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Theme: Scientific Ethics

The Interrelationship between Research Integrity, Conflict of Interest, and the Research Environment

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Quite distinct regulatory measures have been established to try to deal with research misconduct and conflict of interest. To decrease research misconduct, the emphasis has been on education aimed at promoting an understanding of and commitment to research integrity. To decrease the impact of conflict of interest, the emphasis has been on management of the research environment. In this essay I discuss the idea that research misconduct and its close relative "questionable research practices" should be framed in the context of conflict of interest. If we take seriously the implication of conflict of interest regulations that even a $5,000 financial interest might bias the design, conduct, or reporting of research, then how much more risk of bias will be in play when what is at stake is ongoing funding of short-term research grants on which a researcher's salary and job depend? Education is important and necessary to promote research integrity but by itself will not be sufficient. Placing problems of research misconduct and questionable research practices in the context of conflict of interest makes it clear that we also will need to develop new approaches to manage the structure of the research environment. One example of such a management strategy would be for NIH to phase in a limit on the overall percentage of a faculty member's salary permitted to be supported with NIH grant funds, complementing the already existing upper dollar limit that can be used for faculty salaries.

Annual reports from the Department of Health and Human Services (HHS) Office of Research Integrity (ORI) during the period 1994–2012 show misconduct findings in less than 20 cases/year and no signs of an increase (10), a very low level indeed given the size of the HHS research community. Notwithstanding the ORI experience, other data suggest that research integrity of scientists is a significant concern. According to meta-analysis of 18 independent surveys, about two percent of researchers admit to having committed research misconduct at least once and know of such behavior by about 14% of colleagues (2). Over the past 10 years, the rate of retraction of published papers has increased markedly with more than half the retractions resulting from serious research misconduct (3). And questions concerning research reproducibility provoked National Institutes of Health (NIH) leaders Francis Collins and Lawrence Tabak to write, in a 2014 essay published in *Nature,* "A growing chorus of concern, from scientists and laypeople, contends that the complex system for ensuring the reproducibility of biomedical research is failing and is in need of restructuring" (1).

Looking back in time, a series of well-publicized cases of scientific misconduct that occurred during the late 1970s resulted in hearings held in March 1981 by the House Committee on Science and Technology Subcommittee on Investigations and Oversight on the topic of *Fraud in Biomedical Research* (17). Then Congressman Albert Gore, Jr., opened the hearing by posing a series of questions about the scientific research environment, beginning with the following two questions:

> *Is the increased competition for grants and awards stimulating fraud?*
>
> *What, if any, effects will the introduction of profit-making ventures into the university biomedical sciences have on the pressures facing researchers?*

After 1980, the second question became of particular concern in the biomedical sciences. Congress had passed the Bayh-Dole Act, which encouraged universities and research centers to patent technologies that their employees invented with the support of federal funds. The transition of the research community from publish-or-perish to patent-and-prosper (13) was underway, with institutions

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and investigators potentially benefitting from a combination of patents, licenses, and startup companies. By the time the Committee on Government Operations held its 1990 hearing called *Are scientific misconduct and conflicts of interest hazardous to our health* (16), serious questions had been raised about the response of the research community not only to misconduct, but also to conflict of interest (COI).

Quite distinct regulatory measures were introduced to try to deal with research misconduct and COI. In this essay I will discuss the idea that research misconduct and related "questionable research practices" (6) should be framed in the context of conflict of interest. Gore's two questions mentioned above, combined, then would read, "What effects has the introduction of soft money support of researcher salaries from short-term grants and awards had on the pressures facing scientists in the biomedical sciences?"

To decrease research misconduct, the emphasis has been on education aimed at promoting an understanding of and commitment to research integrity. Beginning in 1989, NIH required that teaching the principles of scientific integrity become an integral part of research training (14). Now, more than a generation of graduate students and postdoctoral fellows has gone through some sort of training. Matters of what and how to teach were left to the research institutions until relatively recently, when NIH and NSF instituted robust guidance concerning format, overall subject matter, faculty participation, and duration and frequency of instruction (7, 9).

