Science on Trial by Sheldon Krimsky

Conflicts of interest jeopardize scientific integrity and public health

The notion that scientists pursuing knowledge about the physical or biological universe could have competing interests that might affect their objectivity is, for them, a hard pill to swallow. Most scientists still do not believe that ethical concerns over conflicts-of-interest apply to them. They view this notion as a legal construct designed to ensure that those who serve in our government are not beholden to special interests, especially their own financial self-interest.

Scientists typically believe that they are accountable to a system of norms in which the pursuit of truth and objectivity are the sole considerations accepted by their profession. Whatever other interests they may have in the subject matter of their research are believed to be eclipsed by, and subservient to, the singular objective of their inquiry, namely, the unfettered search for certifiable knowledge. While this is a widespread belief, it is not based on empirical evidence. Practicing scientists are least likely to know whether their conflicting financial interests affect the outcome of their research. Prior to the 1980s it was rare to see the media linking the term "conflict of interest" to scientists. Ethics in public life focused largely on the Watergate Scandal and the subsequent passage of the Ethics in Government Act of 1978.

Academic science, however, became intensely commercialized during the last quarter of the twentieth century, a result of complex events including new laws, court decisions, executive orders, and growing incentives among research universities for partnering with the private sector. During this time, American science policy was developed to establish closer linkages between academic science/medicine and for-profit companies. It was alleged by leading science policy experts that creating corporate-university partnerships was a triple-win strategy. Universities and their faculty would benefit from the new infusion by industry of research and development (R&D) funds and expanding research programs. Industry would thereby gain access to new knowledge and could exploit the low overhead and relatively inexpensive labor of academic research facilities. Finally, society could reap the benefits of accelerated technology transfer bringing new products to market, including therapeutic solutions to medical problems. Without the new incentives for corporate-university linkage, it was alleged that scientific discoveries would remain dormant, collecting dust in professional journals, while the opportunities to turn discovery into useful applications disappeared. However, the new policies that linked science to economic development neglected to consider their effects on the social system of science and its relationship to public trust.

Investigative journalists at the national and regional daily newspapers began to document dozens of instances in which biomedical scientists at America's elite universities and non-profit institutions were evaluating therapeutic products in which they had an equity interest. In many of these cases, the story became newsworthy because the products proved to be hazardous or ineffective, or scientists violated federal or university regulations.

Medical journals were the earliest barometer of discomfiture with the linkages between corporate interests and scientific research at non-profit institutions. In 1984, *The New England Journal of Medicine* (NEJM) became the first of the leading medical journals to require authors of original research articles to disclose any financial ties they had with companies.[1] Since then, many more medical journals have adopted financial disclosure requirements for their authors. Some, including *NEJM*, went further and prohibited authors who had conflicts of interest from writing reviews and commentaries. By 1995, after several congressional hearings, two major federal granting agencies, the National Science Foundation and the National Institutes of Health, issued what were effectively disclosure guidelines for conflicts of interest of grant applicants. The final version of the federal rules gave individual institutions the authority to manage conflicts of interest. There were no incentives to prohibit such conflicts among members of science and medical faculties and no standards were issued that universities were required to meet. The result was a patchwork of institutional policies, which essentially approached conflict of interest as a form of "political correctness."

The poster child for scientific conflict of interest is the tobacco industry. Reports from the World Health Organization (WHO) and documents released during discovery from the multi-state tobacco litigation showed an industry that bought its research from academic centers and well-financed scientists to further its interests in obfuscating studies linking cigarettes to lung cancer and other diseases and in subverting the WHO's efforts to control tobacco use. Among the activities used to create its own science, the tobacco industry secretly funded speakers at WHO conferences, created quasi-scientific front organizations, established an ostensibly independent coalition of scientists, rewarded scientists at prestigious universities for critiquing epidemiological and toxicological studies on tobacco smoke, and held scientific symposia to support

