Introduction

Central to current public debates in North America, the United Kingdom, Europe and elsewhere are issues concerning costs and profits in relation to just healthcare and ethical business practices. These concerns are driven by major shifts in healthcare that took place during the twentieth century. These shifts include the transformation of the professional practice of medicine in the United States from a service orientation to a market orientation; the emergence of powerful pharmaceutical and healthcare corporations with global reach; the development of new, innovative, and expensive biomedical technologies by for-profit enterprises; and steadily increasing healthcare costs in industrialized nations. Furthermore, many of the most important ethical issues regarding the business of biomedicine concern decisions made in healthcare systems rather than in the context of patient–physician relationships. These issues lie at the intersections of two flourishing areas of applied ethics that, at least in recent years, are seldom in conversation: bioethics and business ethics. This volume brings together distinguished scholars from both fields. The shared goal of each of the authors is to evaluate the practices of profit-seeking healthcare organizations, and business-friendly public policies regarding healthcare, and to offer normative guidance regarding the ethical delivery of healthcare products and services by profit seeking organizations operating in a global marketplace.

JUSTICE AND MARKETS IN HEALTHCARE

In industrialized nations increases in healthcare spending continue to outpace inflation. In 2006 national health expenditures (NHE) rose 6.7% in the United States, reaching $2.1 trillion and accounting for 16% of gross domestic product (GDP).[1] Annual rates of increase in the range of 6.5–6.9% have been largely stable[2] since 2002 when the rate of increase peaked at 9.1%.[3] The amount of GDP consumed by healthcare expenditures continues to outpace GDP growth.[4] While the trend is most pronounced in the

United States the problem is common to all members of the *Organisation for Economic Co-operation and Development* (OECD). The average, annual, per capita increase in healthcare spending for all OECD countries was 4% in the period from 1995 to 2005.[5] Additionally, average OECD healthcare expenditure as a share of GDP reached 9% in 2005.[6] Both France and the United Kingdom substantially exceeded this rate of growth (by 1% and 0.6% respectively) while Canada saw their expenditure as a share of GDP drop slightly (by 0.1%) during the same period.[7]

In the United States healthcare spending on pharmaceuticals alone has reached $200.7 billion, a nearly 500% increase since 1990. This accounted for 10% of NHE in 2005. Pharmaceutical spending increased at the highest rate of any component of NHE from 1994 to 2003.[8] On average, per capita spending on pharmaceuticals for OECD countries has risen by more than 50% in real terms since 1995. Pharmaceutical spending constituted around 17% of NHE for OECD countries and growth in spending between 1995 and 2005 has averaged 4.6% per year, outpacing the average annual rise in overall healthcare spending of 4% over the same period.[9]

Increases in spending in all sectors of healthcare serve to drive up health insurance premiums. In the United States between 2004 and 2005, 1.3 million additional Americans became uninsured, raising the percentage of non-elderly uninsured Americans to nearly 18%.[10] This brings the total number of non-elderly uninsured Americans to nearly 46.1 million.[11] Rising premiums coupled with the economic downturn in 2001 are seen as the primary reasons for such large increases in the number of uninsured.[12] The economic downturn of 2008 may result in even greater numbers of uninsured. One result of millions of Americans being unable to afford health insurance coverage is that nearly half of all personal bankruptcy filings have partly resulted from an inability to pay medical expenses.[13]

Health insurance premiums are the fastest growing expense for US employers, increasing 87% since 2000. On average employee contributions to health insurance premiums have increased 143% since 2000.[14] Further, increases in pharmaceutical spending have resulted in the establishment of tiered, cost-sharing formulas and increased drug co-payments. In 2005, 74% of workers with employer-sponsored coverage had cost-sharing arrangements with 3 or 4 tiers, 27% higher than workers in 2000. Average co-payments for non-formulary drugs doubled from $17 in 2000 to $35 in 2005 and average co-payments for formulary drugs increased 69% from $13 in 2000 to $22 in 2005.[15] As a result of increased cost sharing out-of-pocket expenses for employees have increased 115% since 2000.[16] While most OECD countries have some form of universal health coverage, significant increases in spending

have contributed to the higher national expenditures noted above and constitute additional burdens for those systems. All industrialized countries that provide some form of universal healthcare are struggling to finance their systems in the face of rising costs and aging populations.

