Bridging the Academia/Industry Chasm: Proposed Solutions

Paul Beninger, MD, MBA1,2, Marcia Boumil, JD, LLM1, Deeb Salem, MD3,4, Kenneth Getz, MBA5, Henry Klapholz, MD4, Gregory D. Curfman, MD6, Rohan Jotwani4, and Harris Berman, MD4

The New England Journal of Medicine recently published a series of articles revisiting the issue of financial conflicts of interest in medicine in the United States and their influence on medical decision making.1-3 The series, authored by Lisa Rosenbaum, a national correspondent for the journal, and introduced by an editorial from the journal’s editor-in-chief, Jeffrey Drazen,4 highlights the intense scrutiny that currently surrounds research collaborations between academic medicine and industry partners—relationships that are intended to lead to drug, biologic, and medical device discoveries and commercialization. In a 2006 landmark article in the Journal of the American Medical Association, Brennan et al describe the issue as follows:

Conflicts of interest occur when physicians have motives or are in situations for which reasonable observers could conclude that the moral requirements of the physician’s roles are or will be compromised. In terms of industry influences, financial conflicts of interest occur when physicians are tempted to deviate or do deviate from their professional obligations for economic or other personal gain. The bias thus introduced violates both the best interests of patients and the standards of scientific integrity.5

Rosenbaum, in a sharp departure from the prior policy of the NEJM that dates to the tenure of former editor-in-chief Arnold Relman, suggests that current conflict of interest principles may go too far, “thwart[ing] productive collaborations” and “stifling honest discourse.” She points out that physicians with ties to industry may nevertheless have important expertise and that if every physician with ties to industry is “shamed” or “silenced,” the advance of medicine will be compromised.6

In a blistering rebuke to the NEJM’s apparent about-face, specifically centered on the role of medical journals and industry relationships, 3 prior editors of the NEJM, writing in BMJ, described Rosenbaum’s contribution as “a seriously flawed and inflammatory attack on conflict of interest policies and regulations.” The BMJ authors accuse Rosenbaum of minimizing the “importance of conflicts of interest in medicine by publishing articles that show little understanding of the meaning of the term.”8 Noting that the articles contributed no new data and reasserting the 2009 position of the Institute of Medicine report that a perception of bias exists “whether or not a particular individual or institution is actually influenced,” they point out that improper industry influence is by its nature nearly impossible to quantify.6

While also citing no new data, the BMJ authors decline to acknowledge that the research climate has changed since their tenure, such that today academic

1Public Health and Community Medicine, Tufts University School of Medicine, Boston, MA, USA
2Genzyme, a Sanofi company, Cambridge, MA, USA
3Department of Medicine, Tufts Medical Center, Boston, MA, USA
4Tufts University School of Medicine, Boston, MA, USA
5Tufts Center for the Study of Drug Development, Tufts University School of Medicine, Boston, MA, USA
6Harvard Health Publications, Harvard Medical School, Boston, MA, USA

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Corresponding Author:
Marcia Boumil, JD, LLM Professor of Public Health and Community Medicine, Tufts University School of Medicine, 136 Harrison Avenue, Boston, MA
Email: marcia.boumil@tufts.edu
scientists have either left their academic positions for opportunities in industry" or have succeeded in sustaining active and productive research agendas through partnerships with and funding from industry.

Rosenbaum is not alone in broaching a contrarian perspective. Thomas Stossel has recently published a book-length treatise on the subject, in which he addresses the bright line presently separating academia and industry.8

So our intent here is to foster discussion, and encourage research in furtherance of the goal: specifically, how we can develop a new approach to conflict-of-interest rules that recognize the mutual interdependence of academia and industry, that acknowledge established principles of risk mitigation, and that also reflect today's fiscally challenging, clinical research environment.

Industry clearly benefits from the range of expertise provided by collaboration with academic clinical leadership; for example, identifying feasible clinical endpoints, developing scales and grading systems to measure clinical benefit, recognizing adverse drug reactions and new clinical syndromes, and providing expertise on institutional review boards, independent data monitoring committees (IDMC), and end-point committees.

Academia, likewise, benefits from the complementary strengths of industry partners through their efforts to develop, test, and commercialize new products, in addition to the salient effect that greater financial resources have on retention of talent. If adequate safeguards could be developed, industry would benefit from the academic community's perspective on the research, particularly as discoveries find their way into the Food and Drug Administration (FDA) regulatory process leading to commercial marketing.

The challenge, of course, is in proposing new rules. Academia/industry partnerships are fraught with inherent "competing" interests.1-4,8 Industry cannot ignore its for-profit mission and the demands of shareholders, whose primary objective is to maximize return on investment. Thus, judgments about promising discoveries, selection of human subjects, and product promotion are at risk of being overly influenced by industry's profit mission, and the patient-centered focus risks being compromised. The NEJM and BMJ articles highlight these concerns.

Although grievances between academia and industry are long-standing and have been well publicized,8,9 the parties must recognize that they are also fundamentally interdependent in terms of their strengths, interests, stakeholders, processes, and ultimate goals. Indeed, this interdependence suggests that continued medical innovation cannot be achieved without the involvement of both parties. The public sector has historically been the dominant contributor to basic research, but Industry must also be recognized as the primary contributor to discovery, manufacturing, laboratory and animal model testing, drug and biologic clinical development, and regulatory filings. Current economic exigencies thus press for consideration of an approach that fosters productive connections between academia and industry in the US market. Done well, industry/academia partnerships would invigorate technology and promise new discoveries without further escalating the controversy over conflicts of competing interests. Our goal is to construct a state-of-the-art framework to accommodate financial interests in a meaningful way, so that long-standing concerns about such collaborations are addressed with a system of checks and balances.