WHAT IS A CONFLICT OF INTEREST

BY DAVID RESNIK

Scientists, especially clinical investigators, may have financial or personal interests that undermine their ability to perform their primary ethical or legal obligations. Below are some of the situations that can create conflicts of interest or apparent conflicts of interest for individuals involved in research:

- A scientist is the president of a company he started, and that is also sponsoring his research;
- A scientist is on the board of directors of a company which sponsors his research;
- A scientist owns a significant amount of stock or equity in a company that sponsors his research;
- A scientist receives significant gifts, honoraria, or consulting fees from a company which sponsors his research;
- A scientist holds patents on a product which he is testing on human subjects.

Almost all of the controversies regarding conflicts of interest in science have focused on the conflicts that individuals face when they conduct, review, or disseminate research. In the last few years, however, controversy has shifted from individuals toward research institutions, such as universities and academic medical centers. Research institutions, like individuals, have financial and other interests. Research institutions also make decisions and have ethical and legal obligations to students, faculty, patients, and to the public. A research institution could therefore have a conflict of interest when it has interests that undermine its ability to meet its principal ethical or legal obligations. An institution could also have a conflict of interest if someone in a position of leadership in the institution has a financial or personal interest that could undermine the institution's ability to meet its obligations. The following situations could create real or apparent conflicts of interest for institutions involved in research:

- A university owns a patent on a new drug which is being tested on patients at its medical center.
- A university official owns a patent on a new drug which is being tested on patients at the university medical center.
- A university owns stock in a company which is sponsoring research on campus.
- The chair of an institutional review board overseeing research on human subjects is a paid consultant for a drug company which conducts clinical studies at the chair's institution.
- A university receives a large donation from a drug company to build or improve a research center, while the company is sponsoring clinical trials at that university's medical center.

David B. Resnik is Professor of Medical Humanities at The Brody School of Medicine at East Carolina University and Director of New Programs for the Bioethics Center at University Health Systems of Eastern North Carolina. He is also the Associate Editor of the journal Accountability in Research *and is on the Board of Directors for the North Carolina Association for Biomedical Research.*

pro-industry positions.[2] A similar strategy of industry-corrupted science continued after public health scientists began linking second-hand smoke and lung cancer.

The next obvious question was whether the tobacco industry was idiosyncratic. Was it possible that other industry-sponsored research biased the outcome of scientific and medical studies? In other words, is there a funding effect in science?

A series of studies published in the past fifteen years provides support for the hypothesis that privately-funded studies of commercial products tend to yield results weighted in favor of the sponsor's interests compared to similar studies of those products by non-profit institutions. One of the most elegant of these studies was published in the *New England Journal of Medicine* by a Canadian research team. The researchers began with the question: Is there an association between authors' published positions on the safety of a drug and their financial relationships with a pharmaceutical company? They focused the study on a class of drugs called "calcium channel antagonists" (CCAs), which are used to treat hypertension. After identifying medical journal articles on CCAs published between March 1995 and September 1996, each article was classified as being supportive, neutral or critical with respect to the drug. The investigators then surveyed the authors of the articles on whether they received funding from pharmaceutical companies that manufactured CCAs.

The study found that 96 percent of authors classified as supportive of CCAs had financial relationships with the manufacturers, while only 37 percent of the critical authors and 60 percent of the neutral authors had such relationships. The authors of the *NEJM* study wrote that their results demonstrate "a strong association between authors' opinions about the safety of calcium channel antagonists and their financial relationships with pharmaceutical manufacturers."[3] And as more studies were done, the funding effect in science seems to gain in credibility and significance. A study published in the *British Medical Journal* on conflicts of interest and investigator findings, drawn from articles in that journal, found that "authors' conclusions were significantly more positive towards the experimental intervention in trials funded by for-profit organizations alone compared with trials without competing interests."[4]