In Chapter 1, "Medicine and the Market," Daniel Callahan argues that markets in medicine may be divided into three distinct approaches. One approach is that of ever increasing profit spurred by market innovation. A second approach, one favored by many healthcare economists, views the market in instrumental terms and emphasizes greater efficiency in the delivery of care. A third approach, common in politically conservative literature, views a healthcare marketplace as a necessary and appropriate partner for a thriving democracy. Callahan argues that in thinking about the possible role of the market in healthcare, we can learn from these three approaches. We want, he argues, a healthcare system that preserves and encourages the traditional values of medicine such as individual patient welfare; that is based on the most reliable and well-grounded economic theory and evidence; and that balances individual good with the common good. He argues that European and Canadian healthcare systems better achieve this nexus of values than the United States system because of their commitment to universal coverage and because market forces play a small role in those systems. In contrast, the United States healthcare system is fragmented, lacks a commitment to universal coverage, and market forces play a much more prominent role.

The for-profit business of biomedicine includes pharmaceutical companies, medical equipment manufacturers, healthcare providers, medical facilities, group practices, pharmacies, and insurance companies. In Chapter 2, "Broken Promises: Do Business-Friendly Strategies Frustrate Just Healthcare?," Norman Daniels observes that business-friendly strategies in financing and delivering medical services improve profits for businesses, but he argues that such strategies do not promote just medicine. He examines five market-friendly strategies – he calls them promises – regarding managed care, privatization, and intellectual property that have been promoted as ways to improve the US healthcare system. Daniels argues that each of these promises has been broken in ways that put populations at risk and that these failures provide good reason to subject all such promises to careful ethical and scientific review.

PATIENTS, PROFITS, AND PHARMACEUTICALS

The pharmaceutical industry has been the most profitable industry in the United States for most of the last decade.[17] The industry has seen profits as a

percent of revenues between 14.3% and 18.6% for the last ten years compared to a median return of 5.2% for all Fortune 500 companies in 2004, the highest median return in the last 10 years.[18] The industry regards robust profits as the best way to satisfy investors while ensuring the continued development of new and innovative pharmaceuticals. At the same time the industry has received widespread criticism from politicians, bioethicists, clinicians, and consumers. The industry is accused of failing to provide life-saving drugs to the sick and dying in developing nations in order to protect ethically questionable intellectual property rights. It has been accused of exploiting poor, undereducated populations in developing nations in drug trials. And it is alleged to have used the billions of dollars it spends annually on marketing to promote drugs in deceptive and misleading ways.

As diseases ravage developing nations critics have called upon the pharmaceutical industry to expend more resources in efforts to treat diseases that are mainly endemic to the developing world. There are often few treatments for these diseases and what treatments are available are often prohibitively expensive. For example, during an outbreak of malaria in Ethiopia in 2003 the United Nations Children's Fund (UNICEF) was forced to use an outdated combination of chloroquine and sulfadoxine-pyrimethamine (SP) to treat patients. The cocktail was not as effective against newly mutated strains of malaria, with as many as 60% of patients showing resistance to the cocktail. However, the more effective artemisinin was prohibitively expensive at $1 to $2.50 per treatment compared to the $0.20 that the choloroquine/SP cocktail cost.[19] In another case, Melarsoprol, literally the same arsenic found in antifreeze, is used in treatment for sleeping sickness. It kills 5% of those treated and destroys the vein into which it is injected. Despite these side-effects Melarsoprol is used because it is the only viable treatment for the disease. The only realistic alternative treatment, Eflornithine, was so effective at bringing people out of end stage comas it was nicknamed "the Resurrection Drug." However, at $210 per treatment it is nearly four times the cost of Melarsoprol, and access to the drug dried up when Aventis abandoned it upon determining that it was ineffective against cancer, the disease it was originally developed to treat. The fate of Eflornithine highlights another important problem regarding the treatment of diseases in the developing world. How do you get pharmaceutical companies to take an interest in diseases that are largely relegated to the developing world when there is no financial incentive to drive research and development?[20]

One potential solution that has been proposed has been for governments to offer pharmaceutical companies an extension on an existing patent for a drug

of their choice in return for the development of treatments for third world diseases. The idea being that continued patent protection of a blockbuster drug will provide the financial incentive necessary to encourage companies to invest in research and development on third world diseases.[21] However, even if effective drugs are developed to treat diseases in developing nations the problem of how to pay for manufacturing and distributing them remains.

