Introduction

Charting a Sustainable Path for the Twenty-First Century Pharmaceutical Industry

Michael A. Santoro

> This industry delivered miracles, and now they're throwing it all away. They just don't get it.[1]
>
> Dr. Roy Vagelos, former Chairman, Merck & Co.

THE UNRAVELING OF THE "GRAND BARGAIN"

Perhaps no business engages the worlds of science, medicine, economics, health, human rights, government, and social welfare as much as the pharmaceutical industry. As the twenty-first century begins, however, there is growing controversy and even hostility in the relationship between the pharmaceutical industry and the public. The millions of individuals, families, and communities throughout the world that have been stricken by the scourge of AIDS offer the most tragic human face to this controversy, but it is no overstatement to say that the pharmaceutical industry impacts the life of virtually every person in the world.

What we are witnessing is the unraveling of a "grand bargain" between the pharmaceutical industry and society. This grand bargain was a complex, implicit social contract that allowed the modern global pharmaceutical industry to emerge in the second half of the twentieth century. Although the industry prospered immensely, society also enjoyed a bountiful array of life-saving and life-enhancing drugs. As the twenty-first century begins, however, this grand bargain is in tatters and public mistrust and resentment of the industry run feverishly high. Many feel that the enormous industry profits are not sufficiently

matched by contributions to the common good. What factors are behind this growing tension between the pharmaceutical industry and society? Which of the criticisms of the industry are warranted and what reforms of the industry make sense? How can the fragile relationship between the pharmaceutical industry and society be repaired? Will a new social contract develop in the twenty-first century? These are the broad questions addressed in this book from a diverse array of perspectives.

While it is impossible to discuss all the controversies involving the modern pharmaceutical industry, the essays in this book attempt to address the most significant moral, scientific, and public policy issues that underpin the industry's complex relationship with society. Accordingly, the book is divided into four sections encompassing these broad themes. Section I is concerned with the research process by which drugs get discovered and developed. Section II casts an analytical and critical eye on the marketing of drugs directly to consumers and to physicians. Section III contains essays that critically assess the intellectual property rights protecting these discoveries and the related pricing policies this intellectual property regime allows both in developed economies and in third world countries. Finally, Section IV looks to the future and contains essays that reflect on a sustainable path for the pharmaceutical industry to thrive economically while serving the needs of society.

Many of the essays in this book address hot-button issues such as pricing for AIDS drugs and stem cell research. Indeed, several of the authors in this volume press these hot buttons quite deliberately because they believe passionately in the moral and scientific force of their positions. Such passion and commitment are only natural and understandable given the momentous human impact of these matters. When read together, however, the various essays in this book are intended to offer a fair, balanced, and insightful consideration of the troubled relationship between the pharmaceutical industry and society. Given the divergent ends of a for-profit industry and a product with immense public health implications, there will always be some tension in the relationship between the pharmaceutical industry and society. The hope is, however, that this book can help point to a more sustainable path where these divergent interests are better aligned and the inevitable residual tensions are better managed.

THE INDUSTRY'S DETERIORATING PUBLIC IMAGE

In recent years, drug companies have operated in the glare of the global court of public opinion. The verdict has been decisively negative. It is difficult to pick up a newspaper or a magazine these days without reading about some controversial issue presenting the pharmaceutical industry in an unflattering light: ever-rising drug prices in the United States and around the world; egregious overcharging for drugs sold to public health programs such as Medicaid; never-ending vitriolic trade negotiations over intellectual property and generic drug manufacturing in third world countries; sympathetic pleas by senior citizens and others to import drugs from Canada where government controls keep prices low; concerns about the rights of patients participating in clinical trials; troubling revelations that clinical trials are sometimes selectively published in scientific journals to overstate effectiveness and efficacy; the seemingly ubiquitous emergence of consumer advertising; revelations of shockingly large-scale bribes to physicians to prescribe particular drugs; and the international debate over the role of the industry in providing AIDS drugs to third world countries.

