of international trade negotiations, this is a highly policy-relevant finding. It suggests that the prevailing cross-national price differentials, far from representing unfair mooching on the part of other countries, actually fairly closely reflect one of the objectives frequently cited by the critics of current global drug-pricing policies, namely, that cross-national drug prices should reflect cross-national differences in ability to pay.

VI. The Balance of Power in the Pharmaceutical Market

The critics of government-imposed price controls on pharmaceutical products do have a valid point. As long as the price ceilings are set above the incremental cost of producing these products, manufacturers will be tempted to sell at whatever those controlled prices are, because they earn at least a positive margin toward the recovery of fixed costs. The problem is that the price ceilings may be set at levels far below fully allocated fixed costs per unit. If every payer followed that strategy, pharmaceutical companies would soon become insolvent.

Critics of price controls therefore point to "free markets" as the more efficient alternative without, however, specifying precisely how such a market should be structured. The tacit assumption appears to be that the mere absence of government controls on the production, pricing, and distribution of a product *ipso facto* represents a properly functioning market. One could not be more wrong on this point. According to the First Optimality Theorem of economics, "free markets" in an industry will lead to an efficient allocation of productive resources and distribution of output only if these markets are perfectly competitive, which requires that the following exacting conditions be met (Arrow 1963, pp. 942-943):

1. There is full price transparency for all rival products, on both sides of the market
2. The intrinsic qualities of the rival products are fully and accurately understood, on both sides of the market
3. There is unfettered and costless entry and exit of producers for any product sold in the market
4. There are no increasing returns in the production and distribution of products and
5. For every product traded in the market, there are many buyers and many sellers, none of whom possesses monopolistic market power (such as those conveyed by patent laws).

According to the Second Optimality Theorem, in markets meeting these stringent conditions, any *efficient* allocation of goods and services that is desired by society on *ethical* grounds can be attained, in principle, without government interference in the production, pricing, and distribution of products, simply by redistributing purchasing power among the citizenry to allow the market to drive on its own toward the desired outcome (Arrow 1963, p. 943).

The First and Second Optimality Theorems have become the intellectual foundation for current proposals worldwide to "privatize" all production and distribution of health care and to seek politically desired distributions of health care through transfers of cash or vouchers to low-income families. Unfortunately, it would stretch credulity to argue that the markets for health care even approximate the stringent conditions required by these theorems (see, e.g., Rice 2002).

Furthermore, as Newhouse (2004) has argued convincingly in a recent commentary on the pricing of pharmaceutical products, in practice, it is impossible to develop a price policy for pharmaceutical products that is both *statically* and *dynamically* efficient. *Static* efficiency requires that, at a given point in time, price be set equal to the incremental cost of producing more output with a given capacity, lest customers willing to cover at least these incremental costs go unserved. However, given the industry's cost structure, at that price fixed costs (including R&D) will not be recovered. It follows that a statically efficient price *ipso facto* is dynamically inefficient, because *dynamic* efficiency requires that, over the long run, added resources flow into R&D and production capacity up to the point at which the social benefits from further expansion would no longer cover the long-run incremental cost of expansion (including R&D). As a result of this inherent conflict between static and dynamic efficiency, all pricing policies for pharmaceutical products in the real world will be compromises between these two forms of efficiency. Thus far, these compromises have been anything but balanced, even in what were considered by pharmaceutical manufacturers as "free markets."

Before 1990, for example, pharmaceutical manufacturers selling products in Germany believed they were operating in a "free market" there, because the manufacturers were free to set the prices for their products to German wholesalers. The markups of wholesalers and retailers were regulated by government. Insurance carriers, typically covering 100% of the retail prices charged for prescription drugs, had no choice but to pay those prices. Every physician in Germany then enjoyed complete therapeutic freedom to prescribe whatever product he or she deemed appropriate. Occasionally — perhaps more than occasionally — they did so under conflicts of interest created by sundry favors or rewards bestowed on them by the marketing departments of pharmaceutical companies. No economist could possibly describe this arrangement as a properly functioning "free market," because there was no countervailing power whatsoever on the demand side of that market. Naturally, the arrangement was not sustainable over the longer run and was abandoned in the early 1990s, in favor of sundry government controls on drug pricing and prescribing.