To decrease the impact of COI, the emphasis has been on management of the research environment so as to minimize the potential consequences of bias. HHS amended the Code of Federal Regulations in 1995 with a new subpart designated Responsibility of Applicants for Promoting Objectivity in Research, which qualifies "…by establishing standards to ensure there is no reasonable expectation that the design, conduct, or reporting of research funded under PHS grants or cooperative agreements will be biased by any conflicting financial interest of an investigator" (18).

The potential for bias arises especially because value judgments are an inherent part of the everyday practice of science. As I have discussed elsewhere, decisions about experimental design; about which experimental results should be counted as data vs. experimental noise; about which conclusions concerning a hypothesis under investigation can be drawn from the data; and about which results to present in a research paper and how to organize them—all these and more include value judgments influenced by an investigator's experience, intuition, and interests (4).

In the original COI regulations, significant financial interest (SFI) was defined as greater than $10,000. Assessment of whether a SFI might present a conflict of interest with federally funded research was determined by the investigator. In 2011, HHS strengthened the conflict of interest rules (15). The level of SFI was lowered to $5,000 and encompassed all of an investigator's institutional responsibilities. The institution rather than the investigator became responsible for determining whether a significant financial interest might represent a COI. And investigators were required to take a training course regarding COI.

Under the COI regulations, management is accomplished by changing the research environment depending on the particular situation. At one end of the scale, the change might simply require an investigator to disclose the COI in papers and presentations and to potential subjects of human research. At the other end of the scale, the change might result in an investigator being disqualified from participating in the research altogether unless the financial relationship causing the COI is terminated.

One important exclusion of the COI regulations specifies that the term significant financial interest does not include the following types of financial interests: salary, royalties, or other remuneration paid by the institution to the investigator if the investigator is currently employed or otherwise appointed by the institution…

It is this exclusion to which I wish to call attention and which I would like to consider further.

As already discussed, the Bayh-Dole Act, besides promoting development of scientific discoveries into usable technologies, had a major impact on the research environment because of its effects on conflicts of interest. Another far-reaching event, equally important, was the 1960 report *Scientific Progress, The Universities, and the Federal Government* issued by the President's Science Advisory Committee (PSAC) (11). PSAC advised that the number of academic centers of excellence in the United States should be doubled and that to promote this expansion, federal support should be made available to increase the size of university faculties. PSAC's recommendation came with a warning, however:

> *We recognize that many university scientists are strongly opposed to the use of Federal funds for senior faculty salaries. Obviously we do not share their belief, but we do agree with them on one important point—the need for avoiding situations in which a professor becomes partly or wholly responsible for raising his own salary… Just as a professor should not be responsible for obtaining the funds to pay his regular salary, so also there should be no bonus payment for "landing a contract." (11)*

The recommended expansion of American research universities succeeded beyond expectation, but over time, the research community ignored the warning about avoiding situations in which faculty members raised their own salaries. Instead, the soft money system of faculty salary support became commonplace, with many researchers in the United States required to raise much or even 100% of their salaries through research grants that require competitive review every few years.

The National Academies Institute of Medicine report *Integrity in Scientific Research: Creating an Environment that Promotes Responsible Conduct* emphasized the importance of the overall research environment in promoting research

integrity (5). What does that environment look like now? The competition for faculty jobs is fierce, with the growth in the number of trainees easily outpacing the number of faculty positions available (8). The competition for grants is fierce, with overall NIH funding success rates down to around 15% (12). Regardless of whether the goal is to find a job, to win a grant, or to competitively renew one's grants, success will depend on producing an ongoing record of research publications describing discoveries made during the grant period. The possibility that nothing of consequence will be discovered in the short term results in a potentially career-disrupting outcome.

If we take seriously the implication of the COI regulations that even a $5,000 financial interest might bias the design, conduct, or reporting of research, then how much more risk of bias will be in play when what is at stake is a researcher's soft money salary, and possibly job, and indirectly the well-being of one's family, based on grants that come up for renewal every few years?

Education is important and necessary to promote research integrity but by itself will not be sufficient. Placing problems of research misconduct and questionable research practices in the context of conflict of interest makes it clear that we also will need to develop new approaches to manage the structure of the research environment. Making changes in the soft money environment of research would be one good place to start. For instance, in addition to the already existing upper dollar limit that can be used for faculty salaries, NIH could phase in a limit on the overall percentage of a faculty member's salary permitted to be supported with NIH grant funds.

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