

The Market and Medical Innovation: Human Passions and Medical Advancement

MARK J. CHERRY

Saint Edward's University, Austin, Texas, USA

I. INTRODUCTION

Innovation, even medical innovation, is frequently driven by the profit motive. Other motives to innovate surely exist—scientific interest, professionalism, altruism, patriotism, or even civic duty—however, without the profit motive the same level of innovation does not obtain. Historically, the development of an economic sphere in which individuals and groups ventured with others, open to the possibility of success and failure, and charged whatever prices seemed likely to yield the greatest profits, offered a significant incentive to innovate new products and services (Rosenberg and Birdzell, 2002, p. 21). The open market offered both the possibility to profit from one's innovation and to raise the capital necessary for experimentation. Moreover, it diffused political and social authority, freeing innovators to compete with each other as well as to challenge the status quo.¹ To state the matter somewhat rhetorically: greed is a powerful human incentive to create innovative healthcare products and medical services.

Yet, within bioethics, the proposition that the market encourages scientific excellence and virtue in medical research and product development is met with considerable skepticism. Market-based research and development of pharmaceuticals and medical devices, it is more typically claimed, fail to protect the most fundamental interests of persons and public health. In part, there is a concern that intellectual property protection will impede the flourishing of scientific research. As a report from the International Bioethics Committee (Berlinguer & De Castro, 2003), "On the possibility of Elaborating a Universal Instrument on Bioethics" urged:

As healthcare services and medicines become increasingly more expensive, access to them by poor populations becomes more severely compromised.

Address correspondence to: Mark J. Cherry, Ph.D., Department of Philosophy, St. Edward's University, 3001 S. Congress Ave., Austin, TX 78704, USA. E-mail: markc@admin.stedwards.edu

While poor people have at least as much need for these medicines as everybody else, many do not have the resources to guarantee access. . . . Our global society must face the responsibility to use science and technology to promote public health and to equalize access to healthcare and medicines . . . (2003, para 17).

The IBC believes that the promotion of justice requires securing the benefits of scientific and technological advances equally for all of humanity (2003, para 28). The underlying assumption, which must be critically evaluated, is that the results of scientific progress belong to humanity as a whole, rather than to those who invest time, energy, and resources, to create innovations. To put the issue starkly, profiting from the provision of health care services, pharmaceuticals, or medical devices is viewed as morally suspect. As a result, calls for significant, wide-ranging, and extensive governmental regulation, patent limitations, required licensing of generic alternatives, and profit restrictions on pharmaceutical companies are ubiquitous. This issue of *The Journal of Medicine and Philosophy* critically explores such challenges to medical innovation.

II. WHY A CONCERN WITH INNOVATION?

In medicine one must abandon the presupposition that customary or accepted treatments are good simply because they are customary and accepted, and critically examine the standard of care together with new alternatives. Thorough and critical scientific research is integral to reigning in the untutored human desire to ameliorate pain and suffering so that medical treatments do more good than harm. It is often difficult to know truly in medicine, however. Spontaneous remissions and natural cures, remembrance of therapeutic successes more clearly than failures, the placebo effect, and the psychology of discovery, each distort judgments of a treatment's efficacy. At times and in various ways, physicians, scientists, and patients see what they anticipate. The medical field compounds these challenges with the all too human passion to help those in need. As Nicholas Capaldi observes, ". . . a basic presupposition of the contemporary world is that the function of medicine is to improve our lives through the conquest of nature" (2005, p. 573). Yet, as the history of medicine pays witness, many interventions do more harm than benefit. Human suffering caused by ill-founded, but well-meaning, treatments has been significant. Scientific research is central to the advancement of medical practice—including the development of more efficient and effective pharmaceuticals and medical devices.

Yet, many charge that the financial interests of investigators dominate or appear to dominate the goal of obtaining objective research data for the

future treatment of patients, lower scientific standards, impact research priority, i.e., change decisions about what to study;² delay publication of important results, while researchers or others (e.g., pharmaceutical companies or universities) pursue patents and other legal protections; unconsciously distort data or lead to outright fraud; result in loss of public confidence in medicine and clinical research; and negatively affect patient care.³ The forces of for-profit pharmaceutical development and clinical medical research, commentators urge, bring on more harm than benefit. The literature does not usually regard the profit motive as leading to the wise use of resources, the protection of human subjects, or the development of high-quality and innovative pharmaceuticals and medical devices.