In response to this problem Thailand has begun to overrule international patents on several drugs and churn out cheap generic copies. Under a provision of the Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), countries can "compulsorily license" certain drugs, but only under special conditions, which it is not clear that Thailand has met.[22] Similarly, patents are under attack by India's thriving generic drug industry which has won several cases regarding their right to copy patent protected drugs. While Thailand and India's development of generic alternatives to expensive patent protected drugs has demonstrated one way of circumventing the prohibitively high prices of treatments of diseases in the developing world, it is not clear that this will be an effective long-term strategy. With companies feeling the financial impact from the proliferation of cheap generics combined with even less financial incentives for the development of treatments for third world diseases, many have begun to move away from research and development of cures for these diseases.

Nonetheless, some companies have taken positive, unilateral action regarding access to drugs in developing nations. For example, Merck has developed and delivered for free the drug Mectizan, a cure for riverblindness, to hundreds of millions of patients throughout Africa.[23] Novartis has formed the Novartis Institute for Tropical Diseases in conjunction with the Singapore Economic Development Board in order to find new drugs to treat tropical diseases. And the very financial difficulties underlying the development of treatments of diseases in the developing world have led to an innovative decision by GlaxoSmithKline. Hurt by the proliferation of cheap generic alternatives to its AIDS drugs, GlaxoSmithKline chose to sell its AIDS medications at cost to 100 countries and granted 8 local companies licenses to produce generic alternatives. Approximately 90% of their vaccines are now sold at not-for-profit prices to the developing world. By creating 14 different partnerships with the World Health Organization and other non-governmental organizations (NGO's), GlaxoSmithKline has remained profitable while continuing to fund additional research into new AIDS treatments. Additionally, this market model has boosted morale at the company and drawn talented researchers who want their work to improve human welfare.[24]

In Chapter 3, "Are Patents an Efficient and Internationally Fair Means of Funding Research and Development for New Medicines?," Paul Menzel takes up the question of the provision of life-saving drugs to the sick and dying in developing nations. He argues that current global patent law is neither efficient nor fair since it tolerates high expenditures on the development and marketing of non-innovative "me-too" drugs. Moreover, Menzel argues, even with the laudable modification of the Doha Declaration on the TRIPS agreement with respect to patent protection in poor nations, together with the implementation of the most important reforms recommended by critics of current laws, fairness for poor nations will not be achieved without an additional crucial step: an advanced market commitment to purchase medicines for poor nation diseases or a global healthcare research and development fund. These new funding mechanisms, Menzel argues, need not be so comprehensive as to replace patents as partial vehicles for generating and allocating research and development funds.

Many criticisms of the pharmaceutical industry concern the use of undue or illegitimate influence over research subjects, physicians, or patients. The next five chapters are concerned with ethical issues regarding the influence of the pharmaceutical industry. One issue that has arisen in the era of economic globalization concerns the obligations of pharmaceutical companies regarding clinical trials in developing nations. The relatively low cost of conducting trials in developing nations, together with the relative ease of global communication and transportation, has resulted in the developing world becoming a testing ground for new drugs. Conducting trials in nations with minimal regulatory frameworks governing trials has resulted in a concern that the motivation for profit is trumping consideration of basic human rights. For example, recent investigations conducted by the *Washington Post* concluded that, "experiments involving risky drugs proceed with little independent oversight. Impoverished, poorly educated patients are sometimes tested without understanding that they are acting as guinea pigs. And pledges of quality medical care sometimes prove fatally hollow."[25] These concerns are highlighted by the criminal charges and civil rights lawsuit filed by Nigerian authorities against Pfizer in June of 2007. The suit claims that during a 1996 meningitis epidemic Pfizer illegally tested unapproved drugs, in particular the experimental antibiotic Provan, on 200 children without their parents' permission.[26] Nonetheless, in many nations the lure of financial gain from participating in clinical drug trials has created international competition among developing nations as they attempt to entice pharmaceutical companies to conduct drug trials in their countries.[27]

Are pharmaceutical research subjects in developing nations properly understood as exploited? In what ways can pharmaceutical companies be said to exert undue influence over economically disadvantaged individuals who participate in clinical trials? These are the primary questions taken up by Tom Beauchamp in Chapter 4, "The Exploitation of the Economically Disadvantaged In Pharmaceutical Research." As Beauchamp points out, nearly everyone will agree with the abstract rule that we ought not exploit the economically disadvantaged in pharmaceutical research projects, however, it is not so easy to determine what counts as exploitation. And even if we can agree that exploitation is taking place, we still need to determine whether or not such exploitation should always be avoided or whether such exploitation might be acceptable given certain trade-offs. Beauchamp argues that while pharmaceutical research utilizing economically disadvantaged subjects is not inherently exploitative, the issues are more complex and subtle than has been recognized in the literature on the subject.

