Big Pharmaceuticals, Big Money

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> ***"The top 10 drug companies are reported to have profits averaging about 30 percent of revenues—a stunning margin. Over the past few years, the pharmaceutical industry as a whole has been by far the most profitable industry in the United States."*** Angell M, "The Pharmaceutical Industry—To Whom Is It Accountable?" *New England Journal of Medicine*, June 22, 2000.

> ***"In every year since 1982, the drug industry has been the most profitable in the United States, according to Fortune magazine's rankings. During this time, the drug industry's returns on revenue (profit as a percent of sales) have averaged about three times the average for all other industries represented in the Fortune 500."*** Public Citizen Report, "Rx R&D Myths: The Case Against the Drug Industry's R&D 'Scare Card," July 23, 2001.

> ***"Put together, the market capitalization of the four largest [pharmaceutical] companies is more than the economy of India."*** David Earnshaw, formerly director of European government affairs for SmithKline Beecham, now leader of Oxfam's campaign on access to medicines. Quoted in Roger Dobson, "Drug Company lobbyist joins Oxfam's cheap drugs campaign," BMJ, 322, April 28, 2001, p. 1011.

The international illegal drug cartel no doubt makes a lot of money, but the risks are very high and include death by multiple gunshot wounds. The big pharmaceutical companies, on the other hand, make even more money, and the worst risks they face are such things as lawsuits. Furthermore, instead of trying to put them out of business, the U.S. government uses tax dollars to help them develop highly profitable new products.

Just how much money is involved in legal drug sales? According to IMS Health's Drug Monitor Report, pharmaceutical sales in major world markets were $179 billion for the fiscal year ending March 1998. Of that, U.S. sales accounted for $68.7 billion. By March 2000, IMS America reported that in the U.S. alone prescription drug sales had climbed to an astonishing $145 billion, and those monitoring U.S. prescription drug sales expect this trend to continue at least for the next nine years. Since 1993, nationwide spending for prescription drugs has increased at an average annual rate of 12%, while all other types of health spending increased at an average annual rate of only 5%. The cost of drugs is now outpacing the cost of physician care in the U.S. and Canada.

> ***"Historically, hospitals have constituted the greatest of Canada's total health expenditures, followed by the combined cost of all physicians' services, with drug expenditures in third place. In 1997 drug spending vaulted into second place, at 14.5% of the total $79 billion spent on public and private health costs. (Spending on physicians' services represented 14.2% of expenditures; hospitals 32.5%). By 2000, drugs were 15.5% of total expenditure."*** Candis McLean, "The Real Drug Pushers," Report Newsmagazine.

The enormous growth in drug sales isn't due to a growth in revolutionary new drugs. According to a new report by Public Citizen, only about 22 percent of new drugs brought

to market in the last 20 years were truly innovative drugs representing important therapeutic improvements over existing drugs (Public Citizen report, "Rx R&D Myths: The Case Against The Drug Industry's R&D 'Scare Card,'" July 23, 2001). According to many experts, the single biggest factor in the increase in drug sales can be summed up in one word: Marketing.

Breakthroughs Down, Marketing Up

> ***"Last year, the Food and Drug Administration approved just 27 wholly new drugs, down from 53 in 1996."*** Gardiner Harris, "Pitch to Switch," *Wall St. Journal*, May 21, 2001, p.1A.
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> ***"Overall, the industry's marketing and administration expenses are generally more than twice those of research and development. At Pfizer, for instance, marketing and administration make up 39% of expenses, compared with 17% for R&D…. A Pfizer spokesman says the company 'is very optimistic about the future' and relies not only on launching new medicines but increasing the sales of old ones. While that can be done by testing new uses to old drugs and combining them with other drugs, the best means is boosting marketing budgets."*** Gardiner Harris, "Drug Firms, Stymied in the Lab, Become Marketing Machines," *Wall St. Journal*, July 6, 2000, p. A1.
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> ***"If one company epitomizes the modern drugs industry it is Pfizer. Just a decade ago, it was regarded as an industry also-ran. But the US company has powered its way up the global ranking list to its unassailable position thanks mainly to its marketing prowess…. While some of Pfizer's research has been excellent, its success stems largely from its ability to turn drugs—often ones licensed in from its competitors—into multi-billion dollar products."*** David Pilling, "Pharmaceuticals 2001/Sales & Marketing: Relentless rise in role of reps and big launches," *Financial Times*, April 26, 2001.

