

Tuesday, July 20, 2010

Dr. Francis Collins
Director, National Institutes of Health
RIN 0925-AA53
Docket Number NIH-2010-0001-0001

Dear Dr. Collins,

We, the Association of Clinical Researchers and Educators (ACRE), a physician not-for profit association, write this letter regarding the call for opinions and proposed conflicts of interest in medicine¹. We appreciate the opportunity to comment as we have significant concerns that the proposed regulations will have a detrimental effect on biomedical research innovation and patient care.

ACRE recommends that NIH not adopt the proposed rules and recommendations until further discussion occurs, and we offer to be an active participant in this discussion. ACRE members, Educators, Medical Society Leaders and distinguished Professors at academic centers, are engaged in promoting excellence in medical service, education, and innovation, and have substantive track records in these endeavors.

At a minimum we would request that more careful and thoughtful deliberation occur with adequate representation of those who favor healthy interactions between academia, the government and the private sector. Within a framework of mutual respect and well defined guidelines the public has much more to win by a vibrant and high level of engagement between the private sector and medicine. We propose that the ideology that proposes further restrictions on these interactions lacks evidence to support its claims, and will create unnecessary burden on individuals and the government (wasting precious resources). We urge you to consider a delay in implementation until such issues have been carefully considered

Background and definitions

In describing the rhetoric of biomedical ethics *circa* the mid—late 1980s, Marc Rodwin was “*surprised to find how little conflicts of interest – particularly financial conflicts – figured in traditional medical ethics or the new field of bioethics; Codes of medical ethics didn’t even use the term; and that a three-volume Encyclopedia of Bioethics didn’t address the issue.*”²

In the intervening years, ‘financial conflict of interest’ (FCOI) has become “***the***” available *heuristic (or frame)* for characterizing all relationships between the medical professional and private industry.

Like any heuristic, the FCOI frame *simplifies* an otherwise numbingly complex, nuanced, messy reality, by reducing it to a single metric - “risk of corruption.” Instead of offering statistical knowledge about the rate of professional misconduct, the FCOI framing bias substitutes dramatic *anchoring* events - of dubious, unseemly, even deplorable conduct. The numerator, constituted by outrageous or tragic events, is refreshed and amplified by media repetition periodically. The denominator - aggregating all “relationships in place during a year” or “all commercial exposures in a continuing education setting in a given year” - is not provided. Instead, promoters of the FCOI framing bias recur to “often,” or “many.”

Unfortunately, reviewers and journal editors have helped establish the availability of the FCOI heuristic by repeatedly failing to provide their professional audiences with minimal due diligence – by challenging FCOI promoters to answer: “What rate of professional misconduct did you find?” “What scientific basis do you have for claiming that a financial motive caused the misconduct?” “What evidence is there of impaired patient outcomes due to FCOI?” These very simple scientific principles of measuring have been violated in all reports decrying the corrupt nature of interactions between academicians and industry. Making blanket assertions about these recommendations is prejudicial.

In 1993, noting its pejorative connotation, Rothman warned the scientific community that “conflict of interest” had become a banner inscription for a New McCarthyism (in medicine).⁴ And indeed, in 1995 the National Institutes of Health (NIH), the major public source of funds for health-related research, responded to FCOI allegations by requiring academic researchers applying for research grants to disclose to their employers payments above a threshold amount from private companies. The expectation was that the academic institutions would somehow, non-arbitrarily, determine the legitimacy of such payments.

Since then, despite overwhelming evidence that collaboration with industry has yielded immense value and little harm, a massive FCOI ideology has flourished and created a compliance industry that has inherent COI on its perpetuation. Its embrace of the term FCOI represents a framing bias that prejudices judgment, and *dictates* that FCOIs be managed or eliminated.

The NIH proposed new rules to amend the agency’s 1995 regulations, “Responsibility of Applicants for Promoting Objectivity in Research for which Public Health Service (PHS) Funding is Sought and Responsible Prospective Contractors,” are problematic because they espouse the FCOI framing bias.