Among observers outside the industry, the greed and moral failings of the industry approach the status of a truism. Many observers, moreover, have come to question the industry's economic vigor and innovative vitality. Consider the following passing comment in a *New York Times* article: "[The pharmaceutical industry's] profits rely almost entirely on laws that protect the industry from cheap imports, delay home-grown knockoffs, give away government medical discoveries, allow steep tax breaks for research expenditure and forbid government officials from demanding discounts while requiring them to buy certain drugs."[2] What is remarkable about this quotation is that it comes from a *news* article, not an opinion piece. Moreover, the author did not even feel the need to cite a source for his damning conclusions!

Predictably, the barrage of negative media coverage has taken its toll on public perception. According to the Harris Poll, between 1997 and 2004 the percentage of adults believing that the pharmaceutical industry was adequately serving its customers declined from 79 percent to 44 percent.[3] Less than 14 percent described pharmaceutical companies as "generally honest and trustworthy." Fifty-six percent believed that drug prices were unreasonably high and that there should be more

government regulation of the industry. Indeed, public contempt in the United States for the pharmaceutical industry sometimes reaches startling heights of vitriol. A 2003 Gallup Poll revealed that Americans rate the public image of the pharmaceutical industry among the bottom five.[4] Some critics even go so far as to compare the pharmaceutical industry with the tobacco industry.[5]

For pharmaceutical executives, their declining public image is a bitter pill. Despite the fact that the industry has developed many life-saving and life-enhancing products over the last half-century – including so-called "miracle" drugs for treating cancer, AIDS, and heart disease – public trust and confidence are spiraling downward. Most pharmaceutical executives are bewildered by the public's contempt. Typical is the view of one executive who remarked, "We find it quite incredible that we could be equated with an industry [tobacco] that kills people as opposed to cures them." Others, however, are realizing that the industry needs to change quickly and radically to adapt to a fundamentally new political and social environment. Even an industry stalwart such as Roy Vagelos, the former CEO of Merck, has begun to complain about the high prices of drugs and to warn about the inevitability of government price controls.[6]

TWO CORE ISSUES IN NEED OF RESOLUTION: PROFIT VERSUS MEDICAL NEED AND THE NEED FOR COOPERATION

Although the essays in this volume are diverse and far-ranging, two core themes emerge in charting a sustainable path for the pharmaceutical industry. One issue that cuts through virtually all the chapters in this book is the imperfect alignment of private profit-maximizing objectives with public health needs. The central paradox of the public policy debate over the pharmaceutical industry stems from the fact that private enterprise drives creativity and innovation, while simultaneously it restricts access and distorts medical priorities. Important life-saving and life-enhancing drugs, such as protease inhibitors for HIV patients, are invented, but many can't afford those drugs, especially in the third world. Some conditions, such as heart disease and hypertension, which are prevalent in developed economies, offer doctors multiple options for treatment, whereas doctors in third world countries have few options for treating the scourge of malaria. The

airways are filled with ads for erectile dysfunction drugs that make them seem curiously akin to a recreational drug, whereas working-class families wonder how they are going to afford life-saving asthma medication for their children. The disconnect between the profitability of drug companies and the public health manifests itself in a seemingly endless array of such ironies. What are the root causes of this misalignment? How big is the gap between profits and public health? What must be done to bridge this gap? In the process, how do we balance the intellectual property rights of pharmaceutical companies with the basic human right to healthcare? These questions are addressed by numerous thoughtful and knowledgeable authors in this volume.

A second theme that emerges in these pages is the pressing need for the pharmaceutical industry to increase dialogue and cooperation with various stakeholder groups. A number of authors in this volume, including those from within the industry, emphasize that to repair their relationship with society in a sustainable manner, drug companies must learn to think of diverse groups as active partners in the process of drug development and sales. If the pharmaceutical industry is able to adapt and change in this way, it will come to see advocacy groups, the medical and scientific community, governments, NGOs, and international institutions as essential partners in developing useful drugs to solve medical problems that often have social and transnational implications. If the industry is not able to make this transition, it will continue to be vilified and find itself increasingly isolated.