Similarly, until the early 1990s, only about a quarter of retail sales of prescription drugs for the most part in the United States were covered by health insurance. American consumers of prescription drugs paid the full retail price charged them by the local pharmacist, who had complete freedom in pricing those products, as did wholesalers and manufacturers further upstream. Individual physicians had complete therapeutic freedom to prescribe any pharmaceutical product they deemed appropriate, once again under occasional conflicts of interest. Patients either filled the script at the pharmacy or did not, depending on their budgets. Typically, patients had no information on relative prices of these drugs at various pharmacies in their market areas and on the availability of substitute products, let alone on the cost effectiveness of rival products, by which is meant the relative cost for the benefits achieved with the drugs. In fact, even to this day, such crucial information is not generally accessible to American patients. Pharmaceutical executives may have viewed this arrangement as a properly functioning "free market" as well. Once again, however, no self-respecting economist could possibly certify it as even an approximation to a market meeting the conditions of the First Optimality Theorem. Only with the spread of third-party payment in the 1990s in the United States has there been a degree of effective market power on the demand side of the U.S. pharmaceutical market.

Markets for pharmaceutical products worldwide are less than well balanced. Markets dominated by the monopsonistic (single-buyer) power of government can exercise undue power over the supply side of the market and depress prices to dynamically inefficient levels. At the other extreme, markets with an ill-informed and typically feeble demand side, weakened further by moral hazard inherent in health third-party payment, are unduly dominated by the supply side. What is needed instead are markets with more evenly balanced of power, in which both sides of the market are accurately informed about the prices, clinical effectiveness, and cost effectiveness of the rival products being offered for sale. Creating such markets is one of the major challenges confronting health care policy makers around the globe.

This will involve two facets. First, where patients now enjoy full or nearly full insurance coverage for prescription drugs, they are likely to be asked to assume a larger share of the cost of drug therapy, if only to focus their minds on the relative "cost effectiveness" of rival products. Second, however, to allow both patients and their physicians to act as more cost-conscious purchasers of prescription drugs, an information infrastructure will emerge, or should emerge, that can provide potential users of pharmaceutical products with objective, science-based information on the prices and relative

cost effectiveness of rival pharmaceutical products being offered in the market.

Forms of Cost Sharing by Patients

Cost sharing by users of prescription drugs can take a variety of forms, each with its own behavioral and clinical consequences.

Full Out-of-Pocket Spending

The patient may be asked to pay out of pocket the full retail price of prescribed drugs. This is still more common than may be supposed, for example, for the about 45 million persons in the United States without health insurance coverage at any point in time. It is also so for elderly Americans covered by the Medicare Modernization Act of 2003, which requires patients, in 2006, to pay out of pocket fully for the first \$250 of drug spending in a year (the annual "deductible"), then 25% of annual spending in excess of \$250 but below \$2,250, but then it reverts to zero insurance coverage once more for annual spending in excess of \$2,250 but below \$5,100 (the so-called doughnut hole), and thereafter the patient is responsible for 10% of annual spending in excess of \$5,100, with both the deductible and doughnut hole growing over time (Kaiser Family Foundation 2005). Prescription drugs are not covered under the government-run, provincial health insurance plans for Canadians who are neither elderly nor poor. In many of the poor, developing countries, the bulk of health spending is fully out of pocket, including spending on prescription drugs.

Tiered Copays or Coinsurance

Insurance plans around the world that had traditionally covered the full cost of prescription drugs have begun, in the last decade or so, to impose either deductibles or various forms of tiered cost sharing on patients.

The most common form of tiered cost sharing has been flat *copayments* per prescription, staggered in size by generics, brand-name drugs on the insurer's formulary, and brand names not on the insurer's formulary. Although designed to goad patients toward generics or brand-name drugs preferred by the insurer, merely imposing copayments keeps the full price of the purchased products hidden from the patient's view. For that reason, many insurance plans have introduced tiered *coinsurance*. Under such a plan, for example, the insured may be asked to pay 10% of the cost of a generic drug, 20% of the cost of a brand-name drug on the insurer's formulary, 40% of the cost of brand-name drugs not on the formulary,

and, of course, 100% of drugs of any type not covered by the insurance plan at all.

Reference Pricing

By far the bluntest and most controversial form of tiered cost sharing, however, is "reference pricing," so called because the insurer only reimburses patients for the price of a relatively low-cost drug in a larger "therapeutic group" of drugs all declared to be "equivalent" (López-Casasnovas and Puig-Junoy 2001). Patients are then required to pay the entire difference between this low-cost reference price and the actual retail price charged for a drug with a higher price out of pocket. Reference pricing has been used under Germany's Statutory Health Insurance system since the early 1990s. It now is used in a number of other countries, including in some Canadian provinces, in Australia, and in New Zealand (Kanavos and Reinhardt 2003).

