PHARMACEUTICAL RESEARCH: HOW AMERICA LOSES OR WINS

by Irwin Lerner

In considering what is right with American medical care, the pharmaceutical industry has much to be proud of and much to hope for—hope that we can have a significant impact on diseases such as cancer, acquired immunodeficiency syndrome (AIDS), heart disease, and arthritis, and hope that the research community our American pharmaceutical industry has created and sustained will be preserved and strengthened through the uncertain times ahead.

Pharmaceutical Prices

Increases in the price of pharmaceuticals have come only after more than a decade of exemplary resistance to inflationary pressure. Cumulatively, from the base year 1967 through May 1985, the rate of prescription medicine price increases as measured by the producer price index still trailed the rate for all commodities by more than fifty-five points. Further, the share of national health expenditure on drugs continues to decline. In 1960, the money spent on drugs and medical sundries amounted to 13.8 percent of total health care expenditures. By 1983, the latest year for which complete data are available, the share spent on drugs and medical sundries had been cut by more than half, to 6.7 percent, less than a dime of every dollar spent on health.

As for the recent spate of price increases, industry analysts regard them as anomalous. In the face of slower inflation, no competitive industry can resort often or long to across-the-board increases. We have already begun to see price cutting in several highly competitive lines, and as the generics come to market, there will be more cuts.

Realistically, though, the prices of some important medicines may continue to rise. Expiring patents on large sales volume drug products, and the subsequent threatening rush of lower priced imitations into the market—aided and abetted by increasingly widespread substitution by pharmacists—are forcing many research-intensive firms to raise prices on their remaining sole-source, patent-protected products. They do so reluctantly, but they really have no alternative if they are to maintain an adequately profitable revenue stream with which to sustain their organizations and to continue investing in risky and expensive research and devel-

opment. It is somewhat difficult to predict if and when it will abate, short of a sufficient revenue stream from new products; it is clear we are now living with a two-tiered system of pricing in the pharmaceutical industry.

Patient Information

Patient information is the second area of performance on which I would like to comment, and it is a relatively new one for the prescription drug industry. We are much more used to communicating with physicians, pharmacists, and other health care professionals. Nevertheless, here again we seem to be moving in the right direction.

To my mind, patient noncompliance is the supreme irony of modern pharmacology. Scientists take exquisite pains in research leading to the formulation of a new medicine. Laboratory tests are subjected to the strictest controls. Clinical tests on humans are meticulously governed; one missed dose or a mistake in the time of administration can invalidate an entire study. Today, most physicians and pharmacists are highly conscious of the need to make sure that the patient understands when and how to take the medicine. Yet follow-up studies have shown repeatedly that as many as half of all patients fail to follow directions, and as many as a third make mistakes serious enough to endanger their health.

Patient package inserts are not the answer. Research has shown them to be probably the least effective means of fostering compliance. The Food and Drug Administration (FDA) has wisely refrained from making them mandatory, while strongly encouraging the industry to find better ways of communicating. The response to that challenge—not only from individual firms but from industry groups and the medical societies—has been magnificent. The public is being exposed to a variety of attractive and effective compliance messages in the physician's office, at the drug store, on billboards, in magazines, and on radio and television.

Each company, industry group, and medical society seems to be doing something unique. Hoffmann-La Roche, which has distributed some 35 million patient information brochures, also sponsors a quarterly health test series on national television, inviting viewers to test their knowledge of cancer, fitness, nutrition, medicines, and many other health topics. Some ten million Americans regularly view these programs, which besides being entertaining, are crammed with useful information and advice from leading medical authorities.

To bring a new medicine to the market today takes a decade, about $90 million, and the dedicated talents of hundreds of Ph.D.s and M.D.s. All of that can be undone in an instant by a patient who does not know or care enough to comply with instructions. To inform and motivate with the aim of improving patient compliance and benefit is at last receiving the high priority it deserves in our industry. Communicating directly with

the ultimate consumer of our products, in addition to the "gatekeeper physician," is becoming an important part of our mission.

Pharmaceutical Innovation Through Research

The third and most vital area of the pharmaceutical industry's performance is innovation through research. The source of almost all of our modern medicines, unlike the automobiles we now drive, did not originate in Germany and Japan, although that situation may be changing. Nor did our present stock of medicines come from university or government laboratories, which continue to concentrate, as best they can in the face of federal budget squeezes, on fundamental research. Of the 1,134 medicines introduced in this country since 1940, 62 percent originated right here in America, and 90 percent of the originators were name-brand, profitmaking companies. The second most productive country, accounting for just 6.8 percent of our new medicines over this period, was Switzerland. Where did we in the American health care industry obtain the funds to support our very extensive and expensive research operations? From the sales of products which we otherwise could have sold far more cheaply.

The sales of original pharmaceutical products, proudly bearing the trademarks of their inventors, largely rest on the fate of the U.S. pharmaceutical research establishment. From 1980 to 1984, the period of unusual price increases in the industry, member firms of the Pharmaceutical Manufacturers Association doubled their research and development investments in the U.S. This year, the industry will spend more than $4 billion worldwide on pharmaceutical research and development, about four times the amount spent in 1975 worldwide. Hoffmann-La Roche will invest over $400 million on pharmaceutical research in 1985, which is 10 percent of the industry's total expenditure. About 80 percent of this investment is in research for advancement of scientific knowledge and development of new products and related services.

