Testimony

Before the

The Institute of Medicine Panel on

Conflict of Interest in Medical Research, Education, and Practice

Merrill Goozner

Director, Integrity in Science Project
Center for Science in the Public Interest

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Conflicts of interest in medicine are widespread and have negative consequences. Regulation of conflicts of interest has relied on disclosure, which is unevenly defined and poorly enforced. The Institute of Medicine should encourage the medical profession to adopt a new standard for regulating conflicts of interest in medicine. Disclosure rules must be rigorously defined, uniform, and universally enforced. Moreover, they should be reserved for managing the inevitable involvement of medical scientists in the private sector’s efforts to generate new technology and clinical evidence. But the profession should carve out a totally independent sphere where scientists free from conflicts of interest review the evidence, author clinical practice guidelines and evaluate technologies for regulatory purposes. The profession should also reject industry gifts that can influence medical decisions and free itself from dependence on industry funds for continuing medical education. The IOM should play a leadership role by adopting its own more rigorous rules on conflict of interest.

Background

There isn’t a corner of modern medicine unaffected by conflicts of interest. Private industry is the dominant player in applied medical research and the dissemination of results. The share of clinical research funded by industry has doubled over the past 30 years and now accounts for well over 60 percent of all clinical trials. More than a third of institutional review board members overseeing research have ties to industry. Advertising, sponsored supplements, and reprint sales to pharmaceutical firms are major sources of medical journal revenue.

The drug industry and other private firms with a financial stake in how medicine is delivered routinely supplement many physicians’ incomes. Nearly three in ten practicing physicians consult for or speak on behalf of pharmaceutical companies or enroll their patients in industry-sponsored clinical trials. Industry expenditures for direct-to-physician marketing are now well over $50 billion a year. More than 90 percent of physicians report having taken small gifts from the pharmaceutical industry like free food and drug samples. A recent estimate suggests one in ten physicians provide formal consulting for the investment industry about trends in medical practice and how that might affect stock performance.

More than half of continuing medical education is sponsored by industry. More than 90 percent of medical students report having been asked to attend a drug industry-sponsored luncheon, while students typically are exposed to industry gifts or sponsored activities at least once a week at school.
oriented universities, especially their medical schools, have grown dependent on industry funds for clinical research, and have, since passage of the Bayh-Dole Act in 1980, become active participants in the patenting and licensing of new medical technologies and the creation of start-up firms to commercialize those technologies. 

Physicians with ties to industry or with their own proprietary interests have significant influence over the practice of medicine. A survey of authors of clinical practice guidelines written in the 1990s found 87 percent had some form of interaction with the drug industry, and 59 percent of authors had relationships with companies whose drugs were considered in the guideline. Industry underwrites the clinical practice guidelines sponsored by many professional societies and their annual meetings. Physicians often send patients to specialty hospitals that they either partially or entirely own, thereby skirting a 1991 law prohibiting self-referrals at community or teaching hospitals. And specialists, whose financial interests may lead them to overestimate the difficulty and complexity of their own craft vis-à-vis primary care physicians and less influential specialties, dominate the American Medical Association committee that determines the reimbursement schedules of the Center for Medicare and Medicaid Services (Medicare and Medicaid) and private insurers.

The government regulatory and research system has been similarly affected by conflicts of interest and industry’s heavy involvement with the medical profession. About a quarter of outside advisers sitting on Food and Drug Administration advisory committees require waivers of the nation’s conflict-of-interest laws (the Federal Advisory Committee Act) because of ties to industry. After the National Institutes of Health relaxed rules restricting in-house researchers’ ties to industry, hundreds of top-ranking scientists and research administrators forged consulting and other financial arrangements with the private sector.

Negative Consequences

Some observers have dismissed the importance of scrutinizing these far-reaching financial arrangements, especially in the academic arena, and suggest that any efforts to regulate or limit conflicts of interest will retard medical innovation. “The intense energy currently dedicated to demonizing academic-industrial research relationships should be redirected toward developing better ways to identify and facilitate the type of partnerships that have brought more good, by far, than harm,” wrote Thomas P. Stossel of the Harvard Medical School.