Inaction is not an option for the pharmaceutical industry. The void from the absence of cooperation and partnership with stakeholder groups will be filled ineluctably by increased government regulation, including the specter the industry probably fears most – price controls. The loser in this eventuality will not be just the pharmaceutical industry, which will inevitably be less profitable. Society, too, will lose because the heavy hand of government regulation and bureaucracy, although sometimes necessary, can rarely function as efficiently and creatively as coalitions of diverse groups, including government, working together. Therein lies the moral imperative for change in the pharmaceutical industry – the hope for a future where society continues to enjoy a steady stream of drugs to improve health and wellbeing and where these fruits are broadly distributed among rich and poor, and throughout the globe.

PART I

PROFITS, PATIENTS' RIGHTS, AND SCIENTIFIC PROGRESS

The Ethics of Clinical Research Conducted in Private Enterprises

Introduction to Part I

Michael A. Santoro

INTRODUCTION

Pharmaceutical research is a complex social enterprise. It involves persons, commerce, and the advancement of medical knowledge, and it raises a broad array of ethical, scientific, and public policy issues. The chapters in this section analyze and suggest reforms in a number of these areas, including (1) the conflicts that arise between the profit maximization objectives of pharmaceutical companies and the ethical requirements of scientific research and medicine, particularly in regard to safety concerns and the diseases that are targeted; (2) the ethical safeguards for conducting research involving human subjects, particularly vulnerable subjects such as children and citizens of third world countries; (3) the patient's right to be included in drug trials that offer hope for terminal medical conditions, as well as the public health implications of including minority populations in drug trials; and (4) the scientific and ethical issues underlying stem cell research.

MEDICINE, SCIENCE, AND PROFIT MAXIMIZATION: AN UNEASY MIX

The dictates of medical and scientific ethics are sometimes at odds in clinical research, as for example in the administration of placebos to patients in control groups.[1] Such conflicts arise because physicians are trained to cure and treat patients by administering therapeutic remedies, whereas scientists seek to establish facts and advance knowledge. For the most part, however, the advancement of knowledge and the betterment of patients ultimately are complementary goals.

It is the interjection of profit motivation into drug research that creates the greatest ethical challenges. In a sense, these challenges are endemic to the free market system. The power of the free market is that by appealing to self-interest it unleashes powerful incentives that spur creativity and productivity. Bolstered by the added incentive of patent protection – a subject discussed in Part III of this book – the pharmaceutical industry has attracted vast sums of private investment and it has employed these funds to invent and bring to market a wide array of life-saving and useful drugs. The problem with the market, however, is that it does not perfectly correspond to human medical needs. The market responds to consumer demand, which reflects wealth and ability to pay. Human medical needs, however, exist even where consumer markets don't. Conversely, as discussed in Part II of this book, the pharmaceutical industry sometimes attempts to create consumer markets for drugs that do not optimally serve medical needs.

When one considers the disjunction between medical needs and the dictates of capitalism in a global context, the gulf between commerce and medicine grows wider. On purely medical grounds, the needs of a poor child suffering malaria in sub-Saharan Africa should have priority over a middle-aged American man suffering from hair loss. Through the prism of capitalism, however, the balding man is a valued, potential customer and the African child barely exists. The numbers tell the story. Malaria research attracts 20 cents in research dollars for each infection, whereas ailments that are prevalent in developed countries attract hundreds of dollars per case.[2] As a result of such stark economic realities, many of the world's most pressing medical needs will remain unmet without resort to nonmarket solutions.[3]

Jürgen Drews, a physician who has been the research director of a major global pharmaceutical company, is uniquely qualified to examine the interrelationships among medical ethics, scientific ethics, and the profit motive. Drews argues that in recent years an obsessive, and ultimately self-defeating, focus on the bottom line, and the increasing costs of launching a new product, have led pharmaceutical companies to devote their research efforts increasingly to so-called "me too" remedies for conditions such as high cholesterol and hypertension for which useful therapies already exist.