Finally, in a meta-study of 37 original research articles, 23 of which addressed the impact of financial relationships on the outcome of research, the authors concluded: "evidence suggests that the financial ties that intertwine industry, investigators, and academic institutions can influence the research process. Strong and consistent evidence shows that industry-sponsored research tends to draw pro-industry conclusions...that industry-sponsored studies were significantly more likely to reach conclusions that were favorable to the sponsor than were nonindustry studies."[5]

The effects of conflict of interest on science are not only found in tobacco and medicine. Increasingly, reports reveal that chemical companies seek influence over the sciences of

toxicology and epidemiology. In February 2002, thirty scientists co-signed a letter to the Director General of the WHO stating that there was evidence of "inappropriate corporate influence in the decisions of the International Agency for Research on Cancer (IARC)," the cancer research affiliate of WHO. The signatories cited instances in which scientists who promoted the downgrading of classification of certain carcinogens came from corporations producing those chemicals.[6]

In another public letter, forty-five prominent scientists and physicians cited the industry bias of the *Journal of Regulatory Toxicology and Pharmacology*, the official publication of the International Society for Regulatory Toxicology and Pharmacology. The letter requested that the Society reduce the influence of industry representatives on the editorial board and adopt a financial disclosure policy for authors and editors.

The distorting effect of vested-interest science is most visible in relation to science advisory committees [*see sidebar on next page for more examples*]. In 1998, there were nearly 1,000 advisory committees spread across fifty-five federal departments. Approximately one-third of the individuals serving on those committees were appointed by the Department of Health and Human Services.

WHAT CAN BE DONE TO REGAIN THE INTEGRITY OF ACADEMIC SCIENCE AND MEDICINE AT A TIME WHEN TURNING CORPORATE AND BLURRING THE BOUNDARIES BETWEEN NON-PROFIT AND FOR-PROFIT INSTITUTIONS IS IN SUCH FAVOR?

The U.S. Federal Advisory Committee Act (18 U.S.C. Sec. 203) prohibits a person from serving on an advisory committee if that individual has a financial interest in the subject matter under discussion and if the particular matter will have a "direct and predictable effect on that interest." That is the first of two rules. The second rule is that Rule #1 can be waived. And waivers for advisory committee members are given quite liberally. In 2000 an investigative report published in *USA Today* revealed that "more than half of the experts hired to advise the government on the safety and effectiveness of medicine had financial relationships with the pharmaceutical companies that will be helped or hurt by those decisions."[7]

In response to the rising tide of such conflicts of interest, scientific journals, government, universities and professional societies are looking toward transparency as the universal antidote. However, the trend toward disclosure rather than prevention unfortunately will legitimate the multi-vested roles of scientists and their institutions. And if conflicts of interest in the funding of science continue to grow, then we can anticipate systematic skewing of the research agenda and biasing of research results toward the interests of its for-profit sponsors and scientists who hold equity in companies that fund their research.

Two other changes are likely as the partnership between corporations and universities expands. First, the public's trust in the integrity of academic science will decline. Universities and their faculty will be viewed as just another set of special interest groups. This was the reaction of the citizenry toward some members of the University of Pennsylvania faculty after the death of Jesse Gelsinger, who volunteered as a subject in a human gene therapy experiment. When it became known that the chief clinical investigator of the trial and the University of Pennsylvania had equity in a biotechnology company seeking to profit from the experiment, the Gelsinger family sued the university. One of the grounds for the suit was the financial conflict of interest held by the university and the clinical investigator.

In the aftermath of the Gelsinger case, the Department of Health and Human Services (DHHS), under the leadership of DHHS Secretary Donna Shalala, held hearings on whether the financial interests of clinical investigators should be listed on informed consent information given to prospective candidates for clinical trials. In a draft guidance document DHHS suggested that researchers involved in clinical trials disclose any financial interests they have to Institutional Review Boards that monitor other ethical issues and possibly to the patients who are deciding whether they plan to participate as human subjects. Leading scientific and medical associations, including the Federation of American Societies of Experimental Biology (FASEB) and the American Association of Medical Colleges (AAMC), opposed the idea of such a guidance document for clinical trials, arguing that it would over-regulate medical research without contributing to the safety of patients.