But there is substantial anecdotal evidence suggesting that conflicts of interest in medicine have negative consequences, and there is no scientific basis for claiming that the alleged benefits of increased innovation outweigh the risks. Indeed, while correlation does not signal causation, the proliferation of industry
gifts and payments to practicing physicians and financial collaboration between
the pharmaceutical industry and academic investigators has coincided with a
prolonged decline in the number of new drugs and biologics approved by the
FDA.\textsuperscript{17} A hypothesis worth further study is that innovation is being harmed by
excessive financial entanglements between physician-researchers and the private
sector by channeling scarce scientific resources into medically insignificant
research endeavors, inhibiting scientific collaboration, fostering a culture of
secrecy, and creating an anti-commons effect through the extensive early-stage
patenting of basic science insights and research tools.\textsuperscript{18}

The observable negative consequences fall into three categories: 1)
individual episodes of violations of basic ethical principles of research,
publication, education and patient care; 2) general influence over the practice of
medicine in ways that are detrimental to patients’ health and financial wellbeing;
and 3) fears that disclosure of conflicts of interest will diminish the public’s
perception of the medical profession’s integrity.

1. Financial conflicts of interest in research have been implicated in the
suppression of negative research results; delays in publication; failure to report
serious adverse events in clinical trials; the slanting of research reports; the
slanting of systematic reviews of medical evidence;\textsuperscript{19, 20, 21} and a systematic bias in
the direction of delivering outcomes that favor study sponsors.\textsuperscript{22, 23} Ghost-writing
has become common at medical journals\textsuperscript{24} as has efforts by industry sponsors to
control study data and statistical analysis, and to dictate where to submit the
finished manuscript.

Basic principles of scientific collaboration have been undermined by
proprietary concerns, thus retarding biomedical innovation, the very thing that
close ties to industry was supposed to promote. A national survey of life scientists
showed that 46 percent of scientists had been denied access to data by fellow
scientists, and that data withholding was strongly associated with
commercialization of research. Nearly three-quarters of scientists (73 percent)
said data withholding had slowed the rate of progress in their field.\textsuperscript{25}

2. Financial conflicts of interest are also a major driver of waste and
underperformance within the U.S. health care system.\textsuperscript{26, 27, 28, 29} They contribute to
what Jerome Kassirer, the former editor of the \textit{New England Journal of Medicine},
has called “the greed culture that permeates medicine.” They create an
environment where physicians over-prescribe useful drugs; engage in or fall prey
to “disease mongering”;\textsuperscript{30} discourage use of cheap generic medicines; over-utilize
diagnostic and imaging tests; engage in self-referrals for procedures and
operations; and skimp on or ignore primary prevention health promotion and
health care strategies that are undercompensated. Systematic reviews underwritten
by industry sometimes have misrepresented the evidence\textsuperscript{31}, and clinical practice
guidelines underwritten by industry have led in some cases to the propagation of
unsound advice for practitioners.\textsuperscript{32, 33, 34, 35}
3. From the death of 18-year-old Jesse Gelsinger in a gene therapy experiment where the university and a researcher with a proprietary interest in the technology failed to adequately warn parents about the risks of the experiment, to the skewed vote at an FDA advisory committee considering the safety of rofecoxib (Vioxx), 36 financial conflicts of interest and the over-commercialization of medicine have been at the heart of a steady drumbeat of scandals that have rocked the medical profession in recent years. The press focus on conflicts of interest in medicine may be affecting the public’s perception of the profession. While a 2006 Harris Interactive poll found physicians are still ranked as the most trusted profession with 85 percent of the public saying they trusted their doctors, participants in a series of Consumer Reports focus groups in the summer of 2007 said they “believed the system was designed to make money for doctors, hospitals, and drug companies rather than provide high quality care.”

