Conflicts of interest in biomedical research—the FASEB guidelines

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ABSTRACT **The rise in academia-industry relationships has been accompanied by increasing concerns about financial conflicts of interest. To date, policy recommendations addressing financial conflicts of interest have focused on the role of academic institutions in reviewing and overseeing investigator relationships with industry. However, investigators as a group determine the effectiveness of policies and practices. Therefore, there is a clear need for a consensus statement of standards for academia-industry interactions from the scientists' perspective. To meet that need, we propose conflict of interest guidelines for individual biomedical investigators to address the critical challenges faced when financial relationships with industry exist.—Brockway, L. M., Furcht, L. T. Conflicts of interest in biomedical research—the FASEB guidelines. *FASEB J.* 20, 2435–2438 (2006)**

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The vast majority of biomedical researchers are guided by the highest ethical and professional motives. However, the rise in academia-industry relationships has been accompanied by increasing concerns about financial conflicts of interest. These concerns include the potential for industry involvement to bias research, compromise efficient and wide dissemination of research results, delay trainee progress, harm human research participants, and decrease public trust in medical research (1–3). The distress has permeated both the media and Congress, and sparked discussions about expanding regulatory requirements for investigators.

Academia-industry collaborations can benefit society by leading to the development of new medical treatments, diagnostic tools, or other practical ramifications of the research. Academic scientists, administrators, and institutions carry out research and provide the benefit of their knowledge or intellectual property to industry. In return, they receive research support, honoraria, consulting fees, royalties, equity, and/or other payments. Investigators also benefit by interchanges with industry colleagues that facilitate the flow of knowledge and materials, increase productivity, and enable them to participate in the application of their research.

The scope and nature of industry-academia collaborations have increased in size and complexity (4, 5). As scientific questions become more complex, securing Federal resources to support the large-scale collaborative and interdisciplinary research needed to answer them becomes more difficult. Due to funding pressures, financial relationships with industry may become even more important for many academic investigators to achieve their research objectives.

NEED FOR GUIDING PRINCIPLES FOR INVESTIGATORS

To date, policy recommendations addressing financial conflicts of interest have focused largely on the role of academic institutions in reviewing and overseeing investigator relationships with industry (6, 7). But there is a clear need for a consensus statement of voluntary standards for academia-industry interactions from the scientists' perspective. To meet that need, we propose conflict of interest guidelines developed for individual biomedical investigators (**Table 1**). We are particularly concerned with the perspectives of investigators who work in the public interest in all research-based institutions, particularly academic and not-for-profit institutions.

The debate about academia-industry interactions in science and medicine is muddled by an unfounded and common assumption that there is an inextricable link between financial conflict of interest and wrongdoing. Our goal is to provide guidance to academic scientists to address challenges that may occur due to financial arrangements with industry, not to judge whether or not a real or perceived conflict of interest exists. By focusing on relationships and not conflicts of interest

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TABLE 1. *Guiding principles for investigators in academia-industry relationships*

- Investigators have a responsibility and commitment to conduct scientific activities objectively and with the highest professional standards.
- The primary responsibility of full-time investigators is to their institutions. Outside activities shall complement, not compromise, institutional responsibilities.
- Investigators shall have access to, and be involved in, the analysis and/or interpretation of all data generated in the research.
- Mutual understanding of constraints, principles, and policies regarding access, analysis, and dissemination of research information, data, and materials among investigators and their students and trainees, institutions, and sponsors is beneficial.
- Investigators shall not enter into agreements with companies that prevent publication of research results. Prepublication review by an industry sponsor shall occur in a timely manner (no more than 30 to 60 days) so as not to unnecessarily delay study publication.
- Investigators shall be aware of and adhere to individual journal policies on disclosure of industry relationships.
- Consulting and advisory board relationships shall be carried out in a transparent and accountable manner and be disclosed as they are initiated.
- When investigators have consulting relationships with investment firms related to their area of expertise, all parties shall be aware of the specific circumstances involved.
- Investigators shall not use federal funds to the benefit of a company, unless this is the explicit purpose of the mechanism used to fund the research (*e.g.*, Small Business Innovation Research and similar grants).
- When investigators own significant equity in a company with which research is conducted, all parties shall be aware of the special circumstances involved.
- When holding a significant role in a start-up company, investigators shall be guided by agreed-upon limits as to the scope of the relationship.
- Investigators shall be aware of and adhere to requirements of federal funding related to disclosure of inventions. Investigators shall adhere to patent law and institutional requirements. Investigators shall not seek to unduly influence their institution's technology transfer decisions for personal gain.
- A mentor's outside commercial interests shall avoid impeding a trainee's timely progress toward his/her degree, restricting a trainee's right to publish his/her dissertation research in a timely manner, compromising a trainee's career progress, or restricting a trainee's freedom of inquiry. Mentors and institutions should make trainees aware of their rights and responsibilities in industry relationships.
- Investigators shall regard all significant financial interests in research involving human subjects as potentially problematic and thus requiring close scrutiny.