Framing Bias perpetuated by the Proposed Rules

As stated above a framing bias represents a one-sided, prejudice view on a complex topic that disarms the arguments of the accused. The term FCOI is now used as unquestionable indictment of any individual labeled with such attributes. It assumes that all FCOI are malignant by nature. FCOI is one such example of such framing bias.

Using the term “conflict of interest” implies that in order to receive the funding to do the research, CME, consulting, etc., the physician had to do something that had an adversarial or undesirable impact on the patients he was caring for. This implication makes the term inherently negative, and misattributes negative motives to the interested parties involved in the collaboration. As a result, this framing bias has rhetorically reconstructed what were once termed “relationships” between physicians and industry and has instead designated them as conflicts.

Using this broad-based term is a fallacy, and it presents and connotes a negative image of something that, in reality, is almost always positive. Instead, physician-industry collaboration should be regarded as a “win-win” relationship because it adds value and aligns the interests of medicine.

Purpose of Proposed New Rules and Transparency

To suggest that a more rigorous approach to investigator disclosure, management of financial conflicts, and Federal oversight is required because of “the growing complexity of biomedical and behavioral research and the increased interaction among government, research institutions, and the private sector” is exactly the opposite approach NIH should be taking. The paradoxical claim that diverting resources from conducting research, to regulatory oversight, will somehow accelerate translation of basic research to useful treatments is without basis (and honestly perplexing). The NIH's proposed ‘complexifications’ hold promise for little, but obstruction to innovation.

We at ACRE believe **transparency is needed** to quench this otherwise overwhelming negative environment, but this transparency needs to be simple, non-redundant, and already underway with the passage of the Physician Payment Sunshine Act. The new proposed rules state that “If NIH-supported researchers fail to disclose the full extent of their financial interests, universities fail to comprehensively manage FCOI, or NIH fails to diligently oversee the entire system, public trust will be jeopardized in ways that may have far-reaching implications for the future of science.”

The above conjecture has no basis in fact. The proposed NIH rule will require the creation of financial conflict of interest websites. The institutions would have to update the posted information at least annually, and NIH would also require the institutions to update the web site within sixty days of receipt or identification of information concerning any additional SFI that was not previously disclosed. Information on the website must be accessible for at least five years from the date that the information was most recently updated.

Transparency needs to be treated cautiously and explanations associated with the information provided are essential. Often time transparency has been used in a sensationalistic way to chastise highly productive individuals, who happen to have revenue as a consequence of their knowledge or contribution to the medical field. Moreover, placing this information on a public website without the proper context or information for consumers and patients also risks strengthening the misperception that all SFIs constitute “FCOI”. This will leave patients with the idea that working and

collaborating with industry is unethical and wrong, when to the contrary, such partnerships have always benefited patients significantly. It is now routine that every time a pharmaceutical company discloses publicly what they have paid physicians, this is immediately followed by a front news stories in local newspapers, highlighting in a completely negative and derogatory context the income of such (local) physicians (see link below for two examples)⁵⁻⁶. While transparency is not sufficient for the creation of proper behavior it has been used so far only as an intimidation technique and material for sensationalistic journalism. The level of public transparency imposed on to physicians is without much parallel on other private and public sectors. Often times *bone fide* activities that physicians receive payment for (e.g. consulting) are given the derogatory label of “gift” in the various state legislatures that have broached the topic (e.g. Minnesota Pharmacy Board).

When faced with tremendous breakthroughs in prevention, diagnosis, and treatment of complex and chronic diseases, NIH should be *encouraging* such relationships to help find answers and solutions to common public health goals, not chilling the research that will help discover them.

Diverting Money from Research will Hurt Institutions, Patients

The new proposed rules will shift the responsibility for managing financial interests from the investigator to the institution, placing a significant burden of paperwork and verification on NIH recipient institutions. For instance for SBIR/STTR Phase I Applicants only, this shift will affect approximately 5,000 applicant institutions, 2,800 awardee institutions, and an estimated 40,500 investigators, with approximately 2,000 new applicant institutions and 700 new awardee institutions.

