# The $800 million pill

*The truth behind the cost of new drugs*

Merrill Goozner
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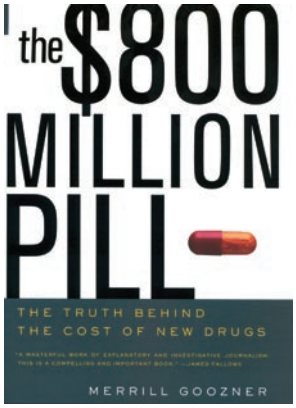


Does it really take the oft-quoted $800 million to make a new drug? Merrill Goozner would argue not — a more accurate figure might be about one-fifth that sum, although the range is considerable and all the estimates are dependent upon which particular economic theory one chooses to believe in. Whatever the reason, Goozner pillories the price of pills and places the blame squarely on the pharmaceutical industry, backing his case by presenting fascinating histories of the development of individual drugs by both Big Pharma and smaller biotechnology companies. Goozner's central premise is that the industrial development of almost all drugs is heavily reliant on basic research funded by the taxpayer and conducted by scientists working for universities, nonprofit research centers, or the NIH. There's no doubt that Goozner's sympathies lie with the traditional academic. He views the pharmaceutical and biotechnological industries rather less favorably, particularly in their marketing practices. Overall, I enjoyed reading this book and was impressed by its thoroughness. Goozner writes well, has a command of his subject, and makes very few scientific errors. Hence it seems reasonable to assume that he also has his facts straight when covering the economic and political aspects of his subject — his specialties, but not mine.

Goozner examines the relationships between academic and corporate research at some length, using as one example the development of protease inhibitors as a critical component of combination therapy to treat HIV infection. He rightly points out that some absolutely crucial basic research on protease structure was carried out by academic researchers in the United Kingdom and the US, and he correctly emphasizes the outstanding quality of the science carried out in some corporate programs and the huge costs incurred, notably by Merck. Conversely, Goozner excoriates both Roche and the NIH's clinical trial network for critical mistakes made during saquinavir development and exposes some absurd treatment decisions made on purely financial grounds. Yet, in the end, the protease inhibitors will save millions of lives, for which much of the credit must go to industry scientists whose contributions have been overlooked by the popular press. The quality of science in Big Pharma, in my own experience, has been outstanding — when academics look down their ivory-towered noses at their industry counterparts, they are making a serious misjudgment.

Rather than cooperating, academic and biotechnology industry researchers raced for the human genome sequence, with all its long-term implications for drug development. Goozner rightly deplores the profit motive as an impetus to generate information that should belong to all humankind. And he notes that neither group could have succeeded as quickly as it did without the development of better DNA sequencing technologies — something accomplished by corporate America, but only after the federal government made the critical initial investments in the methodology. Again, this relates to the book's central position that industry does not work in a vacuum and that many cooks contribute to the chemicals we all throw down our throats.

Drug pricing is now a sensitive topic for the pharmaceutical industry. One of the strongest arguments for high prices is that the profits from one generation of drugs must be invested in the next. That thesis is the thrust of current, and no doubt very expensive, TV advertising campaigns intended to make the public feel happy about the prices they pay today. Still, it makes a change from hearing how Lance Armstrong's testicular problems were resolved or seeing yet another warm and fuzzy discussion of erectile dysfunction. Marketing practices are, however, a very serious problem, particularly for "me-too drugs." Among the more eye-popping tales in the book are those of Astra's stunts with Prilosec and Nexium, how Schering-Plough promoted Claritin, and the dubious nature of Pharmacia's claims for Celebrex. Goozner writes of corporate rivalry, expensive hype, and high prices — and all for "new drugs" that provide little additional benefit to many patients compared to older, cheaper products. The cost of dubious trials aimed solely at "proving" that company X's hyped-up blockbuster is marginally better than company Y's heavily touted wonder-drug is enormous. Goozner's magnum opus pours a magnum o' pus over this practice. He quotes Marcia Angell: "Important new drugs do not need promotion. Me-too drugs do."

To be fair, though, the high price of drugs is not the sole responsibility of the pharmaceutical industry. There are societal causes too, and Goozner addresses many of these, though perhaps not always as well as he might. Ideally drugs should be perfect, safe and cheap, but perfection and safety come at a price. Making drugs 100% safe for a genetically diverse population is a tough task, yet the benefits of a drug to the majority can be outweighed by harm, real or perceived, to a very few. Many candidates fail to make it through the development process, and the price of failure needs to be factored in — there's no money to be made from a drug that never reaches the pharmacists' shelves; there are only losses. And drugs can be approved then withdrawn on safety grounds, with lawsuits the seemingly inevitable consequence. That's fine if a drug's truly at fault,

but some litigation is frivolous or unjustified by the scientific facts; not everyone who sues successfully has been harmed by the drug. My sense is that in our safety-first, suing-in-a-second society, all this contributes to the price of pills; in the end, the legal bills and the payouts are charged to all of us in the drugstores.