While they have not run completely dry, the pharmaceutical industry's labs simply aren't producing many important new medicines. As one industry spokesman put it, all the low-hanging fruit has already been picked. Because the big companies' own labs aren't coming through, they are increasingly relying on licensing new drugs from universities, government or smaller companies that hold the patents for them.

Sometimes these licensing agreements are very complex. For example, Advanced Therapeutic Products (ATP) patented the technology forming the basis of both the Nicorette and Nicotrol nicotine inhalers. Pharmacia acquired the production rights for the inhaler from ATP for a percentage of product payments. Pharmacia, in turn, manufactured the Nicorette inhaler for SmithKline Beecham and the Nicotrol inhaler for Johnson & Johnson subsidiary McNeil, and these two companies market the inhalers under their own trademarks.

Many, if not most, of the biggest-selling drugs are actually developed through government grants to universities or individual researchers.

> ***"According to NIH [National Institutes of Health], taxpayer-funded scientists conducted 55 percent of the research projects that led to the discovery and development of the top five selling drugs in 1995."*** "Rx R&D Myths: The Case Against the Drug Industry's R&D 'Scare Card,'" Public Citizen report, July 23, 2001.

Though it has not yet been clinically tested for FDA approval, the new orally ingestible nicotine for smoking cessation drugs was developed by two Duke University researchers with funding by the U.S. Department of Veterans Affairs. The researchers have already sold production rights to a small pharmaceutical company. This company in turn will no doubt sell ingestible nicotine formulations to one or more of the big pharmaceutical companies, which will fund the clinical trials, get FDA approval, and then market the new cessation drugs under their own trademarks.

Thus, the taxpayers, not the big pharmaceutical companies, actually pay for much of the basic research for new drugs entering the market.

> ***"In 1999, the National Institutes of Health (NIH) provided $17.8 billion for research, and the major proportion was expended for basic research; the top 10 pharmaceutical companies spent $22.7 billion, primarily on clinical research."*** DeAngelis CD, "Conflict of Interest and the Public Trust," JAMA 284(17), Nov 1, 2000.
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> ***"45 of the 50 top-selling drugs from 1992-1997 received government funding for some phase of development, according to an investigation by The Boston Globe. In all, taxpayers spent at least $175 million helping to develop these 50 drugs."*** "Rx R&D Myths," Public Citizen report, July 23, 2001.

In addition to licensing new drugs to market, the big drug companies are also focusing on developing "me too" drugs (products almost identical to drugs already on the market), finding new medical applications for existing drugs, and marketing "new" formulations of older drugs. But all of these require little investment in basic research. In fact, they are more akin to new marketing tools than anything else, despite the clinical testing that must be conducted for FDA approval.

> ***"Consider the welter of very similar drugs to lower cholesterol levels. Developing genuinely innovative drugs is difficult and chancy. It is easier to make 'me-too' drugs or minor variants of established products. To be profitable, the variation need only be sufficient to secure a new patent, and the rest is marketing."*** Angell M, "The Pharmaceutical Industry—To Whom Is It Accountable?" *New England Journal of Medicine*, June 22, 2000.

Johnson & Johnson's Nicotrol patch is essentially the same as SmithKline's Nicoderm patch and neither was developed by the companies marketing them. Glaxo Wellcome's Zyban for smoking cessation is exactly the same thing as Glaxo Wellcome's older drug Wellbutrin for depression. GlaxoSmithKline's see-through patch is the same old wine in a new bottle as is the company's "new" orange-flavored Nicorette gum.

Direct-to-Consumer Marketing

Since 1997, when the FDA relaxed television and radio advertising restrictions for prescription drugs, the big pharmaceutical companies have increasingly turned to direct-to-consumer (DTC) marketing to increase their profits.

> "***Last year pharmaceutical companies spent $1.8 bn on 'direct to consumer' advertising, mostly on television. Advertising expenditure in 1999 rose by 38.5% from the 1.3 bn spent in 1998, and was 33 times the amount spent on media advertisements in 1991."*** Fred Charatan, "Prescription drug sales boosted by advertising," BMJ, 321, Sept. 30, 2000, p. 783.