As already noted, the Republican Policy Committee (2003, p. 5) singled out reference pricing as one form of restraint of free international trade, although on its face reference prices strike at least some economists (Huskamp et al. 2000; Kanavos and Reinhardt 2003) as a reasonable precondition for a genuine, price-competitive market for pharmaceutical products, especially if patients and their physicians are well informed about the distinct attributes and relative cost effectiveness of the drugs within a therapeutic group. The idea is that insurance carriers will socialize through full coverage the cost of only basic prescription drugs that are considered adequate, leaving it to the suppliers of more expensive substitutes in a therapeutically equivalent group to persuade patients in a free market that the benefits of the higher-priced products are worth the extra out-of-pocket outlay on them.

The approach is nothing other than the analogue of the more general concept of "defined contribution" now widely recommended by many economists for the purchase of health insurance (Pauly et al. 1991). Under that approach, government or employers make a defined contribution to an individual's purchase of private health insurance, leaving the individual to pay the full difference between that contribution and the insurance premium actually charged by the private insurer.

Remarkably, however, economists can be found who reject the idea of reference pricing on two grounds (see, e.g., Danzon 2000 and 2001, and the series of essays in López-Casasnovas and Jönsson 2001). That opposition comes even from economists who favor the idea of defined contributions for health insurance (see, e.g., Danzon, coauthor in Pauly et al. 1991).

First, these economists have argued that patients typically are not sufficiently informed about the cost effectiveness of rival drugs in a therapeutic

group and that physicians will not take the time to explain it to them, because they are not explicitly paid for that service. That argument, of course, calls into question the entire idea of applying a market approach to the pharmaceutical market or to health care markets in general. Second, these economists have warned that reference pricing violates horizontal equity, because poorer patients are more likely deprived by it of superior, higher-priced products than are wealthier patients. That argument, however, would apply with equal force to any defined contribution approach to health insurance and any proposal to impose high deductibles and coinsurance on patients for any health service, as such arrangements always entail the price rationing of health care at the margin (see Reinhardt 1996).

Much of the controversy over reference pricing, in particular, the strong opposition of pharmaceutical manufacturers to that approach, arises from the definition of "equivalence" in the construction of the relevant "therapeutically equivalent groupings" of prescription drugs. These groupings can be narrowly or widely construed. At the narrow end, a "therapeutically equivalent group" of drugs may include only drugs with the identical active, chemical ingredients, which inevitably confines the grouping to generic drugs only. At the other extreme, very much frowned upon by research-based pharmaceutical manufacturers, the "therapeutically equivalent grouping" can be defined by insurers to include all products with the same therapeutic target, including off-patent and on-patent drugs.

Additional controversy arises from the selection of the reference price within a therapeutically "equivalent" group of drugs. If only the lowest-priced drug in the group serves as the reference price, all other products are exposed to cost sharing by patients, and their prices may well be pushed down toward the low reference price. Even so, this would have to be regarded as a market solution, rather than price control, because patients' preferences and willingness to pay had forced the migration of prices toward the reference price. But if a higher-priced product, somewhere in the middle of the therapeutic grouping, were used as the reference price, then the prices of lower-priced products, including generics, would migrate up over time toward the higher reference price. It might lead to very high profit margins on noninnovative products that do not contribute toward financing R&D.

A more in-depth discussion of reference pricing lies beyond the compass of this essay (in this regard, see Kanavos and Reinhardt 2003). Suffice it to say, it is a powerful method of introducing market power on the demand side of prescription drugs covered by health insurance, and one likely to be embraced, sooner or later, by private health insurers, as they seek to cope with the ever-rising cost of health care.

Consumer-Directed Health Care (CDHC)

After the demise of "managed care" in the United States during the late 1990s, the latest novel idea in American health policy is what is euphemistically called consumer-directed health care, which is in effect nothing other than health insurance with very high annual deductibles, ranging, in the United States, from \$2,000 per family to \$10,000 or more. Just as American management consultants sought to market "managed care" around the globe during the 1990s, so they are apt to market CDHC in the early twenty-first century as a novel American invention, even though it is but a particular variant of the medical savings account (MSA) approach long used in Singapore.

Whatever may be said for or against the CDHC approach, it cannot be judged supportive of the research-based pharmaceutical industry, as patients will be exposed to the full cost of prescription drugs within the high deductibles. Unless special insurance arrangements are made for prescription drugs, on the plausible argument that lowering their cost to patients can help avoid costly hospitalizations and other more expensive acute care, the approach is apt to impinge severely on the profit margins and funding of R&D in the industry. It is a development that ought to give the industry pause.

An Information Infrastructure of the Pharmaceutical Market

If the market power inherent in the decisions of patients is to be more effectively harnessed in the control of health care costs, then it becomes essential that patients, as well as their physicians, are better informed than they now are about the relative costs and benefits of rival products with the same therapeutic target, in short, on their relative "cost effectiveness." The development of such an information base will be another major challenge of health policy makers in the coming decades.