per se, we hope to direct the guidance toward smart practices and other useful tools for scientists.

Investigators are individually responsible for maintaining accountability in their choices to enter into relationships with industry, complying with policies and requirements, and taking responsibility to guard against bias in research. The purposes of the proposed guiding principles are to:

- Help academic investigators become aware of potential challenges in academia-industry relationships (sufficient awareness may be lacking);
- Encourage ways for investigators to interact with their institutions to address these challenges (the variety of conflict of interest policies investigators must conform to may cause confusion); and
- Promote voluntary measures that guard against research bias and foster transparency and accountability.

MAJOR RECOMMENDATIONS

There is a wide variety of academia-industry relationships that individual scientists may have. We discuss the major categories below and recommend ways for academic investigators to address challenges that may occur due to the specific kinds of financial relationships they have with industry.

RESEARCH ACTIVITIES

When industry funds academic research, there is the allegation by some that scientific conclusions are favorable to industry (1). All academic investigators participating in research (industry-funded or not) have both a professional and public obligation to conduct unbiased research, and companies must always adhere to established good clinical practice standards (8). In addition, investigators should have access to and be involved in the analysis and/or interpretation of all data generated in the research. To avoid bias, investigators should establish a data analysis plan and research committee (in the case of multi-institution studies) or choice of a principal investigator and define their responsibilities prior to the start of the study (9). This will not only help coordinate data access and analysis, but ensure that data analyses are not being skewed to support conclusions favorable to industry. Academic investigators should always be aware of, and adhere to, agreed-upon

design elements, including patient inclusion criteria for enrollment in clinical studies.

Research success, promotion, and tenure for academic investigators depend heavily on openly presented and published research findings (as well as carrying out mentoring and teaching responsibilities). There is concern that commercial ties can undermine academia's commitment to such openness. Sometimes the need to publicly disseminate research findings, and the data and materials on which they are based, conflict with industry's need to restrict such access in order to develop a product. Investigators should not enter into agreements that prevent or unduly delay publication of research results.

It is common for industry to want to formally review a manuscript prior to journal submission to secure intellectual property rights. This should occur in a timely manner (ideally, within 30–60 days). While there may be circumstances that make this time frame impractical, an industry review time of more than 60 days should not become commonplace. In addition, once a study is published, academic investigators should make reasonable efforts to provide data and materials to other investigators for replication purposes. Investigators should also voluntarily disclose relevant industry relationships in publications and presentations. When in doubt, investigators should err on the side of transparency when communicating with other investigators and the public.

CONSULTING AND ENTREPRENEURIAL ACTIVITIES

In academia, experts in a particular scientific field or inventors of technologies often have the most expertise to help translate that technology into a useful product, and should be encouraged to do so. Investigator participation in entrepreneurial activities (*e.g.*, start-up companies) is translational research in its truest sense (10) and serves the public interest when managed appropriately. But investigators with dual roles (*e.g.*, research faculty and company consultant or founder) face unique conflict of interest challenges. It is important for such investigators to delineate their individual responsibilities up front and in accordance with a contract that defines the activities, the agreed-upon scope of the relationship, and the method of compensation with the collaborating private company. This contract should be altered accordingly as the relationship evolves with time.

Key to such a contract is specifying exactly how investigators are to be compensated for their industry activities and tailoring scrutiny according to the degree of risk each type of compensation poses. For example, equity—stock or options—is an important mechanism of compensation (particularly for small start-up companies) and can be an effective incentive. But it is important that investigators realize that equity poses greater conflict of interest challenges because it has a greater potential for financial gain than other forms of compensation, such as fees or research grants. Equity relationships also need diligent monitoring because the value of the compensation varies according to the perceived success of the company, particularly in publicly traded companies.