Market-based medical research in the United States has drawn significant recent attention in part because of a changing research environment that encourages collaboration between commercial industry and the non-profit academy. However, the ever-present calls for reform and regulation risk enacting facile and oversimplified solutions to what is a complex problem. Realistically to assess the risks involved in financing science through commercial interests one must also consider the background risks involved in a medicine bereft of the significant bolus of funds the commercial industry provides to support both patient treatment and medical progress through the development of pharmaceuticals and medical devices. Insofar as the market leads to greater innovation of life-saving and life-enhancing pharmaceuticals and medical devices than alternative strategies, then constraining product development through the restriction of financial rewards and profits, or limitations on patent protections, would hinder the pace of innovation. This would in turn lead to significant harms to both present patients and future persons.

Moreover, because of the diffusion of social and political authority the market defines social space for peaceable consensual human interaction, even amongst those who do not share the same background moral or religious beliefs and commitments. Here morality exists as the marketplace of moral ideas and moral understandings within which each peaceably pursues his own ends without sharing a common, content-full moral vision or concrete view of justice (Engelhardt, 1996). The market secures the possibility of diversity within particular countries and cities, as well as for the emergence of a worldwide network of non-geographically based communities with their own particular understandings of moral probity, including bioethics, health care policy and institutional restrictions. Fenton and Lomasky, for example, critically explore the question of whether pharmacists who object to abortion may permissibly refuse to dispense RU-486. In itself, the market does not seek morally or scientifically to resolve the abortion debate; rather, it leaves such decisions to free and consenting persons. Respecting the freedom of persons to interact with free and consenting others defaults to protecting liberties of association, contract, conscience, and religion, and thereby to protecting the

possibility of substantial moral diversity, including divergent incommensurable instantiations of the good life (e.g., Orthodox Jew, Orthodox Christian, or atheist cosmopolitan). Fenton and Lomasky conclude that within the diverse medical marketplace, absent prior contractual commitments, pharmacists are not morally required to dispense abortifacients.

As I have argued elsewhere (Cherry, 2005), while often perceived solely in terms of pursuit of profit, the market does not preclude altruistic action. Churches and other charitable organizations could play a significant role in creating health care resources for the poor. In this issue, Benjamin Hippen, a transplant nephrologist and member of the United Network for Organ Sharing Ethics Committee, explores the role that a market in human organs for transplantation might play in increasing access to a scarce medical resource. As Hippen documents, there are significant health risks associated simply with queuing for available organs. He argues that the market would create social and political space to explore for-profit opportunities and incentives for organ procurement and allocation, without thereby forbidding altruistically based incentives and opportunities. For example, one might envision individuals donating rights in organs directly to local churches, which would guarantee high quality health care for surgery and minimize other risks associated with donation. The organs could then be sold to the rich to raise funds to purchase health care, food, and medicine, or be made available for transplantation to the poor. Such opportunities could easily exist side-by-side with active organ donation programs.

Market transactions and contractual relationships draw moral authority from the consent of the participants to be bound by their agreement. The parties to the transactions, themselves, freely convey authority to the enforcement of the specified conditions. The actual agreement of actual persons creates and thereby limits the moral authority to interfere in the free interaction of consenting persons. Here, moral authority is not drawn from assertions of so-called "moral consensus," ideal theories of rational action, or even deep moral intuitions regarding consequences, human rights, or cardinal moral concerns, but rather from the agreement of the parties to collaborate. Collaborators need not agree regarding the background ranking of values or moral principles, cultural or religious assumptions; they need only affirm the content of their agreement. Nor must one presume a particular value standard or canonical order—just the recognition that collaboration is possible through agreement. Agreement or permission is the ground of the moral justification of such collaboration. Here, one does not affirm the market, or even its outcomes, as in itself good; rather, the idea of the market is the creation of social space for unencumbered personal interaction. The market is simply the result of respecting the moral authority of persons over themselves and their private property. As Fenton, Lomasky, and Hippen explore, market incentives thereby also encourage the efficient and effective procurement and dissemination of innovative health care.

III. FOR-PROFIT PHARMACEUTICAL DEVELOPMENT: A HEURISTIC FOR ASSESSING INNOVATION

In 2000, U.S. private industry devoted approximately fifty-five to sixty billion dollars to research and development, which represented more than twice that spent by the United States government. Licensing income for universities increased from approximately \$186 million in 1991 to approximately \$735 million in 1997 (Barnes and Florencio, 2002, p. 526; see also Culliton, 1981). In a survey of two hundred and nineteen university and academic institutions, the Association of University Technology Managers reported a 2002 licensing income of \$1.337 billion (AUTM, 2003, p. 28). Faculty researchers, and sometimes the academic medical centers themselves, are increasingly incorporating private start-up companies further to test and develop products based on the research conducted at the academic institution. Some 4,320 such start-up companies have been formed since 1980, with approximately 2,741 or 63.4 percent still operational (AUTM, 2003, pp. 32–33; see also Council on Governmental Relations, 1999). Over time such innovation has advanced health care science and patient care through the development of innovative pharmaceuticals, medical devices, and medical techniques.