And it appears to be working. As the big drug companies have poured more and more money into DTC television ads, drug spending has risen enormously, and the bulk of the rise was accounted for by increased sales of the most heavily advertised prescription drugs.

> ***"Doctors wrote 34.2% more prescriptions in 1999 than in 1998 for the 25 drugs promoted direct to consumers that contributed most to overall drug spending. Doctors wrote only 5.1% more prescriptions for all other prescription drugs."*** Charatan, BMJ, Sept. 30, 2000, p. 783.

However, some physicians and industry watchdog organizations are becoming increasingly alarmed by the influence of the drug companies' direct-to-consumer advertising tactics. They point out that not only do all drugs—especially prescription drugs—have negative side effects, but that such continual bombardment by drug ads "normalizes" taking drugs.

> ***"It's insidious; companies want you to think there's something wrong with you. It's saying in effect, 'If you've got a problem, the way to deal with it is through pills.' It's also 'medicalizing' a problem which may not be a problem you need to deal with, like male pattern baldness or shyness. Once you have a drug, it becomes a medical problem."*** Dr. Joel Lexchin, a Toronto physician and member of Medical Reform Group. Quoted in Candis McLean, "The real drug pushers," *Report Newsmagazine*, Mar 19, 2001.

Americans appear ready to pop a pill to alleviate almost anything they feel is a problem, from feeling blue to thinning hair or stopping smoking or having more sex or losing weight or quieting unruly children. Though none of these problems is a genuine disease in and of itself, the drug ads suggest that they need "treatment" using one of their "medications."

In addition to increasing numbers of these highly profitable "lifestyle" drugs, the pharmaceutical industry has capitalized on the current medical focus on *prevention* by turning out more and more medications designed to prevent disease, such as drugs to lower cholesterol and blood pressure levels and a host of new vaccines. While some of these drugs undoubtedly do help prevent disease for some people, they are sometimes

prescribed when there is not a clear and compelling need for them (or when industry-friendly quasi-government panels lower the bar for what is deemed high blood pressure or high cholesterol).

Even such toxic and costly pharmaceuticals as chemotherapy drugs are sometimes used without sufficient justification, despite their serious side-effects.

> ***"Many patients with cancer receive chemotherapy at the end of life, even if their kind of cancer is known to be unresponsive to the drugs, according to a study reported at the recent annual meeting of the American Society of Clinical Oncologists held in San Francisco."*** Gottlieb S, "Chemotherapy may be overused at the end of life," BMJ, 322, May 26, 2001, p. 1267. Dr. Ezekiel Emanuel, lead author of the study, also noted that chemotherapy is very expensive, $38,308 for treatment of a patient in the final year of life as compared to $27,567 for a patient not in the final year of life.

While treating cancers known to be unresponsive to chemotherapy with these drugs may do nothing to help suffering patients, it certainly benefits the pharmaceutical companies providing the drugs.

The fact is that *all* drugs, not just chemotherapy drugs, have potentially serious side effects, and no drug should be prescribed unless it is truly necessary to the health and well-being of a patient. Not even if the patient insists on having it because he or she has seen an upbeat television ad and is convinced that the advertised wonder drug will cure all of life's pains and anxieties.

Side-effects and Medication Errors

> ***"[P]rescription drugs…account for more deaths each year than all murders, auto accidents and airplane crashes combined. It is estimated that 100,000 people die every year from the adverse effects of prescription drugs, and 1 million are injured so severely they require hospitalization."*** Thomas Moore, "Prescription drug risks are too high," *The Miami Herald*, April 12, 1998, p. 6L.

> ***"It has been estimated that fatalities directly attributable to adverse drug reactions are the fourth to sixth leading cause of death in US hospitals, exceeding deaths caused by pneumonia and diabetes. The economic burden resulting from drug-related morbidity and mortality is equally significant and has been conservatively estimated at $US30 billion dollars annually, and could exceed $US130 billion in a worst-case scenario."*** White TJ, Araakelian A, Rho JP, "Counting the costs of drug-related adverse events," *Pharmacoeconomics*, 15(5): 445-58, May 1999.