In developing such a framework, we begin with the "twin pillars" of risk mitigation, transparency and accountability, which continue to be recognized as key elements of the governance process. Defined, transparency is information that should be managed and published so that it is relevant, accessible, timely, and accurate. Examples are described in Table 1.

Defined, accountability is the demonstration that persons in a given organization are answerable for their actions, and there is redress when duties and commitments are not met. Examples are provided in Table 2.

Turning to potential solutions, the following may play a role, with further research needed to assess viability.

A Joint Venture (Transparency and Accountability)

In 1984, Braude15 proposed a joint venture of programs for the development of antimicrobial drugs that may seem prescient in light of today's global difficulties with epidemic and highly lethal (Ebola) or teratogenic (Zika) viruses and endemic multidrug-resistant pathogens, notably M. tuberculosis. The proposal articulated a comprehensive, systems-based approach that would put in place infrastructure for basic science, translational development, clinical development, training, and commercialization.

In response to the AIDS crisis of the 1980s, there are examples that predate the Physician Payment Sunshine Act by decades of successful multilateral collaborations that included academia, regulatory agencies (FDA, European Medicines Agency, others), industry, and patient groups: AIDS Clinical Trial Group16 and Oversight Committee for the Evaluation of Metabolic Complications of HAART.17

More recently, Fordyce et al described a program of multilateral partnerships to address the 2 decades of stagnation in drug development for cardiovascular disease.18 Likewise, this included the range of
stakeholders, although specific governance mechanisms were not discussed. Also recently, Agnandji et al described a highly collaborative, multilateral, coordinated effort involving parties from 3 continents to conduct a dose-escalation program to assess the safety and immunogenicity of a replication-competent recombinant vesicular stomatitis virus–based vaccine expressing a Zaire ebolavirus glycoprotein. This timely, extremely well-managed program was supported by public (multiple governments, public health agencies, and universities) and private (foundation and trust) sources.

What all these programs have in common is a focused, issue-driven agenda in need of urgent attention, collaboration of professionals with broad-ranging expertise, and multifaceted resources, which, together, are strongly reminiscent of the original concepts proposed by Braude. In addition, such efforts could help to restore, support, and even secure a threatened balance of talent between public and private sectors.

**Required Reporting (Transparency)**

Enacted in 1997 as part of the FDA Modernization Act, clinicaltrials.gov began the process of creating transparency mechanisms to enable the general public to learn about clinical trials in progress and to provide professionals with a summary of their results following completion. Several authors have noted variable compliance by both industry and the public sector, including academic medical centers, with reporting requirements. The National Institutes of Health (NIH), which funds but does not itself conduct large-scale trials, has recently extended its policy of required data sharing to include all interventional clinical trials, including those with negative results. Further, the Institute of Medicine has proposed recommendations that may mitigate corporate risk of sharing clinical trial data, including data use agreements and the establishment of independent review panels. In principle, this concept could readily be extended, as the NIH proposes for publicly funded studies, such that results of all clinical studies, including those funded by private sources, beginning from first-in-human, would be made available in a timely way.

### Independent Data Monitoring Committees, Also Known as Data Safety Monitoring Boards (Transparency and Accountability)

To preserve integrity and competence of a clinical trial, an IDMC draws its membership from independent experts with no direct study involvement and no conditions that might affect committee member impartiality. Transparency, in terms of access to complete data sets, and accountability, in terms of decision making about the status of the clinical trial, are essential to IDMC effectiveness. Professional access to participating IDMC membership largely depends on informal networks and apprenticeship to more senior and experienced members. It would be of significant value to industry to develop a pool of trained professionals from which industry could draw. Professional medical associations could make a substantial contribution in this area by providing broadly accessible training, for example, through daylong courses at national meetings, with periodic updates and refresher courses to their memberships and by setting credentialing standards.
Education (Transparency)

The examples cited have primarily been in response to acute crises that demanded immediate action and required collaboration. From a broader perspective, Stossel focuses attention on educational efforts of “rebut[ting] the unjustifiable assertions of the conflict-of-interest narrative” (p 53). However, it is likely that a deeper systemic, even culture-altering approach to the standoff is needed to sustain any desired changes. As a first step, there is an opportunity to include modules in the national medical school curriculum and residency training programs that identify and explain the many clinical and nonclinical roles that contribute to the drug/biologic development enterprise. A second step could be a series of national dialogues to deliberate the components of a thorough reconsideration of our approach to drug/biologic/device development.

In conclusion, such endeavors would not be without challenges. Mistakes, problems, conflicts, and other challenges should be expected and considered opportunities for building trust by developing greater understanding of the issues, gaining insights into the perspectives of other stakeholders, and for enhancing relationships for the long haul and the benefit of patients. Academia and the pharmaceutical industry have been at arm’s length for some time. The present financial pressures that are expected to continue on both sides favor an environment for developing creative solutions, such as giving an independent organization the opportunity to find common ground on which to build trust and to consider the multiple opportunities for developing collaborative paths of give and take that would benefit both as well as the patients they serve. The time for meaningful dialogue is upon us.

References