Leading medical educators fear standards are eroding in a way that will ultimately undermine the profession’s standing. “Inconsistency in research standards can affront human research ethics, undermine academic integrity, distort public policy and medical practice, and impair public health,” wrote David Korn and Susan Ehringhaus of the Association of American Medical Colleges. “Many leaders and administrators at academic medical centers are asking how scientific objectivity can be maintained considering the potentially compromising relationships that can ensue from gifts, grants, royalties, equity holdings, and business ownership – not only to individual investigators and clinicians, but also to academic institutions,” wrote David J. Rothman of the Center on Medicine as a Profession at Columbia University. “The practice of medicine in a system that treats medical care as if it were a market commodity cannot meet the expectations that drew you to a life in medicine,” warned former *New England Journal of Medicine* editor Arnold Relman in an open letter to the profession at the conclusion of his latest book, “A Second Opinion.”

**Poorly Regulated**

The main tool for attempting to manage conflicts of interest in medicine is disclosure – in the medical literature, within continuing medical education activities, on government advisory committees, on clinical practice guideline-writing committees, on institutional review boards, and in the direct payments between firms and physicians. Disclosure assumes that a conflict of interest, once exposed, can be taken into account by other researchers, physicians, patients, insurers, and government officials when they consider either the research or opinion offered by the conflicted person.

However, disclosure is poorly enforced and has itself become enmeshed in scandal. In research and continuing medical education, disclosure relies on the good will and self-awareness of researchers, editors, and educators who self-regulate within a patchwork of confusing and sometimes contradictory rules.
Unsurprisingly, patient advocates, consumer groups, and the press have continually exposed instances when researchers failed to disclose relevant conflicts of interest in journals where their articles appeared. Very few journals have adopted sanctions for failing to disclose conflicts of interest, and at least one leader in the field has explicitly rejected that approach. Among practicing physicians, information on drug industry payments is hard to come by. In the two states that have adopted disclosure laws, patients cannot easily access the data, which in any case is incomplete.

Voluntary disclosure in hampered by varying definitions of what constitutes a conflict of interest. There is no common standard for relevance, although most policies declare only relevant conflicts of interest must be disclosed. There is no common standard for how long a conflict of interest persists. The Journal of the American Medical Association says five years. The Institute of Medicine says only current financial arrangements merit disclosure. There is no consensus on the desirability of a minimum standard below which reporting need not occur, and no agreement on what that level might be.

When it comes to disclosing intellectual property, determining when patents or patent applications are relevant to a published article is especially difficult. Researchers today are encouraged to file patent applications on basic science insights that decades ago would have been considered part of the public domain. The ultimate value of that intellectual property may not become apparent for years. Moreover, scientific advances in one area may increase the value of patented technologies in another area that at first blush years earlier may have seemed only marginally related. This has already led to accusations that prominent researchers are covering up relevant patent disclosures. That many journals and organizations with conflict of interest policies make no attempt to define relevance makes enforcement difficult if not impossible.

In the wake of numerous prosecutions involving anti-kickback and false-claims act claims involving drug industry payments to physicians, professional associations including the American Medical Association, the American College of Physicians, the Accreditation Council for Continuing Medical Education, and the Pharmaceutical Research and Manufacturers Association adopted voluntary guidelines governing financial conflicts of interest that might unduly influence the physician-patient relationship. What is notable in all the voluntary guidelines is that they seek to limit, not eliminate conflicts of interest from the relationship. The AMA says meals provided by drug representatives “must be modest.” ACP says physicians should accept industry honoraria “only for services rendered and reasonable travel costs.” The ACCME, which sets the rules for continuing medical education (CME) seminars that most physicians must take to maintain their state licenses, says industry support for CME must be “only in the form of educational grants.” The PhRMA excludes takeout meals from its guidelines.
This consensus that small gifts and unrestricted grants do not matter ignores a broad stream of social science literature that shows that gift-giving, no matter how small, creates a feeling of reciprocity on the part of the recipient. The evidence in medicine suggests that physicians are influenced by small gifts, even when they don’t believe that they are.\textsuperscript{50, 51} When it comes to accepting gifts, food, and financial support from industry and allowing industry grants to underwrite continuing medical education, no professional medical group has found it expedient to follow in the footsteps of the No Free Lunch campaign and just say \textit{no}.\textsuperscript{52}