> ***"David Lawrence, CEO of Kaiser Permanente, the nation's oldest HMO, calls medication errors 'the number one public health risk in the United States, ahead of tobacco, alcohol, [illegal] drugs, or guns."*** Ted Sandoval, "Cutting Medication Errors Requires Proactive Steps," Web MD, Medcast, June 20, 2000.

All drugs have negative side effects, even aspirin. However, prescription drugs have far more potentially dangerous side effects than do over-the-counter medications. Most people who take these drugs according to their physicians' directions do not experience serious side effects, but some do. Some people have severe allergic reactions, some suffer heart attacks or seizures, and some experience organ damage because of the

prescription drugs they take. One of the most common serious drug problems is liver damage because most medicines taken by mouth are ultimately processed through the liver.

In addition to the negative side effects induced by individual drugs, some drugs interact negatively with certain foods or with other drugs.

Another factor involved in the large number of people killed or made ill by prescription drugs are medication errors, and the primary reason for medication errors can be traced to the sheer number of prescription drugs on the market.

> ***"There are currently more than 17,000 trade and generic names for drugs in the United States, according to the Institute for Safe Medication Practices in Huntingdon Valley, Pa. The organization also estimates that the number of drugs on the U.S. market has grown 500% in the last decade."*** Braus P, "Want to avoid drug errors? New software can help," American College of Physicians-American Society of Internal Medicine *Observer*, April 2001.

The vast majority of these drugs are not important, breakthrough medications, but "me-too" drugs, generic versions of name-brand drugs, new variations of older drugs, and old drugs with new names for new medical applications. But with so many medications and so many names for the same medications, it is not surprising that there are medication errors, including negative drug interactions.

> ***"With so many people on so many pills, small wonder that part of the increase in healthcare costs is illness caused by drug interactions. A Queen's University study of seniors' medication released in January, for example, found that in 96% of cases studied, doctors' knowledge of their patients' medication use was inaccurate. On average, the patients had a daily dose of seven medications."*** Candis McLean, "The real drug pushers," *Report Newsmagazine*, March 19, 2001.

Given so many potential hazards—from prescription errors to life-threatening side effects—it is clear that pharmaceutical products can kill as well as cure. Nevertheless, most people naïvely continue to believe that FDA approval means a drug has been thoroughly tested and is safe for them to use.

Clinical Tests

> ***"Baycol is the 12th prescription drug to have been taken off the U.S. market because of dangerous side effects since 1997. Some critics said many of those bans happened because the FDA, under political pressure, had sped up drug approvals during the 1990s. Baycol was not a 'fast-track' drug: The agency spent 11 months reviewing it before approving it in 1997."*** "Bayer Pharmaceutical's Cholesterol-Lowering Drug Baycol Linked to Deaths, Pulled Off Market," AP, Aug. 8, 2001. One of the statin drugs, Baycol destroyed muscle tissue and was linked to 31 deaths in the U.S. and 9 abroad.

> ***"Rezulin [a diabetes drug] was taken out of pharmacies and off the market. But by then it was linked to 63 deaths from liver failure."*** "FDA: Guardian Or Rubber Stamp?" CBS Evening News, July 12, 2001.

Critics of the FDA point out the agency's close ties to the big drug companies as one of the problems in the drug approval process. A *USA Today* report found that more than half the advisors to the FDA have "financial relationships" with drug companies that have an interest in FDA decisions (De Angelis C, "Conflict of Interest and the Public Trust," JAMA, Nov 1, 2000). But even if panel members involved in approving a drug are scrupulously honest, they still depend on data from that company's clinical trials to approve the drug as safe and efficacious, and the data can be misleading.

Pharmaceutical companies are well aware of how to manipulate clinical trials and the resulting data to show their products in the most favorable light.

> ***"Efforts by drug companies to suppress, spin, and obfuscate findings that do not suit their commercial purposes were first revealed to their full, lethal extent during the thalidomide tragedy. Although government drug regulation schemes around the world are now in place, the insidious tactics of big pharma have changed little."*** "The Tightening Grip of Big Pharmaceutical Companies," Editorial, *The Lancet*, April 14, 2001.

For example, a clinical trial might over-select young, healthy subjects when the drug being tested is intended for use primarily on older patients.