The influence of pharmaceutical companies on the prescribing practices of physicians continues to trouble many observers. One of the primary means by which the pharmaceutical industry maintains high profit margins is through their immense investment in marketing, nearly $30 billion in 2005 in the United States alone.[28] Of this amount $6.7 billon was spent on direct-to-physician (DTP) marketing. If one includes medical journal advertising and free drug samples, the total amount spent on marketing to American physicians comes to $25.6 billion. Often DTP expenditures are utilized for ethically questionable, but legal activities such as purchasing meals and providing gifts to physicians. Physicians are educated in a culture permeated by the influence of pharmaceutical companies. Medical students attend drug-company-sponsored lectures and seminars. Modestly paid residents are courted by pharmaceutical representatives at expensive restaurants. And medical students, residents, and fellows are keenly aware that some of their faculty are paid handsomely to represent drug companies. Is it any surprise, then, that physicians are quite receptive to "drug reps" after they complete their training? Recognizing the role that medical education plays in shaping the perspectives of physicians regarding drug companies the University of Pennsylvania School of Medicine, Yale School of Medicine, Vanderbilt University Medical Center, and other prominent medical schools, have recently restricted the activities of pharmaceutical company representatives on campus.

Marketing budgets are also used to illegally market drugs. For example, pharmaceutical companies regularly find themselves in legal trouble over the promotion of off-label uses of medications, where drugs are promoted for uses

not approved by the FDA. Schering-Plough has settled three times in five years regarding indictments that it has promoted off-label uses of its drugs and lied about drug prices, costing the company a total of $1.3 billion.[29] In 2004 Pfizer pled guilty to charges that it paid doctors to prescribe their epilepsy drug Neurontin for off-label uses, paying $430 million.[30] Pfizer is currently battling lawsuits that claim that it encouraged the prescribing of its cholesterol drug Lipitor to a broader population than allowed under federal rules.[31] In 2006 InterMune settled a suit for $37 million regarding the off-label promotion of Actimmune. Additionally, InterMune recently halted clinical trials designed to approve Actimmune for the very off-label uses InterMune was accused of encouraging after it showed no effectiveness in prolonging the lives of pulmonary fibrosis patients.[32] Cephalon was investigated in 2004 when it came to light that half of prescriptions written for its narcolepsy drug Provigil may have been for off-label uses.[33] Eli Lilly, in their marketing of the antipsychotic medication Zyprexa (Olanzapine), intentionally downplayed health risks and pitched the drug for uses not approved by the Food and Drug Administration. In 2007 Eli Lilly's total payout for Zyprexa-related legal claims came to $1.2 billion to plaintiffs who contracted diabetes or other diseases as a result of taking the drug.[34] Lilly is contemplating a $1 billion dollar settlement with state and federal governments to settle civil and criminal charges that resulted from the false and misleading marketing.[35] In 2008 Merck agreed to pay the US government $671 million to settle, in part, charges that they used money and perks to induce doctors to write more prescriptions for their drugs.[36]

Appealing to a large body of empirical data, Jason Hubbard argues in Chapter 5, "The Dangers of Detailing: How Pharmaceutical Marketing Threatens Healthcare," that many of the techniques that pharmaceutical sales representative's employ actively aim to deceive and manipulate physicians. Hubbard argues that these deceptive and manipulative practices interfere with the capacity of physicians to fulfill their fiduciary duties in prescribing the best treatments for their patients. As a result, he argues DTP marketers act disrespectfully toward physicians and harm patients. Given these problems he calls for a voluntary ban on many of the practices that surround DTP marketing. The industry has recently responded to such criticism with revised guidelines for marketing to physicians that take effect in 2009.[37] However, since the industry lacks transparency with respect to compliance and has not put enforcement mechanisms in place, the new guidelines are unlikely to curb widespread abuse. Hubbard argues that regulatory solutions may be required in order to stop ethically illegitimate marketing to physicians.