Consulting and entrepreneurial activities must proceed with transparency, accountability, and strict adherence to contracts that conform to institutional policies:

- Investigators should not prematurely communicate unpublished or nonpublicly discussed information regarding ongoing research studies, particularly clinical trials, to individuals or organizations other than to a company sponsoring those studies unless indicated by a Small Business Innovation Research or similar grant.
- Federal grantees must disclose inventions resulting from federally funded research to their institution as an obligation of the Bayh-Dole Act. Investigators should disclose inventions in a timely manner, as required, and not condone or participate in moving discoveries "out the back door" to companies with which they have a relationship.
- Patent law requires listing all collaborating inventors (including trainees). The criteria for an inventor are different from those for someone who might typically be included as an author on a paper, and this may be a source of confusion and tension. Investigators should be cognizant of these criteria.

ACTIVITIES AFFECTING TRAINING AND EDUCATION

Mentoring and educating trainees is an important and often primary responsibility assumed by academic investigators. Trainees may have a direct relationship with a company, such as a training or travel grant, or an indirect relationship through their mentor that supports their research. It is important to understand whether such relationships involve restrictions that might cause fewer publications or delays in publication of manuscripts and dissertations, as well as constraints in the type of research conducted. Mentors must ensure that trainees understand their rights and responsibilities in industry relationships prior to their involvement in order to make fully informed decisions. An investigator's outside commercial interests should never impede a trainee's research progress, career progress, or publication of research results.

ACTIVITIES AFFECTING HUMAN RESEARCH PARTICIPANTS

The most intense scrutiny of academia-industry relations focuses on risks to human research participants. High profile cases, such as the death of Jesse Gelsinger in a gene therapy trial at the University of Pennsylvania, highlight the need for protections. The potential risk to human research participants has created a consensus within the medical and scientific community to in-

crease attention to this issue. Clinical researchers have a special responsibility to ensure protection of research participants and patients against any negative consequences of financial relationships while maximizing the societal benefits of such interactions.

One of the core principles put forth by the Association of American Medical Colleges (7) is that institutions should regard all significant financial interests in human subjects research as potentially problematic and thus requiring close scrutiny. Clinical investigators should also be guided by this principle. Investigators with significant financial interests should not play a role in the research, absent very compelling circumstances. However, it may not be in the best interest of the public when the excluded investigator has the most knowledge and expertise to carry out the study. For example, the excluded researcher may be a surgeon who has developed a unique surgical technique. Thus, all risks and benefits of excluding conflicted researchers should be weighed and considered in each case. In addition, investigators should understand that many institutional review boards may require that relevant financial relationships be disclosed to patients and human research participants (11). How and when this is done needs to be determined.

SHARED RESPONSIBILITY AND INDIVIDUAL INTEGRITY

Academic institutions, industry, government, professional associations, journals, and investigators need to share responsibility to meet conflict of interest challenges. Our recommendations rely greatly on the observation that institutions attempt to fairly and diligently review and oversee investigator relationships with industry. How well or uniformly they may do this across the country, however, may be something that needs greater attention by university leadership. In addition, timely oversight and avoidance of undue bureaucratic delays are critical so as not to impede research progress. Therefore, the proposed guiding principles should be used to complement and improve, not substitute, for any requirements from institutions, government, and journals.

Federal regulations give institutions the flexibility to be responsive to specific circumstances regarding industry collaborations with academia. While this is important, we urge that some uniformity of policies, particularly disclosure requirements (4), among others, would be beneficial for investigators. The scientific community and the academic leadership community should continue to study the effectiveness of their conflict of interest policies and practices, and strive to balance the need for more common standards with preserving case-by-case analysis and situational-driven decision-making, when warranted. Investigators must be involved in these discussions because investigators, as a group, determine the effectiveness of policies and practices.

Many important benefits are derived from scientific collaborations between academia and industry. But investigators should ask themselves if they would be able to adequately defend their industry collaborations if they were publicly questioned (*i.e.*, the "headline test"). Individuals may decide not to enter into a relationship with industry based on their own analyses of benefits and risks, and this type of assessment is encouraged. With careful disclosure and oversight, investigators can minimize or eliminate the risks of such collaborations while maximizing the benefits to the scientific community and public. Failure to do so could have damaging effects on the future of the scientific enterprise. FJ

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