> ***"Rochon et al. found that only 2.1 percent of subjects in trials of nonsteroidal anti-inflammatory drugs were 65 years of age or older, even though these drugs are more commonly used and have a higher incidence of side effects in the elderly."*** Bodenheimer T, "Uneasy Alliance—Clinical Investigators and the Pharmaceutical Industry," *New England Journal of Medicine*, 342(20), May 18, 2000.

After FDA approval, it was discovered that Glaxo Wellcome's flu medication Zanamivir could be dangerous for patients with underlying respiratory diseases such as asthma or other chronic pulmonary illness. After some deaths were reported, the FDA issued a warning and required labeling changes for the drug.

Or in comparison trials, the drug being tested might show that it is more efficacious than the drug it is being compared with simply because higher dosages of the new drug were administered. And, since the data from the trials are generally housed and often analyzed by the drug companies themselves, unfavorable results can be suppressed or long-term data showing negative effects might not be presented.

The highly advertised (and expensive) anti-inflammatory drug Celebrex was hailed by an article in the *Journal of the American Medical Association* as vastly superior to existing (and far less expensive) anti-inflammatory drugs such as aspirin and Ibuprofen (Motrin and Advil) because it eliminated the problem of gastric bleeding associated with these drugs. However, researchers at the Therapeutics Initiative in Canada discovered that the study's authors had cut the trial data off at six months. The longer-term results showed that Celebrex was also associated with gastric bleeding, but that it just took longer for these side effects to manifest themselves. The FDA had concluded that there were no major differences between Celebrex and the existing medications, but the published study in JAMA left out the longer-term data.

> ***"Perhaps even more importantly, the [Therapeutics Initiative] report suggests significant safety concerns. 'Any benefit in serious gastrointestinal side effects appear to be cancelled by increased cardiovascular events, including heart attacks, clotting, hypertension and heart failure,' Dr. Wright [director of TI] declares. Celebrex may be 'trading off a decreased chance of stomach ache and ulcer for potentially serious cardiovascular problems.'"*** Candis McLean, "The real drug pushers," *Report Newsmagazine*, March 19, 2001.

Celebrex is now being clinically tested for lung cancer prevention and has already been approved by the FDA for use in preventing colon cancer in patients who are at particularly high risk for the disease ("Celebrex Under Study for Lung Cancer Prevention," *ScienceDaily Magazine,* Aug. 8, 2001).

As bad as some of the manipulations of clinical trials and study data and published clinical reports are, none approach the sheer immorality of some of the drug companies' clinical trials conducted in developing countries. Test subjects in developed countries today are legally protected against abuse, but protective laws in some poorer countries are more lax and are not as rigidly enforced.

> ***"An investigation into corporate drug experiments in Africa, Asia, Eastern Europe and Latin America reveals a booming, poorly regulated system in which experiments involving risky drugs proceed with little independent oversight, and impoverished, poorly educated patients are sometimes tested without understanding that they are guinea pigs. These foreign trials speed new drugs to the marketplace—where they are often sold mainly to patients in wealthy countries."*** Joe Stephens, "Testing drugs: Overseas trials lack oversight: Companies target patients in poor nations," *The Miami Herald,* Jan 7, 2001, p. 1L.

> ***"'We're colonizing a region for clinical trials' declared Juan Pablo Guzman, who has worked on clinical trials in Latin America for Searle and Pharmacia, at June's annual meeting of the Drug Information Association in San Diego. 'We have to believe there is gold at the end of the journey.'"*** "Latin America is fertile ground for experiments," *The Miami Herald*, Jan 7, 2001, p. 3L.

In one such instance, researchers for Pfizer clinically tested what the company believed to be a promising new antibiotic on Nigerian children who had fallen victim to the country's meningitis epidemic. Among the 200 test subjects, 11 died and others suffered meningitis-related symptoms such as seizures, blindness, deafness, and lameness. The drug being tested, orally-administered Trovan, had never been approved or tested for use with children, and chemically similar drugs had caused joint damage in animal experiments. According to an article in the *Miami Herald,* Pfizer's own internal report showed children did die shortly after taking oral Trovan.

> ***"The experiment's final report concluded that Trovan and the comparison drug were equally safe and effective."*** Joe Stephens, "Testing drugs: Overseas trials lack oversight," *The Miami Herald,* Jan. 7, 2001.