Implementing the new proposed rules, which require institutions to verify conflicts of interest greater than \$5,000, would cost approximately \$12,047,525, a burden that may necessitate a whole office to manage the process, and develop a management plan for every FCOI. Many of these costs will ultimately be shifted to other revenue generating areas of medical institutions, not uncommonly patient care. Altogether, implementing the new rules would require an additional 344,215 hours of work. Conversely, NIH notes that:

“... expanding the public disclosure requirement could increase the administrative burden on the Institutions in some respects (due to an increase in volume of posted information) and raise privacy concerns among impacted Investigators given the increased scope of financial interest information, not all of which is related to PHS-funded research, that would be made publicly available.”

If institutions are faced with more significant financial burdens to carry out the new rules, and their staffs are more widely expended, this will divert resources from other critical areas. And all to protect what? Since NIH predicts the negative and perhaps unintended consequences of its own rules, it is obvious that more research is needed by the agency to ensure that the benefits of such rules truly outweigh these risks.

Rules Hurt Willingness to Participate in Research

The proposed rules and requirements “risk strengthening the misperception that all significant financial interests (SFI) constitute FCOI.” Coupled with the fact that NIH believes that public disclosure “does risk strengthening the misperception that any FCOI necessarily causes bias,” their proposed rules have the potential to significantly harm the willingness of investigators to carry out PHS-funded research. NIH must create rules that *minimize* these risks and misperceptions about bias, especially since numerous institutions sufficiently manage FCOIs.

Rules Are Harmful to Translational Medicine

Translation basic research into effective therapies is a low yield activity. If physicians and researchers are hesitant to work with industry because of a negative perception bias of relationships with industry, this will undoubtedly result in stymieing of biomedical research. We may end up with a corporate sponsored research silo that focuses on medications and improved technologies, and a cadre of basic science NIH funded physicians and researchers that focus on basic science, further amplifying the so called “valley of death.” The problem with separation is that it will undoubtedly hurt patients. Taxpayers want medications, and new technologies that provide cures. They are less concerned with some false “purity” that potentially shuts down translational (curative) research.

Rules Impact Non-Profits

The new rules change the requirements of reporting. A non-publicly traded entity must report a SFI if the value exceeds \$5,000, or the Investigator (or spouse/dependent children) holds **any** equity interest (e.g. stock, stock option, or other ownership interest), intellectual property rights (e.g., patents, copyrights), royalties from such rights, or agreements to share in royalties related to such rights.

NIH anticipates that the revised SFI definition would result in the disclosure by Investigators to Institutions of a wider array of interests on a more frequent basis. How much money and resources would be spent sifting through meaningless interests that have no impact on the subject grant, other than slowing the eventual discovery or research?

Rules Will Hurt CME

One area that will have an immediate negative impact is the requirement to disclose payments associated with continuing medical education (CME). CME content, whether organized by academic or commercial entities, is independently developed from the supporter, and physician attendance is voluntary and uncompensated⁷. There are currently significant checks and balances in the system to ensure fair balanced education. Including payments for speaking at CME events on behalf of a non-profit and travel expenses for all types of relationships will cause University programs to withdraw from paying for outside speakers for their grand rounds and other activities. They may up considering all of the administrative costs that come with being in

compliance with the newly proposed NIH rules as not worth bringing in an outside speaker. It also creates a false innuendo that CME is something that creates a FCOI. The report ignores now three peer-reviewed studies that show that physicians at large value industry sponsored CME, and find it not to be biased⁸⁻¹⁰.

The proposed regulations will lead physicians that teach CME programs to be less willing to teach, because of the implicit label of “having done something wrong.” This will negatively impact the training of current and future generations of physicians because often the only individuals truly qualified to train physicians in the earliest stage of adoption of a new medical device, technique, or technology, are often those who developed the innovation.

New Rules Ignore Relevant Evidence

NIH’s reliance on the Wazana paper violates a major requirement of serious scholarship by not citing research that shows the many benefits of commercial contributions to medicine¹¹. Wazana exercised confirmation bias by referring only to publications critical of industry influences on medicine, although others refuting these criticisms existed. The Wazana paper is often cited as the sole evidence of the harm done by having FCOI in medicine and its negative impact on patient care. It is never cited that Wazana explicitly stated in his discussion that of the publications reviewed “...**no studies used patient outcome measures.**”

NIH’s proposed rules only cite literature supportive of its conclusions and treat the benefits of commercialism in medicine cursorily. Today, there is evidence that public trust in doctors is high and stable, according to a series of Harris polls on “most trusted professions.”¹². There is evidence that the public worries about incentivizing physicians to economize on resources, and that the public associates more resource use with better care.