In our country, pharmaceutical innovation through research depends on financial support from research-intensive firms. These firms in turn depend on revenue partly from patented and partly from off-patent products. When, for whatever reason, income from off-patent products declines and new products become stuck in a company or regulatory pipeline, the research-intensive firm faces a crisis, and its options are few. First, a company may decide to diversify into other health or nonhealth-related businesses that require far less research expenditure. Second, a company may decide to go more or less generic, in terms of additional business, taking advantage of some other firm's expired patents and of the recently liberalized FDA rules for gaining approval of imitative products. Both strategies allow a firm to hedge on its pharmaceutical research bets, reducing the risks that necessarily accompany an all-out commitment to pharma-

ceutical innovation. While these strategies may not curtail research in absolute terms, at least not immediately, they always do so in relative terms, because they divert a portion of the firm's resources from the original research mission.

For companies like Hoffmann-La Roche and a small group of others, however, the optimal strategy remains one of reliance on internal research and development to generate new drug products that make a genuine difference in patient management. Since the research investment dollars are now harder to come by, far greater attention is given to research strategies and programs, and to the focusing of effort. In some cases, research portfolios have been trimmed to permit greater concentration on higher potential compounds. But the fundamental commitment to research remains undiminished. We hope in this way to accelerate a stream of original products through the Hoffmann-La Roche pipeline so that they reach the market, begin paying off their development costs, and become profitable revenue producers that will keep regenerating the discovery cycle and keep our company growing.

Policymakers in our national and state capitals should note that while other nations, like Japan, are modifying policies both to build up their research establishments and to contain drug prices, we seem to be concerned with price alone. A number of forces are already working to reduce revenue for the research-intensive firms: disinflation, overseas competition, unreformed regulatory delays, the rising costs of bringing new medicines to the market, and costly delays inherent in the need to master the new biotechnologies, such as genetic engineering. On top of factors intrinsic to the market or the nature of scientific research, policymakers are piling a host of regulations designed to encourage pharmaceutical manufacturers whose only concern is imitating existing medicines, not discovering new ones. Government is encouraging the generic industry not only through policymaking, but directly through promotion akin to press agentry. New product launches can be expensive and risky. Psychologically and substantively, the effect of heedless boosterism for generics is to magnify the risks attendant upon original research and thereby further deplete the ranks of firms willing to make an all-out commitment to that vital mission.

Today, the nation's major health problems are those that only original research can tackle. In the lengthening life expectancy that is resulting in enormous growth in the number of senior Americans, we have multiplied the incidence of degenerative diseases primarily associated with age—cardiovascular disease, cancer, arthritis, mental and emotional disorders. Products that merely imitate existing medicines cannot address these problems. The nation needs new medicines and must have them as soon as possible. Even the generic drug industry depends on new medicines—to copy when the patents expire.

Generic drugs do fill a social and economic niche if they are truly equivalent to the medicines they imitate, so that patient benefits can be truly assured. Still, is it wise to encourage the growth of the generic drug industry as a matter of public policy, without regard for the effects on the research-based industry? One consequence of a national policy of cheap drugs is to foster a shift of research effort out of this country and the availability of research fruits elsewhere in the world long before American physicians and patients have access to them. Would it be healthy for our nation if we were to reward imitative behavior more highly than innovative behavior?

This is hardly the time to make pharmaceutical research an endangered species. This is the time, rather, to strengthen the American research community, even as other nations are strengthening theirs. Society does not owe the research-intensive firms a living, much less a profit. But it does, I believe, share with us the responsibility of helping to accelerate promising lines of research investigation, enhance the security of researchers, support their exchanges of knowledge and ideas, and expedite the availability of new and useful drug products to the public.

In assessing what's right about American health care, I think that pharmaceutical research productivity has certainly been among our greatest successes. The problem is that we in the industry have apparently failed to let the rest of society know what we have been up to in research all these years. The man in the street may have a perception of high-cost health care and prescription drugs. At the same time, he may have come to expect a never ending succession of new wonder drugs. But he probably knows little of the dynamics of the pharmaceutical research community or of its relation to the health care industry, or how both are affected by public policy decisions. And the politicians and bureaucrats seem to feel that the great promise and potential of original research in biology, chemistry, and medicine will continue to be fulfilled, no matter what.

There is much the industry does well, but one thing it needs to do better is to communicate to all of its constituencies its role in improving the quality of life. Unless we begin to do that very soon and very well, America will be the loser in terms of technological leadership and the health of its citizens. We also need better public policy on pharmaceutical research. Together, we must devise solutions that sustain the emerging generic drug industry while at the same time preserving all the fecundity and vitality of the pharmaceutical research community.

In sum, what's right about the American pharmaceutical industry is its dramatic record of achievement and contributions to the world's improved health status, its world leadership position, and its continuing commitment to alleviating or eliminating the health problems that still affect so many millions of people. Good medicine is good business, and America has been the winner for that.