But of course many of the sick and dying in these countries will never be able to afford treatment with the successful drugs once they are approved as safe and efficacious by the FDA.

Maintaining the High Cost of Medicines

Increasingly the big multinational drug companies are coming under fire for doing everything in their power to maintain the high costs of their products, even when those costs mean that essential drugs will not be available to the poor (or even to some of our own elderly who have limited incomes).

> ***"Using big money, creative court challenges and a regulatory system prone to delays, the nation's leading manufacturers of brand-name drugs are fighting harder than ever to keep cheaper generic imitations off the market…. Generic drug makers have at times enriched themselves by keeping their products off the market, deliberately, in exchange for payments from patented drug companies."*** Greg Fields, "Brand-name drug makers' tactics slow generics," *The Miami Herald*, Aug. 17, 2000, p. A1.

By far, the greatest public outcry over the high cost of drugs came as a result of the AIDS epidemic in Africa. AIDS drugs, such as those manufactured by GlaxoSmithKline, are extremely expensive, far too expensive for them to be used in developing countries where the disease is truly at epidemic proportions.

> ***"These drugs aren't expensive because of the cost to develop and manufacture them (many were actually invented at public universities using grants from taxpayers). Rather they're expensive because some of the pharmaceutical giants that market them demand huge profits, estimated by Brazil's health minister, Jose Sera, at up to 10 times cost, or 1,000 percent."*** Tom Fiedler, "AIDS fight boils down to dollars vs. lives," *Miami Herald* editorial, June 24, 2001, p. 5L.

Smaller drug companies in such countries as India and others in sub-Saharan Africa sought to manufacture affordable versions of the AIDS drugs for use in their own and other poor countries, but the big multinationals sued the smaller companies, alleging they were pirating patented drugs.

GlaxoSmithKline ultimately bowed somewhat to public pressure and lowered the cost of its antimalarial and newer HIV and AIDS drugs to developing countries. However, as critics pointed out, even with the lowered prices of the AIDS drugs, they will still be too expensive for the huge majority of Africans.

At the same time, the burden of medication expense for many of our own elderly citizens, who often take multiple medications, means that they are either doing without essential drugs or are lowering their use of the medications by deliberately skipping doses (which in some cases could be more dangerous than not taking the drugs at all). Medicare does not cover prescription drugs except those administered in hospital. According to Public Citizen, the big drug companies are charging these seniors twice as much on average as the companies charge their most favored customers such as HMOs and the Departments of Veterans Affairs and Defense. Public Citizen claims that the mark-up for Medicare outpatients for Merck's high cholesterol drug Zocor is 144%. The organization says that the mark-up for Pharmacia's diabetes medication Micronase is a whopping 363%, and that Abbot Laboratories' hormone treatment Synthroid is even worse at an incredible 1,446%.

The current political solution to this problem of medication cost to seniors is to have the taxpayers assume the burden for it, but since the taxpayers have already paid for the basic research to develop many of these drugs and have even paid for some of the clinical trials, that seems asking a bit much of the taxpayers. Perhaps a better solution would be to put pressure on Big Drugs to come up with a reasonable plan to lower the cost of necessary medications for seniors—or at least give them the same price breaks they give their "favored" customers.

There is no question the pharmaceutical industry provides important and necessary products to improve the health of Americans and save the lives of those who have infectious and parasitic diseases. However, the big drug companies' marketing and testing abuses and their almost unbridled influence on public policy (and government agencies) are major problems in this country and in the world. It could be that their control of the practice of medicine and of public health policy is even more dangerous to the health of society in the long run than some of their drugs are to the health of individual consumers.

Suggested Supplemental Reading Online

"The real drug pushers," by Candis McLean, *Report Newsmagazine*, March 19, 2001.
http://193.78.190.200/10a/the%20real%20drug%20pushers.htm

"Rx R&D Myths: The Case Against The Drug Industry's R&D 'Scare Card,'" Public Citizen report, July 23, 2001.
http://www.citizen.org/congress/drugs/R&Dscarecard.htm

"The Drug-Induced Lung Diseases," Pneumotox Online.
http://www.pneumotox.com