Federal regulation of conflict of interest rules is similarly lax. The National Institutes of Health is required by law to ensure that its extramural grantees, who expend about 80 percent of the NIH budget, work at institutions that have enforceable and enforced conflict of interest policies. But NIH collects very few of those documents and makes no effort to collect data. Its “primary method of oversight is reliance on grantee institutions’ assurances that regulations are followed.”\textsuperscript{53} The result is wide variations in campus policies driven by local context and individual institutional values.\textsuperscript{54} NIH rules for its own scientists, adopted in the wake of \textit{Los Angeles Times} revelations that dozens of top scientists were reaping huge consulting fees from private industry,\textsuperscript{55} were more restrictive than prior rules but allowed senior researchers to own some stock in drug companies and give lectures at industry-funded medical education seminars.\textsuperscript{56}

In 2004, the Department of Health and Human Services encouraged academic institutions to adopt policies for managing institutional conflicts of interest. A survey of 86 medical schools revealed that just 30 had done so by the end of 2006, and 29 more had policies under consideration. The survey also found a “substantial gap” in the policies – a general failure to inform institutional review boards about institutional conflicts of interest.\textsuperscript{57}

Finally, the Federal Advisory Committee Act, which sets ethics rules for outside advisers to the Food and Drug Administration and other federal agencies, allows agencies to waive its rule that advisers not have conflicts of interest if they think the conflict is minimal or the expertise of the scientist is unobtainable elsewhere. The FDA, which approves the safety and efficacy of new and existing drugs, is among the most profligate users of this exemption, granting waivers to 21 percent of outside advisers on 16 committees, according to a recent study.\textsuperscript{58} The data in the report indicated the agency could have found advisers without conflicts who were equally or more qualified than the conflicted panelists had its staff expended just one additional week searching for unconflicted panelists.\textsuperscript{59} Still, the recently enacted FDA reform law only required that the number of waivers be reduced by 25 percent over the next five years.

\textbf{Principles for Reform}
Given this background, the questions posed by the Institute of Medicine’s Panel on Conflict of Interest in Medical Research, Education, and Practice are crucial to the future of the profession and the health of the American people. The scope of the Committee’s work includes “propos(ing) principles to inform the design of policies, guidelines, and other tools to identify and manage conflicts of interest in these contexts without damaging constructive collaboration with industry.”

It is curious that constructive collaboration with industry is the value highlighted in the scope of work. Why not protecting patients; or improving health; or fostering objectivity and independence? As noted earlier, even on the narrow field of fostering collaboration with industry, the committee ought to consider the counterintuitive notion that excessive interaction with industry may be harming medical innovation since the rise to dominance of industry’s role in medical research, education and practice has coincided with a steady decline in new drugs and biologics emerging from industry’s labs.60 61

But even if one grants that financial (as distinct from intellectual) collaboration with industry is an important activity worth preserving because it fosters innovation, the question remains what principles should govern those arrangements. Jerome Kassirer, in his concluding chapter in “On the Take,” laid out these principles:

1. Financial considerations must never be allowed to compromise physicians’ decisions about the care of individual patients or the safety of subjects involved in medical research;
2. Because the integrity of scientific knowledge directly affects patient care, the information on which physicians base their clinical decisions must be free of bias generated by financial entanglements;
3. The profession must be accountable for insuring that undue commercial influence does not make the cost of care so high that it excludes many from receiving it; and
4. We must aspire to the ideal of eliminating financial entanglements, but if physicians cannot or will not, we must have clear and enforceable methods that protect patients and complete disclosure about the conflicts.62

“The highest standard, and the one that would engender the most confidence,” he said, “is elimination of financial conflicts of interest.”

Over the course of the 20th century, the healing art was transformed into a science. In the 21st century, the best practices in medicine will likely be determined by scientific evidence.63 Given the importance of private enterprise in the U.S. innovation system, individual companies will play a central role in the generation of medical evidence through financial support of some basic, much
applied, and most clinical science. These companies will inevitably utilize outside researchers, scientists, and educators to supplement their internal efforts.