Whereas it is commonplace to comment that such research has become a lucrative enterprise, it would be shortsighted not to note that it has also played a crucial role in demonstrating that many treatments thought to be important parts of the standard of care were ineffective or at least less effective than new alternatives. Such innovation has increased longevity while decreasing morbidity. Here one might consider advancements in material well-being represented by increasing life expectancy and decreasing infant mortality in the industrial world.⁴ Medical research requires the investment of capital, and while governments fund some innovation, with private charity providing some additional funding, charitable resources are limited, as are the governmental monies that can be devoted to basic science. As Pythagoras Petratos argues in his contribution, the market is likely the most effective means for securing capital and productively directing such investment towards innovative medicine (2005). Analyzing recent developments within the British National Health service (the Private Finance Initiative) as a heuristic, Petratos explores the advantage that private investment of financial resources and talent bring to medical innovation. Petratos provides yet another example of Capaldi's observation that innovation cannot simply be planned and straightforwardly controlled; rather, one must establish the conditions and incentives that make innovation more likely (2005).

The competitive stimulus to gain financial and professional rewards drives innovation; it possesses significant motivational force independent of a disinterested concern for civic duty and scientific curiosity. Such financial

rewards also finance research and development. In the U.S., industry finances approximately 57% of biomedical research, with the NIH funding approximately 36% and non-profit organizers 7% (Senate Joint Economics Committee, 2000, p. 9). According to the industry group Pharma, it costs approximately 10–15 years and 800 million dollars to bring a new drug to market (Pharma, 2004), and only approximately three in ten drugs will be sufficiently profitable to recoup this research and development expense.

The U.S. Senate Joint Economics Committee estimates that the direct and indirect costs of illness in the U.S. exceeds three trillion dollars annually (2000, p. i); as a consequence, effectively treating illness also directly impacts productivity and the Gross Domestic Product. In one statistical study that considered the aggregate impact of new pharmaceuticals on health care costs, hospital and surgery indicators declined most for those illnesses that had the most significant increase in pharmaceuticals prescribed. The study demonstrated that increased prescriptions and innovative pharmaceuticals reduced hospital admissions, number of hospital days, and the number of surgical procedures. It concluded that on average a one dollar increase in pharmaceutical spending translated into a three dollar and sixty-five cent reduction in overall health care expenses (Lichtenberg, 1996). Thus, while the pursuit of innovative pharmaceuticals and medical devices is an important key to decreasing morbidity costs and mortality risks, it also improves productivity and very likely reduces long-term health care expenditures.

Frank Lichtenberg argues in this issue that economic research demonstrates that research and development investment is directly impacted by the incentives offered for actual product development. Pharmaceutical companies focus most extensively on diseases that impact the developed world. It is such research that most likely to recoup the research and development investment as well as, perhaps, show a profit. "Two analyses of the relationship between pharmaceutical innovation and the burden of disease indicated that the amount of pharmaceutical innovation is positively related to the burden of disease in developed countries but not to the burden of disease in developing countries" (2005, p. 687) The challenge for creating pharmaceuticals for the developing world is that incentives for innovations are weak or nonexistent. To increase pharmaceutical innovation for diseases primarily afflicting individuals in developing countries, incentives must be created and strengthened that encourage such innovation. Lichtenberg's suggestion is the establishment of purchase commitment funds: "Under such programs, the public pays only if a successful drug is actually developed. This gives pharmaceutical firms and scientists strong incentives to self-select research projects that have a reasonable chance of leading to a drug, and to focus on developing a viable drug rather than pursuing other goals" (2005, p. 687). Such commitments would very likely spur new, competitive, and innovative research.

Voluntary partnerships between government and industry, Timothy Goodman argues, are also a very productive means to expand access to health care, while also preserving innovation incentives. "Recognizing the need for greater access to health care in developing and developed nations alike, in recent years private-sector pharmaceutical firms have established a range of voluntary initiatives to provide innovative medicines to indigent patients and build capacity for delivering health care" (2005, p. 656). He argues that there is no consensus on the existence of a right to health care, much less on what such a right would include or on whom the burden for providing it would fall. What is clear is that removing patent protections and the profit motive dramatically lowers incentives for innovation.

