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'The Truth About the Drug Companies' and 'Powerful Medicines': The Drug Lords

By STEPHEN S. HALL

During the past year, when I was driving my children to school, I'd hear the same advertisement on the radio again and again. You've probably heard it too: as somber music played in the background, a young man, his voice cracking, explains how he developed a rare and deadly form of cancer. He wonders if he will ever play baseball with his son, and then relates how, thanks to a company called Novartis and its new cancer treatment (never mentioned, but a drug called Gleevec), he's been given a new lease on life.

What is most fascinating about this ad is that it should seem necessary. As Marcia Angell points out in "The Truth About the Drug Companies: How They Deceive Us and What to Do About It": "Truly good drugs don't have to be promoted. A genuinely important new drug, such as Gleevec, sells itself." So why advertise a cancer drug that cures a fatal leukemia and has no competition? The answer, of course, is that Novartis is not advertising Gleevec, but the company itself -- and the virtues of the drug industry as a whole. Why? Because, as Angell notes, a "perfect storm" of indignation -- on the part of consumers, regulators+and even doctors -- may be developing around the pharmaceutical business.

In just one week this summer, the news included reports that Schering-Plough pleaded guilty to cheating Medicaid; the city of New York sued leading pharmaceutical companies, including Amgen, Bayer, Bristol-Myers Squibb, Eli Lilly, Johnson & Johnson and Merck, for inflating costs and defrauding taxpayers; Janssen Pharmaceutica Products admitted it had withheld from the public information about potentially fatal side effects in a schizophrenia drug it markets; and Wyeth settled yet another in the multibillion dollars' worth of lawsuits against it by people who suffered permanent injury from use of the fen-phen weight-loss drugs. All this against a broad public perception of price-gouging, lack of innovation and bombastic self-congratulation. And that brings me back to the Novartis ad.

An alternative history for Gleevec is recounted in both Angell's methodical multicount indictment of the drug industry and Jerry Avorn's entertaining jeremiad, "Powerful Medicines: The Benefits, Risks and Costs of Prescription Drugs." In this less heroic version, several decades of dogged research by academic scientists -- much of it paid for by American taxpayers through the National Institutes of Health -- had teased out the molecular details of chronic myelogenous leukemia, a rare and fatal hematological cancer. Researchers at Novartis (then Ciba-Geigy) created several compounds that in theory might throw a monkey wrench into the process by which blood cells become cancerous. But these potential miracle drugs sat on the shelf untested, until Brian Druker, a researcher at the Oregon Health and Science University, asked for the compounds and became the first to discern their anticancer properties in the lab dish. Even that wasn't

enough. As Avorn tells it, "Novartis had so little interest in committing resources to the drug's development that cancer researchers had to resort to the bizarre tactic of sending a petition to the company's C.E.O., signed by scientists in the Leukemia and Lymphoma Society of America, imploring him to make more drug available for clinical studies."

Novartis has overcome its lack of enthusiasm -- it now charges $27,000 for a year's supply of Gleevec. But those heart-warming ads, now the centerpiece of the Novartis corporate identity, say more than intended about how today's pharmaceutical industry takes credit where little is due. As both Angell and Avorn lay out in painstaking, often enraging, detail, a self-serving mythology -- promulgated on a scale possible only in a business with annual worldwide revenues of $400 billion -- has enveloped the pharmaceutical industry. Angell and Avorn cut through the haze, arguing persuasively that Americans are paying an enormous amount of money for some very mediocre medicines.

The rising voices of disillusionment have the credentials to back up their scorn. Two of the season's most stinging anti-drug-industry analyses come from former editors in chief of The New England Journal of Medicine. Marcia Angell is one. Jerome P. Kassirer is the other; the title of his book, "On the Take: How America's Complicity With Big Business Can Endanger Your Health" (Oxford University, $26), says it all. Jerry Avorn, a professor at Harvard Medical School, helps decide what drugs are used in Boston's Brigham and Women's Hospital. And John Abramson was a doctor in family practice until, as he recounts in "Overdosed America: The Broken Promise of American Medicine" (HarperCollins, $24.95), he began to detect what might politely be called statistical legerdemain in articles promoting new drugs in the aforementioned New England Journal.

These books are not simply diatribes against high prices and lagging development of new medicines. More disturbingly, the authors contend that the drug industry has polluted the scientific basis of modern medicine with rigged market-driven clinical studies that inflate the effectiveness of new, high-priced drugs while concealing their risks to patient safety. Angell's occasionally strident language, laced with terms like "bribes and kickbacks" and "faux research" seems hyperbolic -- until you consider that one week's worth of headlines.

The reasons for the transformation of the industry's image from life-saving pioneer to robber baron are many. But at root is a profound shift in the hierarchy of influence and decision making within the companies themselves over the last two decades, as the traditional emphasis on research and development has given way to marketing. The change is everywhere apparent: in the background of many company executives, in the annual balance sheets (in 2001, Angell estimates industrywide marketing budgets at $54 billion, almost double research-and-development outlays, which the industry lobby puts at $30 billion), in the army of 88,000 salesmen (or detailers), trained to bird-dog doctors and persuade them to prescribe their company's drugs. Though much drug industry research remains outstanding, the system rewards what Avorn calls "trivial pseudo-innovation"; shifting the emphasis from research to marketing was, he says, "just

responding rationally to the legal, regulatory and economic pressures of a marketplace that had become perverse."