I would also argue that, even before a drug is approved, the regulatory costs of the research and development processes adversely contribute to pricing. Pressure from patient-oriented lobby groups and animal-rights activists causes the government to wrap research in red tape. However well intentioned the goal of each new rule, the overall effect is that the costs and time involved in taking a drug to market are skyrocketing. Excessive bureaucracy also rusts the drug-discovery engines of basic research. Political lobbying groups cause federal agencies to pour out a torrent of new rules and regulations, costing academic scientists and institutions millions of man-hours and billions of bucks to comply. All this adds, eventually, to the cost of drugs, all too often without significantly improving patient safety or welfare. The Health Insurance Portability and Accountability Act (HIPAA) was a farce too far. If the rule makers are not themselves reformed, they will soon have no research left to regulate. Then there will be no more drug-pricing decisions to complain about.

Another problem area is the patent system. Patents, Goozner rightly notes, are critical to the conversion of basic discoveries into practical therapies. No company will spend its money to develop a product that will merely be copied by its rivals after the hard yards have been gained. But the system is deeply flawed, as Goozner emphasizes in his discussion of the patenting of genome sequences without any understanding of their functions. The US Patent and Trademark Office (PTO) has made other quixotic, arguably absurd decisions to award patents on single-nucleotide polymorphisms, signal transduction and metabolic pathways, even enzymes, to corporate and academic scientists alike. Important policy decisions affecting many aspects of biomedical science are, one suspects, made at a rather low level within the PTO without consideration of their strategic consequences and real-world implications — a boon for lawyers and lobbyists, but not for science and society.

Could the system be improved? Goozner does present some imaginative ideas that deserve consideration. He would like to see the NIH and nonprofit organizations play a bigger, more direct role by, for example, conducting comparative trials to determine which me-too drugs work best (or at all). As an example, Goozner discusses Vioxx and Celebrex, rival COX-2 inhibitors for arthritis pain. This turns out to be a highly topical issue; a very recent FDA-funded study has indicated that long-term Vioxx use causes cardiological complications. Merck has now withdrawn Vioxx at enormous expense, and this cost will presumably have to be recouped in the price of future drugs. The downfall of Vioxx will probably benefit sales of Celebrex (now owned by Pfizer), but the cardiac safety of all the COX-2 inhibitors is now being questioned. Goozner uses these compounds as but one example of the impact that slick advertising and promotional freebies have on the prescription and purchasing habits of physicians and the public.

Any academic who interacts with the pharmaceutical industry will eventually realize that making drugs is an incredibly complex process. Identifying a drug target or a lead compound is often the easy bit compared to what it takes to convert a hit into a practical, safe, and effective drug. In general terms, only the industry can make practical drugs. Academics can't, nor can NIH. Indeed, federal officials all too often back obviously defective approaches because, unlike the captains of industry, they will not have to go down with their flagship when it hits the rocks — stockholders usually complain about expensive, bad decisions; taxpayers rarely do. It seems right, though, that the NIH should continue to indirectly support the drug-development process as part of its duty to improve the health of the nation; we all benefit from effective new drugs. And Goozner correctly emphasizes how important it is that the NIH and nonprofit organizations develop drugs for diseases, such as tuberculosis and malaria, that happen to be prevalent in countries that won't generate much sales income — diseases of the poor that industry sadly ignores.

Goozner's central argument is that taxpayers don't receive a suitable financial return for their investments in the basic science that underlies drug discovery. This raises complex political issues. The fundamental reason drugs cost so much in the US is surely because they are made by corporations with immense political clout and a duty to their stockholders to maximize profits. Whatever a drug actually costs to make and market, American consumers sometimes have to pay twice what Canadians do for the identical product! The pharmaceutical industry even has the chutzpah to argue that drugs safe enough for Canadians are not necessarily suitable for Americans. It has somehow managed to arrange FDA support for this curious, and obviously specious, argument. The recently approved Medicare Bill, signed after Goozner's book was published, even makes it illegal for the US government to negotiate the prices of drugs with their manufacturers. Why can Uncle Sam haggle over the price of a tank from General Dynamics or a truck from General Motors, but not a therapy from Genentech? The answer lies in the influence of pharmaceutical industry lobbyists — a few million dollars to the Bush campaign reaps a few billion in extra profits. If we want cheaper drugs, a change of Administration might help. One hopes that the Democrats would be less willing to enact policies favorable to the pharmaceutical industry after first pocketing a share of the profits. But the Democrats also take industry money, and they have historically been the party most willing to respond to social lobby groups seeking to stifle science by supervising it into stagnation. And I don't believe that helps the price of pills either.

Goozner's book raises the question: Where, then, should the balance be struck between the taxpayer, the consumer, and the stockholder in such a complex seesaw of conflicting pressures? I feel the answer has to lie in Washington, but no politician has yet been able to find it. In the United Kingdom, the Chancellor might simply respond to excessive corporate profits (typically 23–25% of total pharmaceutical industry revenue) by slapping on a windfall tax, as has happened several times to the banking industry. To do this in the USA would be political suicide, even if the money went to subsidize Medicare and Medicaid. Isn't that the fault of all of us?