For example, commercial industry stepped up to fund university-based research as federal budget deficits decreased the amount of money available to universities and academic scientists. Competition for research dollars has become increasingly steep with academic medical centers no longer receiving the bulk of research dollars. Compounding difficulties, as Marcia Angell notes, reductions in reimbursements from Medicare and third-party insurance payers left academic medical centers financially strapped (Angell, 2000). In a survey of research leaders, nine out of ten reported that the pressure to treat patients, and insufficient revenue from such clinical work, poses a moderate to large problem for clinical research (Campbell Weissman, May, & Blumenthal, 2001, p. 805). This perception was greater in academic medical centers located in markets with a high degree of managed care penetration. External funding from the private sector—e.g., pharmaceutical companies and so forth—often helps to make up such shortfalls, facilitating the academic missions of research, education, and clinical care (Angell, 2000, p. 1517).

IV. CONTROLLING CONFLICTS OF INTEREST

A central challenge remains, however: controlling conflicts of interest as an issue of institutional and professional virtue and character. The usual practice is to rely on the use of scientific criteria, including publication of data and methods of investigation, through the peer review process, to sustain the practice of impartial professional scientific investigation. Still, the federal government, most states, and academic institutions have developed conflict-of-interest policies to monitor university and researcher financial entanglements. Commentators typically place conflicts of financial interest within three categories: those that are small enough that they are unlikely to affect research, those that are manageable, and those that regulations should prohibit or that preclude the researcher from engaging in the research. While the design of clinical trials typically avoids fraud—e.g., random assignment to various treatment arms; that the trial is double blinded, i.e., that neither

the researcher nor the patient know which treatment the patient is receiving; that independent groups often gather and analyze data—as Baruch Brody has pointed out, there is still opportunity for the investigator’s secondary interests to affect the study’s design, conduct, and data analysis (Brody, 1996, pp. 407–417; see also Lo, Wolf, & Berkeley, 2000).⁵

The most popular strategy for reducing conflicts of interest has been the disclosure of financial holdings and arrangements that may present potential conflicts to the institutional review committee, department chair, university official, or legal counsel. At times, even public disclosure is specified, such as in public presentations or publication of research. Policies frequently prohibit research, if such economic entanglements exceed a certain threshold amount, usually \$10,000. Disclosure requirements generally apply to the equity holdings, stock, and stock options, as well as income from salary, honoraria, and consulting fees. Such reporting usually applies to the researchers as well as to the holdings of their spouses, and dependent children, although some institutions request disclosure from parents, siblings and adult children as well.⁶ Other methods include oversight of the research, either by a supervisor or a committee, divestiture of financial entanglements, or modification of research. Universities have at times assigned a different faculty member to lead a research project or requested that the faculty member for whom there exists a potential conflict take a leave of absence (Cho, Shohara, Schissel, Drummond, 2000).

The federal Office of Research Integrity of the U.S. Department of Health and Human Services guidelines for managing conflicts of interest and promoting objectivity in research, for example, requires that all institutions wishing to do research with public health service funds maintain and enforce a written conflict of interest policy. Institutional responsibility includes collecting financial disclosure statements from each investigator of interests that would reasonably be assumed to constitute a conflict of interest, and to update such disclosures periodically during the period of award. Such conflicts might include “anything of monetary value, including but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights)” (ORI, 2000). Researchers are not required to disclose equity, salary, and other financial arrangements that do not exceed \$10,000.⁷

Similarly, the Association of American Universities task force on conflicts of interest recommended that universities assess the adequacy of their procedures for managing conflicts of interest, so that risks to the objectivity of research could be minimized. They urged that universities, together with their research partners—commercial industry or governmental agencies—understand themselves as fully accountable for the design and integrity of their research. Institutionally, the disclosure process allows a university to

assess and monitor such concerns. Many have developed review committees to assess potential conflicts, consider costs and benefits, and make recommendations regarding appropriate actions. The review committee judges, for example, whether to modify the financial arrangements, to establish a process to monitor the integrity of the research, to establish procedures to insulate financial decision-making from research decision-making, or to recommend that the research be prohibited (Hasselmo, 2002, p. 426).

Insofar as the protocol involves research on human subjects, the institutional review board (IRB) must first approve the study. IRBs are charged with ensuring that research is performed safely; assessing the protection of human subjects, and that the study meets the institution's standards for scientific conduct. IRBs often also review adverse events. Importantly, this process has led to another area of concern, namely conflicts of interest in the composition of IRBs at academic medical centers and in the use of commercial or independent IRBs. Whereas the intent of the IRB is to harmonize the interests of clinical researchers with the protection of research subjects, the concern is that the IRB's primary function has apparently become the protection of the institution rather than the research subjects (Annas, 1991). IRB membership is typically almost exclusively researchers from the particular institution, who therefore have a vested interest in the ongoing success of the institution. As Leslie Francis states the concern: members of the IRB may have "interests in job security; interests in the prestige or research reputation of the institution in which the IRB is located; commitments to scientific colleagues or to the advancement of technological medicine" (Francis, 1996, p. 422; see also Slater, 2002). Moreover, grant applications may include overhead reimbursements, payments for patient care, and so forth, which for a non-profit academic institution may be important sources of income. Similarly, members may be interested in the overall financial status of the for-profit or not for-profit entity. The IRB is likely aware that the success of particular protocols may attract other profitable studies to the institution. Members may be friends, mentors, or colleagues of the investigators. At times, IRB members may informally coach the primary investigators on a research project regarding how best to phrase the protocol so that it will be approved. Also, members may bring a particular social, political or moral agenda with them to the IRB; for example, they may be in favor of unfettered access to abortion or to unrestricted research on embryonic stem cells, and thus be more likely to approve even poorly designed studies that support such moral claims.