Angell, who gives a vivid historical context, dates the "watershed year" to 1980, on the cusp of a era in which it became "not only reputable to be wealthy, but something close to virtuous." The Bayh-Dole Act of 1980 basically turned academic labs into farm teams for industry research, allowing publicly funded researchers in academic institutions (where much of the real enterprise and innovation occur) to patent their discoveries and license them to the private sector; the law has created a thicket of licensing and royalty relationships, wink-and-nod consultancies and conflicts of interest. As Angell tellingly relates, the authors of one New England Journal article collectively owned up to so many financial conflicts that they had to be listed separately on a Web site. The headline on the editorial she wrote about the episode was "Is Academic Medicine for Sale?" One cynical reader replied: "No. The current owner is very happy with it."

Then there was was the Hatch-Waxman Act of 1984, which did what it was ostensibly designed to do, make it easier for generic drug makers to put cheaper medicines on the market -- but at enormous cost to the consumer. In Angell's view, Hatch-Waxman was a Trojan horse bill; its loopholes meant that pharmaceutical companies could, with patent infringement suits costing, say, a mere $5 million, extend government-granted monopolies on popular drugs like Prilosec and Claritin, in some cases for more than four years, yielding them billions of dollars in additional revenue.

It gets worse. Laws passed in the 1990's gave drug companies extraordinary financial influence over their primary regulator, the Food and Drug Administration, through so-called user's fees to expedite reviews of new drugs. And both Angell and Avorn quote Senator Bill Frist's devastatingly candid remark revealing that one respected candidate for the agency's top job in 2002 apparently lost industry support because "there was a great deal of concern that he put too much emphasis on safety."

As for the recent Medicare reform bill, with its prescription drug benefit, Angell considers the measure a huge windfall for industry, because it explicitly forbids Medicare to bargain on prices. Indeed, Angell foresees a grim day of reckoning, and calls for its immediate repeal.

Pharmaceutical Research and Manufacturers of America, the industry's lobbying group, has tirelessly argued that high drug prices are needed to support the high-risk endeavor of drug discovery and development. Yes, the business is risky. But Angell gives us good reason to dispute the much-quoted figure of $802 million as the average cost for developing a new drug, and the assertions of innovative research and development. She cites studies showing that between 1998 and 2002, 415 new drugs received F.D.A. approval; only 133 were "new molecular entities," or genuinely novel compounds, and of those, only 58 -- or 14 percent of all new drugs for the five-year period -- were considered likely by the F.D.A. to be "a significant improvement" over existing products.

Avorn covers much the same ground, but comes at it by statistical analysis of drug effectiveness and safety. As a "pharmaco-epidemiologist," he studies large patient databases to determine how often certain medications are used and how well they work. His watchword is "evidence-based medicine" -- the use of randomized controlled clinical trials, in which participants are randomly assigned to receive, for example, a drug being tested or a dummy pill, or of large-scale epidemiological studies to determine with statistical rigor exactly which drugs are safest, most effective and, increasingly, most cost-effective. He laments that "we have begun to allow the marketplace to usurp the place of evidence in determining which treatments are effective." The marketplace has also been very good about playing down side effects: Avorn's accounts of the systematic "obfuscation of risk" for two drugs ultimately withdrawn from the market, the diet drug Redux and the diabetes drug Rezulin, are stomach-turning in their detailing of corporate indifference.

What to do? Angell's most urgent recommendation (among many) is to establish an independent mechanism within the National Institutes of Health, for testing prescription drugs against each other without involving the industry. Avorn, in arguing for more evidence-based medicine, lays out several nonprofit and for-profit scenarios for precisely that kind of independent, data-driven drug assessment. (My own view is that there will be a McDonald's on Mars before drug companies relinquish head-to-head clinical testing of their products -- precisely because high-quality data is a poison pill to most of their marketing.)

In 1906, Upton Sinclair documented abuses in the meat-packing industry; his book, "The Jungle," catalyzed outrage and helped lead to the Food and Drug Act of 1906, which set the first national food and drug regulatory processes. I doubt either of these books will have a similar impact. Public policy these days is mostly driven by events, not books. My guess is that it will take the pharmaceutical equivalent of a plane crash -- perhaps a devastating new influenza epidemic, a disease for which, as this flu season's experience makes painfully clear, fewer and fewer companies bother to make vaccines; or a hugely successful life-saving cancer drug whose high cost would make the economic wall between the haves (who get to live) and the have-nots (who don't) politically unsustainable. That unpleasant day of reckoning is almost upon us. These fine books go a long way in explaining how our medicine, once so vaunted, has become so bitter. hThe authors of one scientific article had so many conflicts, they needed a Web site to list them.

Stephen S. Hall is the author, most recently, of "Merchants of Immortality: Chasing the Dream of Human Life Extension."