Since this collaboration is inevitable, it is crucial that industrial support be fully disclosed in the academic literature, in regulatory filings, during continuing medical education activities, to physicians and to their patients. These disclosures must be uniform, universal and accessible to the public. To meet these standards:

1. Publishers should adopt a uniform code of conflict of interest disclosure rules and adopt penalties for failure to comply;
2. The NIH Library of Medicine should make abstract listing in PubMed depend on adoption of these uniform rules, and the abstracts must contain the funding source of the study or article and conflict of interest disclosure statements and/or links to such information for the authors;
3. NIH, the National Science Foundation and other government science agencies should require all institutions that receive extramural grants to make publicly available on their websites institutional and individual conflicts of interest of grantees and non-grantees within their institutions; and
4. The federal government should require private companies register all payments to researchers, physicians, and other health care personnel on a government-run, publicly available database.

Private firms and non-profit institutions that collaborate with the private sector must also adopt the highest possible standards for managing conflicts of interest through the process of generating medical evidence. All clinical trials, their protocols, and, eventually, their results should be registered in a form that makes the data accessible and usable by outside researchers. Institutional review boards should be free from all institutional and individual conflicts of interest. And institutions that conduct clinical trials, and journals that publish their results, should insist that statistical analyses be conducted by independent biostatisticians. That rule needs to be adopted by all journals in a field, since the one leading journal that implemented such a policy – the *Journal of the American Medical Association* – discovered shortly after rejecting one paper for failing to adhere to the rule that it quickly popped up elsewhere and received substantial media coverage. “I can only hope that the decision by the sponsor (to go elsewhere) was based on something other than not wanting an outside analysis of data that might have uncovered flaws in the original analysis,” wrote editor Catherine DeAngelis.

But generating new technologies and clinical evidence is only the first step in the process of diffusing technology and elevating the practice of medicine. And it is here – diffusion – that Kassirer’s line in the sand should be drawn. The system for reviewing the body of evidence in a field (beyond peer review, where disclosure rules should apply); deriving best practices through systematic reviews;
writing clinical practice guidelines; conducting and evaluating comparative research; and, vitally important, evaluating evidence for regulatory purposes should be entirely free from conflicts of interest.

Continuing medical education should be weaned from its dependence on industry support. State licensing laws require CME. Those state laws should be amended to prohibit firms from financing CME or allowing anyone who derives income from a firm with a stake in what is being taught to deliver a CME lecture. It is entirely reasonable to expect physicians to pay fees for their continuing medical education sufficient to adequately reimburse the institutions and individuals who specialize in and prepare those activities. These costs will inevitably be passed along in the cost of physician services, which should be adequately reimbursed so that physicians can afford to finance their own continuing education free from industry funds.

Similarly, the practice of industry sales personnel offering physicians an endless shower of free gifts, meals, and other gratuities whose ultimate purpose is fostering sales of specific products must come to an end. Professional codes of conduct should be amended to prohibit these near ubiquitous practices.

The bottom line is that the relationship between physicians and researchers, whether as evaluators of medical evidence or practitioners in the field, with any firm with a financial stake in the outcomes of the evaluations or individual medical decisions, should be the same as the relationship between financial and political journalists and the companies and politicians they cover. Journalists are strictly prohibited from any engagement, financial or otherwise, with the subjects they cover. In the regulatory arena, advice and decisions should be offered by medical scientists whose relationship to regulated firms are the same as officials at the Federal Reserve Board are to regulated banks and financial institutions. Again, no relationships are allowed.

Why should medicine be held to a lower standard than either of those professions? Where there is total financial independence, there can be no questions about objectivity.


21 Yank V, Rennie D, Bero LA. Financial Ties and Concordance between Results and Conclusions in Meta-Analyses: Retrospective Cohort Study. BMJ. 2007;335:1202-1205.

22 Bekelman et al. op cit.


For more information on this approach, see the “No Free Lunch” website and campaign developed by Dr. Robert Goodman at [http://www.nofreelunch.org/aboutus.htm](http://www.nofreelunch.org/aboutus.htm) (accessed Feb. 19, 2008).