Similarly, insofar as certain research protocols or scientific theories are seen as supportive of particular political ideologies or socio-political movements, this may provide sufficient reason for some to fund, give credence to, or politically to support such research. For example, pro-abortion activists publicly welcomed the publication of a review study concluding that it is unlikely that fetuses feel pain prior to the third trimester (Lee et al., 2005).

At the same time, pro-life activists criticized the review as biased and poorly conducted. Even external lay members may bring a moral, social, or political agenda with them to IRB discussions.⁸

Possible solutions have included a national or central review board to provide oversight of the local review boards (Christian et al., 2002) and commercial independent review boards (Forster, 2002; Lemmens & Freedman, 2000). In each case, however, the central challenges appear to be unaddressed. Since independent review boards are typically financed through fee-for-service review, they face similar financial conflicts of interest vis-à-vis the institution that is paying for the review (see e.g., Lemmens & Thompson, 2001; Barnes & Florencio, 2002; Cave & Holm, 2002). Moreover, both central and independent review boards may bring a moral or political agenda to their review of protocols.

Consider also the publication of results. Many scientific journals require that researchers disclose their funding sources as part of the manuscript review process, although standards vary regarding the disclosure of such information with the publication of the article. Some, such as the *British Medical Journal*, disclose funding sources; others, such as *Nature*, do not. Here the common view is that scientists should have easy access to the investigational data of scientific inquiry. Sponsors of every type of study have some agenda that might possibly affect study design or data interpretation and presentation. As a result, if journals suppress certain studies because of their funding sources then the scientific community may reach false or distorted conclusions when considering a body of research. Journals usually rely on the use of a body of experts in the field of study, who conduct blinded peer review, to sustain the practice of professional scientific investigation.

A related problem is the under-reporting of negative findings. Insofar as early results are negative, researchers—whether in the academy or commercial industry—may simply halt the trials. If unsuccessful trials typically go unpublished, this may lead to an unbalanced set of information for other scientists and practicing physicians. Commentators have reported that studies funded by pharmaceutical companies are 8 times less likely to report unfavorable qualitative conclusions than non-profit funded studies and 1.4 times more likely to reach positive qualitative conclusions (Friedberg et al., 1999). Such findings do not impeach the quality of the research but they do suggest the need for a larger body of evidence available for clinical researchers to explore. In response to such concerns, in September 2004, the International Committee of Medical Journal Editors announced that their representative journals—including *The New England Journal of Medicine*, *The Lancet*, and *The Journal of the American Medical Association*—established a policy that if companies hope to publish the results of their clinical trials in these journals that they must register the trial in a public database before it begins. Investigators are required to describe the condition the trial

aims to treat, the drug to be tested and the methods for data interpretation, such as specification of the standards that will measure success or failure. The announced goal is to reduce the selective reporting of trials (DeAngelis et al., 2004). In response, the Pharmaceutical Research and Manufacturers Association (Pharma) created a public database to hold the results of all controlled clinical trials completed since 2002 for its members' drug products approved in the U.S. (www.clinicalstudyresults.org).

A central question, though, remains: How far must one go to divest oneself from other interests to preserve the objectivity of research? Should one consider the current holdings of one's mutual funds? Should one accept governmental funds acquired through coercive taxation? If one utilizes governmental funding to conduct research on human embryos, then all citizens are complicit in what many believe to be gravely evil. Commercial and industry private funding sources possess the virtue of only utilizing those who choose to collaborate.

V. CONCLUDING THOUGHTS

How much of one's life must be disclosed to preserve scientific professionalism? In addition to financing sources and commercial entanglements, political, moral, and other epistemic and non-epistemic background commitments often play roles in surreptitious or unconscious distortion of scientific data to acquire research funding, advance one's social standing in the scientific community, or further particular socio-political goals. The protection of careers and the furtherance of other professional and social goals may at times take precedence over scientific accuracy (Bell, 1992; O'Toole, 1991). Indeed, it would be shortsighted to overlook the pervasive and subtly nuanced conflicts that desire for renown, professional advancement, and moral worldview represent (Shimm & Spece, 1996). Given the impact of such social and political prior commitments on the interpretation and significance of scientific findings, as well as on the structure and goals of science, governmentally supported rather than market-based, medical research is no guarantee of truth-seeking behavior.

