Journal of Law and Policy

Volume 13
Issue 1
SCIENCE FOR JUDGES III:
Maintaining the Integrity of Scientific Research and
Forensic Evidence in Criminal Proceedings

Article 2

2005

Maintaining the Integrity of Scientific Research

David Korn

MAINTAINING THE INTEGRITY OF SCIENTIFIC RESEARCH

*David Korn, M.D.**

Historians tell us that science arose in the western world under the moniker of "experimental philosophy" and that, at its birth, science was inseparably conjoined with integrity. This inseparable conjunction took root in the fact that experimental philosophy was an activity exclusively practiced by "gentlemen," whose word was deemed their bond and whose devotion to the ideals of loyalty and honor was considered unshakeable. Quaint though this notion may now appear, it is instructive to note that, in 1968, some 300 to 400 years later, Stanford University's then remarkably terse policy on faculty outside consulting relationships was captured in the following language:

> Most major universities, including Stanford, have taken the position that consulting relationships are on balance overwhelmingly beneficial, and there is no disposition to change that view. At the same time, it would be foolish to ignore the fact that some of the complications arising from this state of affairs can cause damage to the university and to the individual, as well. Chief among these complications is that tangled and thorny set of problems embraced by the general title of 'conflict of interest.'
>
> The issues subsumed under that heading are principally ethical and as such they are not readily codified to rules of behavior. In any event, this university has never found it necessary to spell out the rules or codes of ethics for its faculty and staff. The relationship between the university

* Senior Vice President, Division of Biomedical and Health Sciences Research, Association of American Medical Colleges; Stanford University Vice President, Dean of Medicine and Professor of Pathology, *emeritus*.

> and its staff assumes that full-time staff members owe their primary professional allegiance to the University and that they will be alert to the possibility that outside obligations, financial interests, or employment can affect the objectivity of their decisions as members of the University community. If those assumptions are valid, as we believe them to be, then no codes or monitoring devices are needed; if they are not valid, then none will suffice.[1]

Certainly, academic science has profoundly changed since the days of Francis Bacon and Isaac Newton, and profoundly so since 1968, especially in biomedicine. Today neither the organization nor the culture of science conforms to the trusting, "gentlemanly" code of behavior captured so sparsely and elegantly in Stanford's former policy language. Notwithstanding this reality, I will posit that the integrity of science today continues to rest fundamentally on the integrity of individual scientists and their institutions.

Although it is fashionable to think of scientists as "objective," "detached," or "dispassionate," the truth is that successful scientists are passionate about their work and often become committed to particular hypotheses, experimental approaches, and the correctness of their results. In recognizing this passion, and in part to respond to it, the scientific processes themselves are designed to try to protect scientific integrity and mitigate bias. Among the methods used are peer review, requiring that findings be communicated with sufficient description of methods, materials, and data to permit others to attempt to replicate the work, and caution in the interpretation of data, which are always susceptible to challenge, modification, refutation, or corroboration. Replicability plays a particularly important role in confirming the validity of scientific observations and interpretations. Problematically, the public and the press too often ignore the fact that the publication of research, no matter how rigorously peer-reviewed, is most assuredly not intended to be an attestation of verity.

During the past five decades, there has been enormous growth

---

[1] STANFORD UNIVERSITY, RESEARCH POLICY HANDBOOK (1989) (on file with author).

of the U.S. scientific enterprise, spurred largely by federal policy and largesse. Nowhere has this growth been more dramatic than in the field of biomedicine. Although federal sponsors have vigorously regulated the expenditures of hundreds of billions of dollars of research funds, their regulation of the actual conduct of research and the behaviors of researchers has been astonishingly light-handed. Thus, during this interval of dramatic growth, the matter of institutional integrity has become increasingly important. Indeed, in these matters the government has exhibited remarkable deference to the cherished autonomy and self-governance of awardee universities and academic medical centers. Oversight has been accomplished largely through an "assurance" mechanism, whereby the awardee institutions assure the federal funders that they have put appropriate policies and practices in place and, at least implicitly, are diligent in enforcing them. These assurances deal with such matters as scientific misconduct, financial conflicts of interest, and the protection of human research subjects.