The United States is nearly alone among OECD nations in allowing direct-to-consumer (DTC) pharmaceutical manufacturing.[38] However, that may change soon. Currently the pharmaceutical industry is lobbying for DTC advertising to be approved in Europe and Canada. In the United States spending on DTC advertising has quadrupled since it was permitted by an FDA rule change in 1997. Current spending on DTC advertising in the United States is approximately $4.2 billon.[39] Critics of DTC advertising argue that most consumers are not capable of making informed decisions regarding pharmaceuticals and as a result it is dangerous to expose them to such marketing.[40] The pharmaceutical industry claims that DTC advertising merely makes patients more educated consumers regarding diseases and their treatments. And they point out that physicians ultimately control what prescriptions consumers are given. United States Congressman Henry Waxman (D-Calif.) attempted to restrict DTC advertising of pharmaceuticals to drugs that had been on the market for at least three years – enough time to collect useful data on adverse side-effects – by attaching it to a drug safety bill. However, by the time the bill had passed nearly all restrictions on drug advertising had been removed as a result of industry lobbying.[41] More recently, the United States House of Representatives Committee on Energy and Commerce, Subcommittee on Oversights and Investigation held hearings on the subject entitled "Direct-to-Consumer Advertising: Marketing, Education, or Deception?"[42] However, the hearings do not appear likely to result in Congressional action on the issue.

Current FDA oversight of drug advertising appears to be inadequate. Drug makers are only required to submit their advertisement at the time they begin broadcasting and there is often a significant lag between when drug advertisements begin to run and when the FDA actually reviews them. As a result, there have been several cases of drug advertisements being pulled after they have run for significant periods of time. In 2002 GlaxoSmithKline was forced to change an advertisement for their blockbuster antidepressant Paxil in which they stated that the drug was "nonhabit-forming."[43] Pfizer pulled its Viagra advertisement with a man with devilish horns and the phrase "he's back" in 2004 when the FDA determined that the advertisement went too far in indicating what the drug treats when it was supposed to have been a "reminder ad" which allows drug companies to sidestep the requirement that they list side-effects.[44] In addition, Pfizer was cited four times for misleading television and print advertisements for Lipitor and received seven citations for promotions of Celebrex.[45] Similarly, Bayer and GlaxoSmithKline were forced to pull a Levitra advertisement due to the fact that it inadequately stated the drug's side-effects and could not substantiate

claims that it was superior to competing drugs.[46] Amgen was forced to pull an advertisement and make efforts to correct misleading information included in their advertisement for the psoriasis drug Enbrel. Schering-Plough has been cited 11 times for its advertisements for Claritin (a record for the most FDA citations), and Merck was cited for minimizing the chance of cardiovascular risk with its drug Vioxx.[47]

Critics of DTC advertising typically call for a ban on such advertising.[48] In response pharmaceutical companies and the advertising industry argue for the right to advertise on constitutional free speech grounds.[49] Denis Arnold considers the ethical status of DTC advertising in Chapter 6, "The Ethics of Direct-to-Consumer Pharmaceutical Advertising." He points out that none of the existing literature on ethical legitimacy of DTC advertising takes seriously the distinction between the three classes of consumer marketing distinguished by the FDA: reminder advertisements, product claim advertisements, and help-seeking advertisements. Arnold explains the distinctions between these three classes of advertisements and asks whether any of these classes of advertising can properly be characterized as educational as the industry contends. He concludes that reminder advertisements and product claim advertisements rely on biased information and peripheral, non-cognitive means of persuasion and as such are manipulative rather than educational. However, he argues that help-seeking advertisements can be made genuinely educational and recommends a solution to the current impasse regarding DTC advertising. His solution preserves the right of the industry to advertise while eliminating the worst industry abuses.

The recent debacle regarding Merck's voluntary withdrawl of Vioxx from the market is perhaps the most prominent of a series of drug recalls that have led to widespread concerns regarding drug safety. These concerns contributed to the passage of a new drug safety bill that gives the FDA modestly expanded powers to protect consumers. The bill allows the FDA to require further study of the safety of medications and to mandate new warnings if deemed necessary. Companies are also required to publicly release the results of all clinical trials that indicate how well their drugs performed, although what precisely this entails has yet to be spelled out. Finally, the FDA gained the capacity to fine drug companies for failure to comply with their new powers and the additional ability to fine drug makers for failure to complete follow-up studies after their drug has been approved.[50] However, many of these reforms are quite modest relative to the range of safety issues with which the public is rightfully concerned.

Safety issues have raised serious concerns over the influence of pharmaceutical companies and transparency regarding drug trials. In March of