To address the problem of malaria and other unmet medical needs in the third world, Drews suggests a number of nonmarket solutions, including a call for collaborative intergovernmental–nongovernmental–industry partnerships. One extraordinary example of this kind of effort has been launched by the Institute for OneWorld Health, led by Dr. G. Victoria Hale and funded by the Bill and Melinda Gates Foundation. The Institute accepts industry donations of patent rights and the volunteer services of industry scientists to develop drugs that could be useful in the third world. In return, companies can gain tax breaks and garner positive public relations.[4]

How great is the gap between global medical need and market forces? Is the only way to bridge this gap through resort to nonmarket solutions and charity? Or are opportunities to do good by doing well being missed by the pharmaceutical companies? Drews, who has viewed the pharmaceutical industry from within as a scientific director and from outside as an investment banker, tantalizingly suggests that scientific research is best served by a focus on medical research rather than the bottom line. Ironically, Drews observes, it is precisely the obsession with the bottom line that has led to a slowdown in the drug pipeline that in turn has hurt the bottom line. He regards this development as a fundamental departure from an earlier "golden age" when pharmaceutical research was more closely aligned with medical need and scientific purpose. As a scientist, Drews understands that important breakthroughs often come serendipitously in laboratories when the pursuit of knowledge is undertaken for its own sake, and not as a result of the best laid financial plans of MBAs in executive suites.

Doing Good by Doing Well: The Real Lessons of Merck's Cure for River Blindness

Drews's account of scientific creativity merits further study and debate. On an anecdotal level, however, Merck's development of a drug to cure river blindness offers powerful support for his view. River blindness, *onchoceriasis*, a terrible disease resulting in unbearable itching, swollen body tissue, and ultimately blindness, affects over 80 million people in poor settlements of Africa, the Middle East, and Latin America. In the late 1970s, Dr. William C. Campbell, a scientist at Merck, approached then-CEO Roy Vagelos with a proposal to test and

develop a drug for river blindness. Merck justifiably won praise for devoting substantial resources to developing the drug even without any prospect of achieving a return on investment.

As an example of moral leadership in putting medical needs before profits, the Merck river blindness story is inspiring enough. However, the lessons of this story may run deeper. Invermectin, the drug Merck developed to combat river blindness, also had potency and effectiveness against a wide variety of animal parasites. Indeed, Merck made significant profits serving this market. It was no accident that this drug compound, which turned out to have applications in both profit-making and non-profit-making markets, was developed at Merck in a period when Roy Vagelos, a medical doctor, emphasized basic research and challenged Merck scientists to think of their work as a quest to alleviate human disease and suffering worldwide.

Is there a broader lesson here? Is scientific creativity, as Drews suggests, being choked off by the micromanagement of bottom-line-obsessed corporate executives without scientific backgrounds? It is hard to say, based on this one example, where profits and dedication to medical need seem to go hand in hand. But perhaps drug companies today might do well to heed the words of George W. Merck, the company's modern day founder, who in 1950 wisely said: "We try never to forget that medicine is for the people. It is not for the profits. The profits follow, and if we have remembered that, they have never failed to appear. The better we have remembered it, the larger they have been."[5] Some might argue that this sentiment is hopelessly quixotic and naïve at the turn of the twenty-first century, when drug development costs are ever rising. Perhaps, however, pharmaceutical executives need now more than ever to be reminded that sustainable profitability will result from addressing genuine medical needs.

DRUG SAFETY: PUBLIC POLICY, ETHICAL, AND REGULATORY CONSIDERATIONS

It is remarkable to reflect in retrospect that it was not until the second half of the twentieth century, with the passage of the 1962 Kefauver-Harris Amendments to the Food, Drug and Cosmetics act of 1938 (later followed by similar legislation in Western Europe and throughout the world), that pharmaceutical firms were required to demonstrate the