In proposing its new rules, NIH completely ignores pertinent evidence regarding disclosure and work within federal agencies. Specifically, NIH makes no mention of the fact that the Journal of the American Medical Association in 2006 published a study conducted by Public Citizen of voting patterns at Food and Drug Administration (FDA) drug advisory committee meetings¹³. The analysis covered 221 meetings, of which 73% had at least 1 member or voting consultant disclose a “conflict”. The results did not show a statistically significant relationship between “conflict rates” and voting patterns, however “conflict” was defined. In fact, in all three “conflict categories”, the exclusion of advisory committee members and voting consultants with “conflicts” would have produced margins less favorable to the index drug in the majority of meetings, but this would not have changed whether the majority favored or opposed the drug. As a result, the authors concluded that “excluding advisory committee members and voting consultants with conflicts would not have altered the overall vote outcome at any meeting studied.”

Ignoring relevant evidence in the construct of FCOI policies, and basing national policy on conjectures, represents the antithesis of the scientific process that the NIH is supposed to represent.

Americans Want Better Health Care

Americans want better ways to fight disease and improve health – *period*. It is misguided to assert that Americans do not want “FCOI”s to influence the federally funded research. Innovation, in large part resulting from industry translation of NIH-funded research, has delivered these desired outcomes. However, regulations now in force have done nothing to promote more rigorous research, and the proposed rules will push medicine back even more, creating larger gaps in care and deficiencies in training.

Academic-Industry Relationships are Essential

As Campbell recently pointed out, “some types of academic–industry relationships are an essential component of the research enterprise in the life sciences¹⁴. Empirical data show that more than half of academic scientists have such relationships, which most often involve consulting, receiving research funding, and providing scientific advice, and is most common amongst the most productive of investigators¹⁵.”

“Whether through direct sponsorship of research or through advising, such relationships facilitate the discovery of new drugs, devices, and other medical innovations that often result in the improved diagnosis, treatment, and prevention of human disease.”

Physicians have no incentive to learn about what's new in medicine unless what they currently work with is limited or ineffective, so that they desire to get their hands on something better. Indeed, the "clinical inertia" literature says that physicians resist change to better therapy even when they know and have reason to know that it is better. The idea that physicians mindlessly hanker after novelty and innovation, and that industry panders to this longing is not consistent with the facts.

Delayed Implementation of treatments

NIH's proposed rules also ignore the potential for patient harm by delaying treatment if researchers, scientists and physicians choose to leave academia or research altogether to avoid being labeled “unethical” for working with industry¹⁶. Consequently, if new procedures and therapies are not discussed and explored in research, or taught at CME activities or those activities fail to take place due to lack of support, patients will suffer greatly.

Forced reporting of a physician's participation with industry funded research, consulting, or a CME program, will cause fewer true leaders to participate in these programs. The expertise available to advise industry on drug development will be threatened, and on-label education will be deprived of some of the brightest and most engaging educators. Physicians need the freedom to strive to become leading researchers and educators in their field of expertise. Trying to mitigate the potential influence of “conflict” under these circumstances will only hurt patients and medicine.

Conclusion

ACRE believes there is value to physicians, medicine, medical education, and patients from the working relationship between physicians and industry¹⁷⁻²¹. There is no conflict in advancing science, and there is no conflict in providing the education that is required to do so. We request the provisions are not adopted yet, further discussion ensues, and offer to be active participants in an evidence based discussion.

By working together with industry colleagues, we can explain to the public that the contributions of corporations to medicine are, on balance, more beneficial than harmful and that both medicine and the industries that provide it with its technologies are worthy of public support. Cooperation, instead of antagonism, can help industry develop and market therapies with the highest integrity, by keeping physicians current on the best available evidence, and by providing excellent patient care.

Respectfully submitted,

The Association of Clinical Researchers and Educators

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