With millions of Americans participating in over 40,000 clinical trials in 2002, about 4,000 of which are supported by the National Institutes of Health, research scientists and the companies sponsoring those trials are concerned that additional disclosure requirements, which do not have a direct bearing on the safety or benefits of the trials, would create unnecessary impediments to attracting human volunteers. Yet the decision to volunteer in a medical experiment can be one of the most important life choices a person can make. Why shouldn't prospective volunteers know everything relevant to the trust relationship they are asked to develop with the clinical investigator?

CONFLICTS OF INTEREST: PATTERNS

The chart below is a sampling of the extensive 'revolving door' relationships which exist between industry and government in agriculturual biotechnology.

While the names of individuals listed are publicly available (and easily found) they have been omitted here. What matters is not identifying particular individuals, but recognizing the larger pattern.

Role in Industry	Currentor Recent Federal Government Role
Monsanto's former Vice President of Government and Public Affairs.	EPA Deputy Administrator
Member of Board of Directors of Calgene, Inc.	U.S. Secretary of Agriculture
Member of Board of Directors of 12 companies; Science Advisory Board Member for 30 companies.	FDA Science Advisory Board Chair
Monsanto's lead lawyer at King & Spaulding; former Monsanto Vice President for Public Policy.	FDA Deputy Commissioner for Policy (1991-1994); USDA Food Safety and Inspection Administrator (1994-1996)
Vice President of Public Policy for Monsanto.	USDA Deputy Undersecretary for Food Safety
Chairman of Board of Directors of American Soybean Association; Chair of American Oilseed Coalition.	Member of USDA Advisory Committee on Agricultural Biotechnology
Executive Vice President of DuPont; former CEO of Pioneer Hi-Bred International.	Member of USDA Advisory Committee on Agricultural Biotechnology
Vice President of Corporate Relations at General Mills, Inc.	Member of USDA Advisory Committee on Agricultural Biotechnology
Vice President of Administration and Public Affairs at Syngenta Biotechnology, an agricultural biotechnology company.	Member of USDA Advisory Committee on Agricultural Biotechnology
President of Ag Producer Services at Cargill, Inc.	Member of USDA Advisory Committee on Agricultural Biotechnology
Microbial Biotechnologist at Monsanto.	EPA Research Ecologist, Plant Biotechnology, Western Ecology Division

What can be done to regain the integrity of academic science and medicine at a time when turning corporate and blurring the boundaries between non-profit and for-profit institutions is in such favor? We should perhaps begin by reexamining the principles on which universities are founded and the importance of protecting those principles from erosion and compromise for the sake of amassing larger budgets and providing more earning potential for faculty members. Three principles should guide our approach:

• The roles of those who produce knowledge in academia and those stakeholders who have a financial interest in that knowledge should be kept separate and distinct.

• The roles of those who have a fiduciary responsibility to care for patients while enlisting them as research subjects and of those who have a financial stake in the development of specific pharmaceuticals, therapies, or other products, clinical trials, or facilities contributing to patient care should be kept separate and distinct.

• The roles of those who assess therapies, drugs, toxic substances, or consumer products and of those who have a financial stake in the success or failure of those products should be kept separate and distinct.

The public's trust in the integrity of academic science and medicine is destroyed when these roles are conflated. It is important that universities not lose their special status as institutions where the pursuit of knowledge is not compromised by even the appearance of conflict of interest. ■■■

Sheldon Krimsky *is a professor in the Department of Urban & Environmental Policy & Planning at Tufts University. He is the author of* Science in the Private Interest, *published this year by Rowman & Littlefield.*

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