Further study regarding the impact of researcher religious background, or lack of personal religious belief, political viewpoints, voting habits, or social agendas, should be fruitful for understanding the ways in which such background worldviews subtly affect or unconsciously distort the way that one designs studies, collects, and interprets data. Moreover, a central question is whether the politics of governmental research or the market is better at identifying and accounting for such conflicts of interest, while also creating the conditions most likely to generate significant and creative medical innovation, whether in pharmaceutical development or surgical techniques, new sources of scarce medical resources, or access to controversial medical

services. This issue of *The Journal of Medicine and Philosophy* seeks to extend and deepen this on-going discussion.

NOTES

1. As Rosenberg and Birdzell argue: "The diffusion of authority to initiate innovations served also as the West's way of guarding against a chronic menace to innovative change—the interest of the status quo in suppressing innovation. An innovation will seldom be authorized or financed by government or corporate officials whose careers would be adversely affected by the success of the proposal" (2002, p. 22).

2. Here the concern is that industry support may be shifting research emphasis from basic research to clinical research in the hope of product development with more immediate commercial suitability (Blumenthal et al., 1996; Blumenthal et al., 1986; Rabino, 1998)

3. Lori B. Andrews reports that pharmaceutical companies at times pay physicians millions of dollars a year for enrolling patients in studies, with potentially poor results. "Doctors from one field enroll their patients in drug trials in another field. For example, asthma specialists run studies on psychiatric medications. Patients who are not appropriate candidates for a study have received drugs for conditions they did not have, sometimes without even being told that the drugs were experimental. That not only subjected them to unnecessary risks, which is malpractice, but also compromised the study results" (Andrews, 2000, p. B4).

4. Consider the following changes in life expectancy at birth, comparing life expectancy in 1960 to life expectancy in 2002: United States: women 73.1 vs. 79.8 years; men 66.6 vs. 74.4; Turkey: women 50.3 vs. 70.9; men 46.3 vs. 66.2; Greece: women 72.4 vs. 80.7; men 67.3 vs. 75.4; Mexico: women 59.2 vs. 77.1; men 55.8 vs. 72.1.

Also consider infant mortality per 1000 live births, again comparing 1960 to 2002: United States: 26 vs. 6.8; Turkey: 189.5 vs. 38.3; Greece: 40.1 vs. 5.9; Mexico: 79.3 vs. 20.1.

5. Brody identifies eight possible sources of clinical trial design that can provide opportunity for those with a conflict of interest to promote a favored treatment. These included decisions regarding:

- 1) "Which treatments will be tested in the proposed trial, and which will not be tested?"
- 2) "Will there be a placebo control group as well, or will the treatments be tested against each other or against some active control group?"
- 3) "What will be taken as the favorable endpoint (the result constituting the evidence of the dangerousness of the treatment)?"
- 4) "What will be the condition for inclusion or exclusion of subjects from the trial?"
- 5) "What provisions will be made for informed consent?"
- 6) "Under what conditions will the trial be stopped or modified because there have been too many adverse endpoints in one or more arm of the trial or because the preliminary data have shown that one of the treatments is clearly the most efficacious treatment?"
- 7) "Under what conditions will the trial be stopped or modified because of the newly available results of other trials?"
- 8) "Which patients who meet the criteria will actually be enrolled, and which ones will not?" (Brody, 1996, p. 409).

Those with a conflict of interest might choose in ways, even if unconsciously, that lead to flaws in the study design rather than to flawed data.

6. The Association of American Universities task force on conflict of interest adopted the following definition of individual conflict of interest: "The term conflict of interest in science refers to situations in which financial or other personal considerations may compromise, or have the appearance of compromising, an investigator's professional judgment in conducting or reporting research. The bias such conflicts may conceivably impart not only affects collection, analysis, and interpretation of data, but also the hiring of staff, procurement of materials, sharing of results, choice of protocol, involvement of human participants, and the use of statistical methods. The task force determined that researchers were to disclose financial information that might pose a conflict of interest to the institution, to publications, in oral presentations, to federal agencies, and as part of the human participant review process" (Hasselmo, 2002, p. 424).