The assurance edifice, which in many respects defines the federal-academic partnership in basic research, is still operational today. Notably, however, its foundations began to fray in the early 1980s and throughout the 1990s due to a number of unfortunate and highly publicized episodes that occurred in biomedical research. These cases, which cast long shadows on the integrity of biomedical researchers and their institutions, involved flagrant scientific misconduct. In several of the cases, the perpetrators were found to have significant financial interests in the outcomes of their research. Thus, both scientific misconduct and financial conflicts of interest debuted together on a brightly-lighted public stage. However, this linkage was unfortunate because it ingrained in the minds of the public that financial self-interests in biomedical research are inevitably problematic and likely to lead to scientific fraud.

During the late 1990s, a number of federal reports criticized academic medical centers for inadequate compliance with federal regulations concerning the protection of human research subjects. Several of those reports raised concerns about financial conflicts of interest in research institutions, in essence questioning whether the "institutional watchdog" was still trustworthy. In November 2000,

the Association of American Medical Colleges (AAMC) announced its intention to convene a Task Force on Financial Conflicts of Interest in Clinical Research (AAMC Task Force). It did so primarily because of the concern that its member institutions, which conduct more than 60 percent of the total extramural research funded by the National Institutes of Health (NIH), had not been sufficiently responsive to the profound changes that had occurred in the past two decades.[2]

One can readily identify a number of the most prominent factors responsible for these changes. First, of course, has been the extraordinary progress of biomedical science, which has made the results of even the most fundamental research increasingly attractive candidates for commercial development and clinical application. Second was the invention in academia of recombinant DNA technology, which spawned the biotechnology industry, the scientific agenda of which continues to be *deeply* intertwined with academic biomedical research and researchers. The invention of recombinant DNA technology by Professors Cohen (Stanford) and Boyer (UCSF) in the early 1970s is well known, as is the deep intertwining of academic biomedical and biotech industry research.

A third factor was the 1980 case of *Diamond v. Chakrabarty,* in which the U.S. Supreme Court ruled that a recombinant bacterium was patentable subject matter.[3] The Court stated in its opinion that "anything under the sun" invented by man is patentable.[4] By sweeping living organisms under the reach of patentability, the Court deemed a vast expanse of biomedical research and technology eligible for intellectual property protection, an expanse whose boundaries continue to expand and be hotly contested to this day. A fourth factor was the enactment of the Bayh-Dole Act, also in 1980, which gives the recipients of federal research funds both the right to patent their discoveries and the obligation to spur translation of those discoveries into public benefit, that is, to stimulate the commercialization of federally-

---

[2] I like to refer to this period as the ecology of biomedical research.

[3] 447 U.S. 303 (1980).

[4] *Id.* at 309 (internal citations omitted).

funded research results.[5]

Yet another factor has been the storied accomplishments of Silicon Valley, MA Route 128, and the San Francisco Bay Area in informatics and biotechnology. These successes have reached near-mythic proportions in the minds of local, state, and federal politicians—all of them eager to bring similar bounties to their communities through the commercialization of university research. Thus, America's research universities have become increasingly viewed as "engines of economic development" and have found themselves ensnarled in a tangled web of intensely conflicted political pressures and public expectations.

As a consequence of all of these factors, the breadth, depth, and intensity of interaction between universities and their biomedical research staff and industry has increased dramatically, as has the prevalence of individual and *institutional* financial self-interest in academic biomedical research. Some alarmed observers have opined that science is facing a veritable pandemic of financial conflicts of interest; others have questioned whether academia is busily bartering its very soul for the prospect of material enrichment.

