

VIEWPOINT

Confluence, Not Conflict of Interest Name Change Necessary

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The primary interest of the biomedical scientific endeavor is to benefit patients and society. Frequently, this primary interest coincides with secondary interests, most commonly financial in nature, at the interface of the investigator's relationship with a private sponsor, typically a drug or device company or, increasingly, venture capital firms. Academia and the public have become sensitive to how such a secondary interest might be unduly influential, biasing the interpretation of results, exposing patients to harm, and damaging the reputation of an institution and investigator. This concern has prompted efforts to minimize or "manage" such "conflicts of interest" resulting in a plethora of policies at both the local and national level. Although these policies are often developed in reaction to a limited number of investigators, once introduced, they apply to all. Given the broad array of stakeholders, the diversity of approaches, and the concern that such policies might restrain innovation and delay translation of basic discoveries to clinical benefit, the Institute for Translational Medicine

may be even more seductive than fortune. Thus, the outcome of a study may influence publication in a high-impact journal, invitations to speak at conferences, promotion, salary, and space. Even though an investigator may publicly eschew any direct financial reward from a sponsor, such fiscal and professional benefits may accrue to them indirectly from the institution, if they attract clinical trials with their attendant indirect costs. Estimation of how fame—which again may apply to institutions, funders, and journals—might introduce bias is a considerable challenge. However, even in the case of monetary gain, which can be readily quantitated, bias is complex.² A possible strategy is to consider a terrain-mapping approach to potential sources of bias. Much like a heat map of gene expression, a dashboard would express and give weight to elements of fame and fortune on the y-axis, charted against individuals and entities on the x-axis that are likely to gain from the endeavor. Experience would refine the approach over time. Disclosure of such information on institutional websites and its provision in consent forms to participants in trials would help the public to visualize the complexity of such relationships and aid individuals and institutions to promote confluence of primary and secondary interests with the objective of minimizing bias. Irrespective of such efforts, disclosure is necessary but insufficient; it can serve to mitigate, but not to avoid bias.

Third, the inventor of therapeutics and devices may be barred as a clinical investigator in the course of their development.

Here the potential for bias is substantial. In some cases, the emotional attachment of the inventor to a project may be a liability, restraining the ability to "fail fast." However, the inventor also might have a highly restricted skill set necessary to advance translation of the discovery from "bench to bedside." Hence, there is a move away from blanket exclusion to permitting engagement by the inventor in clinical development, conditional on additional oversight, to assure the public and to mitigate bias.

Fourth, the industry-academia interface has evolved as Big Pharma outsources much of its research and the biotech industry booms, much of it spawned by academic entrepreneurs. On the one hand, such developments represent a direct outcome of the Bayh-Dole Act. This legislation released patent rights of federally funded research from the government and reassigned them to investigators and institutions, freeing investigators to pursue commercialization of their discoveries. By design, this fostered public-private partnerships recognized as necessary

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and Therapeutics at the University of Pennsylvania recently convened an international meeting on conflict of interest.¹ Several themes emerged.

First, the term *conflict of interest* is pejorative. It is confrontational and presumptive of inappropriate behavior. Rather, the focus should be on the objective, which is to align secondary interests with the primary objective of the endeavor—to benefit patients and society—in a way that minimizes the risk of bias. A better term—indicative of the objective—would be *confluence of interest*, implying an alignment of primary and secondary interests. In this regard, the individuals and entities liable to bias extend far beyond the investigator and the sponsor; they include departments, research institutes, and universities. The potential for bias also extends to nonprofit funders, such as the National Institutes of Health and foundations, as well as to journals that might, for example, generate advertising revenue from sponsors.

Second, disclosure policies have focused on financial gain. However, in academia, the prospect of fame

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to the development of novel therapeutics and devices. In general, such engagement should be fostered in academia, for example, by recognition in the promotional process. However, although both partners are united in the desire to benefit patients, the private sector, but not academia, is also answerable to shareholders. Consequently, the interests of these partners may at times diverge. Just as universities foster relationships of their faculty with industry, their responsibility to the public interest behooves them to protect and ensure the independence of their faculty to disseminate the full spectrum of their discoveries, even when they may include uncomfortable truths for the sponsor. Institutions also have an obligation to be governed by their mission, rather than profit, and maximizing profit may not always serve that mission.

Fifth, education—of trainees, investigators, administrators, funders, publishers, politicians, and the public—is essential for progress. Academic institutions have a particular responsibility to inculcate, promote, and reward intellectual honesty in ways more imagi-

native and effective than in the past. Just as scientific discovery is celebrated by prizes and awards and election to societies and organizations, academia needs to celebrate examples of moral courage in the scientific endeavor. These might include predicting and revealing adverse events concealed or denied by industry sponsors or publicly disclosing inappropriate behavior by investigators or institutions. Faculty should be repeatedly educated in their ethical responsibilities, not just to their patients, but also to their students, their colleagues, and their institutions to minimize bias and to serve the primary interest of biomedical research. This might occur as part of the online requirements necessary to retain credentials to function as an academic investigator.

Confluence of interest represents a complex ecosystem that requires development of a uniform approach to minimize bias in clinical research across the academic sector. Such a policy must be at once simple and accessible, capturing the complexity of the relationships while being sufficiently flexible at the individual level not to intrude on the process of innovation.

ARTICLE INFORMATION

Published Online: September 24, 2015.
doi:10.1001/jama.2015.12020.

Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Cappola reports receiving consulting fees from Biomarin, Mannkind Corporation, and Takeda. Dr FitzGerald reports being the McNeil Professor of Translational Medicine and Therapeutics, a council member of the American Association for the Advancement of Science, and a member of the National Academy of Medicine biomarker committee; receiving a stipend for being co-chair of the advisory board for Science Translational Medicine; grants from the Harrington Family Foundation and Eli Lilly; consulting fees from Calico and Pfizer, Eli Lilly, Glenmark Pharmaceuticals, and

New Haven Pharmaceuticals; serving as chair for the Burroughs Wellcome Foundation review group on regulatory science awards, the Helmholtz Foundation advisory board for the network of cardiovascular science centers, and the PhD program committee of the Wellcome Trust, a section committee of the Royal Society; and serving on the advisory boards of the Oklahoma Medical Research Foundation and King's Health Partners in London. He also serves on the advisory boards of the Clinical and Translational Science Awards held by the University of Connecticut, Harvard, the Medical University of South Carolina, Duke University, and the University of California at San Francisco.

Funding/Support: This work is supported by a grant (UL1TR000003) from the National Institutes of Health.

Role of the Funder/Sponsor: The National Institutes of Health had no role in the preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

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