The task force also identified conflicts of interest at the institutional level, including university equity holdings, royalty arrangements or licensing agreements, and the direction of research, as well as university officials who possess financial interests with industry partners. They defined institutional conflicts of interest as: "An institutional financial conflict of interest may occur when the institution, any of its senior management or trustees, or a department, school, or other sub-unit, or a related organization (such as a university foundation) has an external relationship or financial interest in a company that itself has a financial interest in a faculty research project. Senior managers or trustees may also have conflicts when they serve on the boards of (or otherwise have an official relationship with) organizations that have significant commercial transactions with the university. The existence (or appearance) of such conflicts can lead to actual bias, or suspicion about possible bias, in the review or conduct of research at the university. If they are not evaluated or managed, they may result in choices or actions that are incongruent with the missions, obligations, or the values of the university."

7. Section §50.605 Management of conflicting interests, states that "The designated official(s) must: Review all financial disclosures; and determine whether a conflict of interest exists and, if so, determine what actions should be taken by the institution to manage, reduce or eliminate such conflict of interest. A conflict of interest exists when the designated official(s) reasonably determines that a Significant Financial Interest could directly and significantly affect the design, conduct, or reporting of the PHS-funded research. Examples of conditions or restrictions that might be imposed to manage conflicts of interest include, but are not limited to:

- (1) Public disclosure of significant financial interests;
- (2) Monitoring of research by independent reviewers;
- (3) Modification of the research plan;
- (4) Disqualification from participation in all or a portion of the research funded by the PHS;
- (5) Divestiture of significant financial interests; or
- (6) Severance of relationships that create actual or potential conflicts."

8. According to Francis (1996, p. 429), lay members are most frequently clergy or lawyers. Moreover, they tend to have been appointed by high level institutional officials with whom they are associated, either through friendship or other official relationship.

REFERENCES

- Andrews, L.B. (2000, March 10). Money is putting people at risk in biomedical research. *Chronicle of Higher Education*, 46(27), B4.
- Angell, M. (2000). Is academic medicine for sale?. *The New England Journal of Medicine*, 342(20), 1516–1518.
- Annas, G. (1991). Ethics committees: From ethical comfort to ethical cover. *Hastings Center Report*, 21, 18.
- Association of University Technology Managers. (2003). *The AUTM Licensing Survey: FY 2002*. [On-line]. Available <http://www.autm.net>. Accessed: August 15, 2005.
- Barnes, M., & Florencio, P. (2002). Investigator, IRB and institutional financial conflicts of interest in human-subjects research: Past, present and future. *Seton Hall Law Review*, 32, 525–561.
- Bell, R. (1992). *Impure science*. New York: John Wiley & Sons, Inc.
- Berlinguer, G., & De Castro, L. (2003, June 13). Report of the IBC on the possibility of elaborating a universal instrument on Bioethics. International Bioethics Committee, United Nations, Educational, Scientific and Cultural Organisation, Paris, France.
- Blumenthal, D., Campbell, E.G., Causino, N., & Louis, K.S. (1996). Participation of life-science faculty in research relationships with industry. *New England Journal of Medicine*, 335, 1734–1739.

- Blumenthal, D., Gluck, M. Louis, K.S., Stoto, M.A., & Wise, A. (1986). University industry research relationships in biotechnology: Implications for the university. *Science*, 232, 1361–1366.
- Brody, B.A. (1996). Conflicts of interests and the validity of clinical trials. In R.G. Spece, Jr., D.S. Shimm & A. Buchanan (eds.), *Conflicts of interest in clinical practice and research* (pp. 407–417). New York: Oxford University Press.
- Campbell, E.G., Weissman, J.S., May, E., & Blumenthal, D. (2001). Status of clinical research in academic health centers: Views from research leadership. *Journal of the American Medical Association*, 286(7), 800–806.
- Capaldi, N. (2005). The ethics and economics of healthcare. *The Journal of Medicine and Philosophy*, 30(6), 571–578.
- Cave, E., & Holm, S. (2002). New governance arrangements for research ethics committees: Is facilitating research achieved at the cost of participants' interest. *Journal of Medical Ethics*, 28, 318–321.
- Cherry, M. (2005). *Kidney for sale by owner: Human organs, transplantation, and the market*. Washington, DC: Georgetown University Press.
- Cho, M., Shohara, R., Schissel, A., & Drummond, R. (2000). Policies on faculty conflicts of interest at US universities. *Journal of the American Medical Association*, 284(17), 2203–2208.
- Christian, M., Goldberg, J., Killen, J., Abrams, J., McCabe, M., Mauer, J., & Wittes, R. (2002). A central institutional review board for multi-institutional trials. *New England Journal of Medicine*, 346(18), 1405–1408.
- Council on Governmental Relations. (1999). The Bayh-Dole Act: A guide to the law and implementing regulations. [On-line]. Available www.ucop.edu/ott/bayh.html. Accessed: August 15, 2005.
- Culliton, B.J. (1981). Biomedical research enters the marketplace. *New England Journal of Medicine*, 304, 1195–1201.
- DeAngelis, C.D., Drazen, J.M., Frizelle, F.A., Haug, C., Hoey, J., Horton, R., Kotzin, S., Laine, C., Marusic, A., Overbeke, A.J., Schroeder, T.V., & Van der Weyden, M.B. (2004). Clinical trial registration: A statement from the international committee of medical journal editors. *Journal of the American Medical Association*, 292(11), 1363–1364.
- Engelhardt, H.T., Jr. (1996). *The foundations of bioethics*, 2nd ed. New York: Oxford University Press.
- Fenton, E., & Lomasky, L. (2005). Dispensing with liberty: Conscientious refusal and the "morning after pill." *The Journal of Medicine and Philosophy*, 30(6), 579–592.
- Forster, D. (2002). New directions in human subject research: Looking beyond the academic medical center: Independent Review Boards. *Seton Hall Law Review*, 32, 513–523.
- Francis, L. (1996). IRBs and conflicts of interest. In R.G. Spece, Jr., D.S. Shimm & A. Buchanan (eds.), *Conflicts of interest in clinical practice and research* (pp. 418–436). New York: Oxford University Press.
- Friedberg, M., Saffran, B., Stinson, T., Nelson, W., & Bennett, C. (1999). Evaluation of conflict of interest in economic analyses of new drugs used on oncology. *Journal of the American Medical Association*, 282(15), 1453–1457.
- Goodman, T. (2005). Is there a right to health?. *The Journal of Medicine and Philosophy*, 30(6), 643–662.