In response to these concerns, AAMC convened a Task Force

---

[5] Government Patent Policy Act of 1980 (Bayh-Dole Act), 35 USC §§ 200-211 (2004). The Act provides in relevant part:

> It is the policy and objective of the Congress to use the patent system to promote the utilization of inventions arising from federally supported research or development; to encourage maximum participation of small business firms in federally supported research and development efforts; to promote collaboration between commercial concerns and nonprofit organizations, including universities; to ensure that inventions made by nonprofit organizations and small business firms are used in a manner to promote free competition and enterprise without unduly encumbering future research and discovery; to promote the commercialization and public availability of inventions made in the United States by United States industry and labor; to ensure that the Government obtains sufficient rights in federally supported inventions to meet the needs of the Government and protect the public against nonuse or unreasonable use of inventions; and to minimize the costs of administering policies in this area.

Id. § 200.

that produced two reports that address individual and institutional financial self-interests, respectively.[6] The reports are noteworthy in that they reflect the hard-won consensus of a highly diverse group of leaders representing all of the stakeholder groups, including academia, industry, bioethics, law, patients, and media representatives. The reports offer principles, recommendations, and guidelines that are stringent and challenging. They would hold academic medical centers to high standards that the AAMC believes would contribute greatly to buttressing public confidence in the integrity and trustworthiness of academic medical centers and the research they produce.

The AAMC recently reported the results of a year-long survey study that it conducted to assess the current state of financial conflict of interest policies at U.S. medical schools.[7] The participation of 82 percent of the schools makes this study the most comprehensive exploration of this topic to date. The report indicates that the medical schools and their parent universities have made encouraging progress in revising and strengthening their policies and practices in accordance with the recommendations of the AAMC Task Force.[8] At the same time, however, the study reveals many areas in which continued effort is necessary to ensure that *all* medical schools engaged in clinical research on human subjects maintain a consistently high standard of disclosure of financial self-interests. For example, the schools must continue to press for the adoption and credible application of the "compelling circumstances" threshold regarding the permitted participation of financially-conflicted scientists in clinical research, and for

---

[6] *See* ASSOCIATION OF AMERICAN MEDICAL COLLEGES, PROTECTING SUBJECTS, PRESERVING TRUST, PROMOTING PROGRESS (2001), *available at* http://www.aamc.org/members/coitf/firstreport.pdf [hereinafter REPORT I]; ASSOCIATION OF AMERICAN MEDICAL COLLEGES (2002), PROTECTING SUBJECTS, PRESERVING TRUST, PROMOTING PROGRESS II, *available at* http://www.aamc.org/members/coitf/2002coireport.pdf [hereinafter REPORT II].

[7] SUSAN EHRINGHAUS & DAVID KORN, ASSOCIATION OF AMERICAN MEDICAL COLLEGES, U.S. MEDICAL SCHOOL POLICIES ON INDIVIDUAL FINANCIAL CONFLICTS OF INTEREST (2004), *available at* http://www.aamc.org/members/coitf/coiresults2003.pdf.

[8] *Id.* at 5-6.

rigorous management to ensure that financial interests are never allowed to compromise the integrity of the research or the welfare of the human subjects.[9]

The AAMC has devoted considerable attention to the matter of financial conflicts of interest during the past fifteen years because of its conviction that academic medicine should demonstrate strong and unambiguous moral leadership in biomedical research (and medical practice, for that matter) to remain worthy of the remarkable trust and esteem placed in it by the American public.

To this point, there persists a major area of concern that has troubled some academic medical leaders and journal editors for many years and, in recent months, has become the focus of enormous public attention and alarm—the integrity of reporting of the results of industry-sponsored clinical trials. Although the principal targets of concern are pharmaceutical companies and, regrettably, the Food and Drug Administration (FDA), academic medicine is also implicated because so many influential clinical trials are conducted by academic specialists of high repute. These "thought leaders" bring to the trial, and especially to the publication of trial results in prestigious medical journals, not only their expertise but also their credibility as academics.