The establishment of the relative cost effectiveness of rival pharmaceutical products poses extraordinary methodological problems, as is superbly well described in the bible for such studies, Drummond et al.'s *Methods for the Economic Evaluation of Health Care Programmes* (2005). The "costs" used in such evaluations can be narrowly construed to be only those of insurers or of insurers and patients, or very widely to include all social costs, including those borne by family members, employers, and others in society (e.g., though contagion). Benefits in cost-effectiveness studies typically are measured by physical health-status indicators, such as added life years saved or changes in blood pressure, but they must be adjusted for the quality of life, which in turn triggers a host of additional methodological challenges and,

in the end, subjective value judgments. Consequently, different researchers can arrive at quite different conclusions concerning the relative cost effectiveness of a set of rival pharmaceutical products (see Pauly, Chapter 10, and Drummond, Chapter 11). The sources of such differences can be laid bare only if all such studies are open to full, external audit as to the raw data going into the studies, the methodologies used to transform the raw data for analysis, and the analyses themselves (Reinhardt 1997).

Given the many judgments that must be made by researchers in even the best, most objective cost-effectiveness studies, the question arises who should conduct them, to make them truly useful for the market of pharmaceutical products. If those studies are conducted or funded by third-party payers, be they governments or private insurers, they will immediately be suspected by pharmaceutical producers, physicians, and patients to be biased in favor of cost savings, possibly at the expense of quality. But if these studies are conducted or funded by pharmaceutical producers, as now they typically are, they are similarly suspect among third-party payers (Millenson 2004) and among the general public. What is needed, therefore, are research institutes that are fiscally independent of either side of the pharmaceutical market and, therefore, beholden to neither side.

In "An Information Infrastructure for the Pharmaceutical Market," this author proposed such an approach for the United States, although it would be applicable to any country (Reinhardt 2004). One or preferably several private, nonprofit Phamaco-Economic Research Institutes (PERIs) would be established permanently by law and granted a generous initial endowment financed by government, say, a 1% tax on all pharmaceutical retail sales over one or two years. These endowments could be replenished from time or time or be generous enough at the outset not to need such replenishments. Like private universities in the United States, the PERIs would invest their endowments in diversified portfolios of financial assets. The returns from these investments, and perhaps annual take-downs of the endowments themselves, would finance an ongoing set of research studies conducted by high-caliber, highly respected pharmano-economic researchers located either at the PERIs themselves or in academic institutions working under contract from the PERIs. These studies would be fully auditable, at all times, by anyone as to raw data and methodology, including by researchers engaged by the pharmaceutical industry. The PERIs also would monitor the performance of drugs after launch and evaluate new therapeutic applications emerging after launch. The research findings produced by the PERIs would be treated as a pure public good, which means that they would be posted on a Web site and be available worldwide to anyone, free of charge.

Finally, these research findings would not be binding on anyone, but they could be used by all stakeholders in their decisions on drug therapy or new R&D on pharmaceutical products.

VII. Summary and Conclusion

The purpose of this chapter has been to provide a broad, general overview of the role of the pharmaceutical industry in the economy and in the health sector, and to explore a number of problems arising from the industry's cost structure and from the traditional imbalance in the global markets for pharmaceutical products.

There can be no question that governments in all nations must be careful not to harm through their policies an industry on whom (1) the entire world depends for enhancements in the quality of human life, and (2) to which the world will increasingly look for technological breakthroughs to help reduce the currently high labor intensity of the production of health care, which cannot be sustained, given an ever-rising ratio of nonworking to working-age adults.

At the same time, the industry must reckon with sustained efforts in the decades ahead to shore up the market power of the *demand* side of the market. It will be sought by engaging patients more fully in the process of price competition through various forms of cost sharing, including reference pricing. It will be sought also through the natural complement of added cost sharing by patients, namely, greater transparency of the prices and the relative cost effectiveness of rival pharmaceutical products. These particular approaches to shoring up the demand side will certainly be attempted in countries where government controls of pricing have been weak or absent. But even where governments have hitherto controlled drug prices, such price controls may be transformed over time into greater cost sharing by patients and the associated transparency of prices and cost effectiveness.

The challenge for all stakeholders worldwide will be to find a dynamically efficient balance between eliminating whatever current waste there may be in pharmaceutical therapy and encouraging greater price competition, on the one hand, and, on the other, leaving prices at sufficiently high levels to attract adequate resources to the complex R&D enterprise of the industry. This book is intended to be part of the global conversation on how best to achieve that goal.