- Hasselmo, N. (2002). Individual and institutional conflict of interest: Policy review by research universities in the United States. *Science and Engineering Ethics*, 8(3), 421–427.
- Hippen, B. (2005). In defense of a regulated market in kidneys from living vendors. *The Journal of Medicine and Philosophy*, 30(6), 593–626.
- Lee, S., Ralston, H.J.P., Drey, E.A., Partridge, J.C., & Rosen, M.A. (2005). Fetal pain: A systematic multidisciplinary review of the evidence. *Journal of the American Medical Association*, 294, 947–954.
- Lemmens, T., & Freedman, B. (2000). Ethics review for sale? Conflict of interest and commercial research review boards. *Milbank Quarterly*, 78(4), 547–583.
- Lemmens, T., & Thompson, A. (2001). Non institutional commercial review boards in North America. *IRB: Ethics and Human Research*, 23(2), 1–12.
- Lichtenberg, F.R. (1996). The effect of pharmaceutical utilization and innovation on hospitalization and mortality. *National Bureau of Economic Research Working Paper*, 541, 8.
- Lichtenberg, F.R. (2005). Pharmaceutical innovation and the burden of disease in developing and developed countries. *The Journal of Medicine and Philosophy*, 30(6), 663–690.
- Lo, B., Wolf, L., & Berkeley, A. (2000). Conflict-of-interest policies for investigators in clinical trials. *The New England Journal of Medicine*, 343(22), 1616–1620.
- Office of Research Integrity. (2000). Responsibility of applicants for promoting objectivity in research for which PHS funding is sought. 42 C.F.R. 50, 601–607.
- O'Toole, M. (1991). Magot O'Toole's record of events. *Nature*, 351, 183.
- Petratos, P. (2005). Does the private finance initiative promote innovation in health-care? The case of the British National Health Service. *The Journal of Medicine and Philosophy*, 30(6), 627–642.
- Pharma. (2004). The issues: intellectual property. [On-line]. Available: www.pharma.org. Accessed: 6/24/04.
- Rabino, I. (1998). Societal and commercial issues affecting the future of biotechnology in the United States: a survey of researchers' perceptions. *Naturwissenschaften*, 85, 109–116.
- Rosenberg, N., & Birdzell, L.E., Jr. (2002). How the West grew rich: The economic transformation of the industrial world. In E. Heath (ed.), *Morality and the market: Ethics and virtue in the conduct of business* (pp. 10–24). New York: McGraw-Hill.
- Senate Joint Economics Committee (2000) *The benefits of medical research and the role of the NIH*, May 2000. Available <http://jec.senate.gov>.
- Shimm, D.S., & Spece, R.G., Jr. (1996). An introduction to conflicts of interest in clinical research. In R.G. Spece, Jr., D.S. Shimm & A. Buchanan (eds.), *Conflicts of interest in clinical practice and research* (pp. 361–375). New York: Oxford University Press.
- Slater, E.E. (2002). IRB reform. *New England Journal of Medicine*, 346(18), 1402–1404.