Although this interaction between academic medical experts and industry is scientifically and clinically understandable, and indeed may be necessary for a successful study, serious concerns have been raised about just how involved the academic principal investigators really may be in such critically important tasks as the design of the trial, primary data analysis and interpretation, and even at times the writing of the paper itself. In other words, too many documented instances suggest that academic leaders sometimes permit themselves to be used to provide cover and respectability to industry-sponsored studies in return for potentially rich financial rewards. It is worth emphasizing that the AAMC Task Force reports urge medical schools and teaching hospitals to

---

[9] *Id.* at 6-7. The Task Force argued that a financially-conflicted investigator should be permitted to participate in clinical research *only* in the presence of "compelling circumstances." *Id.* at 3. Although the Task Force declined to define "compelling," it believed that a useful standard would be that the research in question could not be carried out as effectively or safely by anyone else. *Id.*

adopt a strong posture against permitting such financially-conflicted practices.[10]

The present crisis of credibility is due in part to company sponsors ignoring or suppressing the publication of negative trial results and choosing instead to publish positive results, thereby presenting to practicing physicians and the public a highly misleading picture of the efficacy and safety of the drugs in question. Questions have even been raised about whether the FDA itself, presumably under industry pressure, has been guilty of such suppression of negative data. Given the FDA's statutory role as the federal watchdog over the purity, safety, and efficacy of nearly 25 percent of the gross national product of the United States, such allegations are extremely troubling. As a result, several state attorneys general, especially New York Attorney General Elliott Spitzer, have played a major role in bringing these grievous matters to light by filing charges of criminal fraud, exacting high financial penalties, and imposing corrective practices on the accused company perpetrators.

The present crisis, which focused initially on the use of heavily marketed anti-depressant drugs in children and, more recently, on the purported efficacy and safety of new generation anti-inflammatory drugs ("cox-II inhibitors"), has created great pressure for the establishment of a federally funded and operated mandatory registry of *all* clinical trials. Although the implementation of such a registry is not so simple a task as the media and some congresspersons would like to believe, both the AAMC and the American Medical Association (AMA) have lent their strong endorsements to this initiative.

Two facts are often overlooked in public discussions of financial conflicts of interest in biomedical research. First, the extraordinarily generous public investment in biomedical research in the post-World War II decades has not been driven by scientific curiosity or the abstract goal of enriching scientific knowledge. Rather, that investment has been driven by the hope and expectation that diseases will be better understood, that preventive and therapeutic interventions will be more rational and effective,

---

[10] *See* REPORT I & REPORT II *supra* note 6.

and that from all of this will come dramatic reductions in suffering and improvements in the public health. Second, in our political economy, which frowns on "industrial planning," the commercial development of scientific discoveries is, with the singular exception of the defense industry, almost exclusively dependent on private capital. It is important to keep in mind that the NIH research dollar, with precious few exceptions, stops at discovery; therefore, partnering among academic institutions, venture capital, and industry is an inevitable and necessary step in bringing the fruits of biomedical research to market.

Given these facts, the challenge for the academic medical community is to oversee and manage the inevitable financial self-interests with stringent policies, scrupulous practices, and a strong presumption against permitting a financially-conflicted investigator to participate in clinical research on human subjects, unless a compelling case can be made that the research could not be performed as effectively or as safely by anyone else. Compelling circumstances do indeed exist; nonetheless, the broad acceptance of such a standard would dramatically reduce the number of instances in which such practices occur as well as the unfortunate misbehaviors that too often result. With that said, proposers of new remedies that call for the blanket elimination of financial conflicts of interest should take care that, in their zeal to attain some idealized state of virtue, they do not interdict a robust developmental pathway of immense social benefit and coincidentally kill the goose that lays the golden egg that supports biomedical research discovery and its realization for public benefit.