

MEETING PROCEEDINGS

**Call to Action:
Managing Financial Relationships between
Academia and Industry in Biomedical Research**



**July 17, 2007
Washington, D.C.**



Federation of American Societies for Experimental Biology



Executive summary

The Federation of American Societies for Experimental Biology (FASEB) has issued a call to the scientific community to adopt more consistent policies and practices for disclosing and managing financial relationships between academia and industry in biomedical research. On July 17, 2007, a framework for a national guideline was put forward at a meeting¹ of more than 75 representatives of scientific societies and other key stakeholders².

The FASEB framework is based on three guiding principles: 1) investigators must conduct research activities objectively; 2) operate with transparency; and 3) be accountable to all stakeholders. A Conflict of Interest (COI) Toolkit website

(<http://opa.faseb.org/pages/Advocacy/coi/Toolkit.htm>) was launched that contains recommendations to achieve these principles and improve the management of academic-industry relationships and promote investigator education. It is intended to serve as a platform for the community to share information and practices.

Delivering the keynote address at the meeting, Congresswoman Diana DeGette (D-CO) described concerns about COI by the public and Congress. Eric G. Campbell (Harvard) presented data on the scope of academic-industry relationships, benefits and risks, and policy implications. James A. Severson (University of Washington) discussed the intersection of technology transfer and financial conflicts of interest. Norka Ruiz Bravo (National Institutes of Health (NIH)) described NIH's role in ensuring objectivity in research funded by the agency. Susan Ehringhaus (Association of American Medical Colleges (AAMC)) highlighted AAMC's activities addressing conflicts of interest in clinical research and education. Catherine D. DeAngelis (Journal of the American Medical

Association) discussed how conflicts of interest impact the publication of research results and the need for transparency.

Participants in the meeting expressed support for a set of common principles and guidelines that they could use to help better manage financial relationships between academia and industry. While Public Health Service (PHS) and National Science Foundation (NSF) regulations exist, more consistency in some areas of policies and practices would decrease confusion and noncompliance by investigators. Consistency would be especially beneficial in research that is funded by multiple sponsors and in cases when some investigators are not covered by the PHS or NSF regulations.

The ability to reach the scientific community is the strength of the FASEB effort. Participants indicated that the COI Toolkit could be important for investigator education and might be used in a targeted manner, for example, for institutional COI committee members or when trainees are involved. While investigators support more consistent policies and practices, implementation hinges on the ability of scientists and other stakeholders to work together. Institutions develop and enforce policies for their investigators. Editors develop disclosure policies for authors. Scientific and professional societies have a role in promoting professional ethics. Industry should help to ensure collaborating investigators are in compliance. As a first step, the community might work towards more consistent disclosures.

FASEB will continue to develop the COI Toolkit based on feedback and continue to work with interested organizations towards implementation.

This work was funded by a grant from the *Association of American Medical Colleges – Office of Research Integrity Responsible Conduct of Research Program for Academic Societies*.

¹ Meeting agenda is at: <http://opa.faseb.org/pdf/July17CalltoActionAgenda.pdf>

² List of participants is at: <http://opa.faseb.org/pdf/July17CalltoActionParticipants.pdf>



Call to Action and “COI Toolkit”

LEO T. FURCHT, M.D.

Past President,
Federation of American Societies for
Experimental Biology (FASEB)

Leo Furcht is the Immediate Past President of FASEB, a biomedical research advocacy organization with over 80,000 members and 21 constituent societies. Prior to this he served as Vice President for Science Policy when he began leading the FASEB program on conflict of interest in biomedical research. He is Allen-Pardee Professor and Chair of the Department of Laboratory Medicine and Pathology at the University of Minnesota. He also serves as Chairman of the Board of Directors for University of Minnesota Physicians, the Medical School practice plan at the University of Minnesota with approximately 700 physicians. For a three year period in the 90's he served as Vice Provost for Research of the University of Minnesota Health Sciences and established a research services organization to provide turn key solutions for faculty and companies to get clinical trials facilitated. He is currently serving on two Association of American Medical Colleges/Association of American Universities task forces working on issues on academic-industry interactions in medical education and clinical research. He is from New York City, completed undergraduate and pre-medical studies at Columbia University, received his MD at SUNY Upstate, and did residency training at Minnesota where he has been on the faculty since. He has published over 175 scientific papers. Dr. Furcht has more than 30 patents, founded a series of companies, and has a drug in development that should be reviewed for Food and Drug Administration approval this year.

WELCOME AND OPENING REMARKS

The benefits of joint research relationships involving academia, industry and government are numerous. They facilitate research and bring resources to the battle against disease. Academic scientists benefit through enhanced resources for their research, participation in the application of their research, and collaborations that might not otherwise be available. However, the increase in number and complexity of these relationships has been accompanied by concerns about financial conflicts of interest that pose challenges to the integrity of research and the public trust on how financial relationships are being managed at institutions.

The Federation of American Societies for Experimental Biology (FASEB) believes that maintaining the public trust and assuring the integrity of research is of the highest importance. FASEB's objectives are to promote a national guideline for the disclosure and management of financial relationships and promote investigator education.

Speakers will discuss their perspective on this issue. FASEB's work that aims to promote a national guideline for the disclosure and management of financial relationships between

academia and industry will be presented. A group discussion will follow the presentations.

BACKGROUND

Academic-industry relationships are beneficial, but challenges exist. Having financial interests in companies related to research does not equal impropriety. The vast majority of biomedical researchers are guided by the highest ethical and professional motives, and scientists want to do the right thing. Investigators, as a group, to the degree they adhere to policies, speak to the effectiveness of policies and practices. Much of the work that had been done on conflicts of interest (COI) in the past focused on institutions' roles but the perspective of investigators had not been well-articulated in the policy debate.

FASEB began working on this issue three years ago. A committee developed guidelines that articulated the issue from the investigators' perspective and these were published December 2006 in *The FASEB Journal*. This article identified challenges facing investigators such as: ensuring compliance with requirements, protecting against bias, addressing issues about data and material access, analysis, and dissemination of results, addressing overlap of roles (such as company founder and faculty researcher), and protecting



trainees/mentorship. The purpose of the guidelines was to help individual investigator decision-making regarding these challenges.

CURRENT EFFORT

Funding by the *Association of American Medical Colleges – Office of Research Integrity Responsible Conduct of Research Program for Academic Societies* allowed FASEB to continue work in this area.

Objectives

Two underlying factors contribute to the challenges for investigators identified in the first FASEB report. First, a lack of clarity and consistency in some areas may cause confusion and noncompliance particularly by institutions. Second, sufficient awareness of these issues on the part of investigators may be lacking. To address these concerns, the current effort has two objectives:

- Promote national guidelines for the disclosure and management of financial relationships between academia and industry in biomedical research
- Increase awareness and promote investigator education

Coalition and advisors

FASEB convened a coalition of stakeholders and experts to develop principles, recommendations, and an action plan to implement them. This activity built on previous work of FASEB, Association of American Medical Colleges (AAMC), Association of American Universities (AAU), Council on Governmental Relations (COGR) and others. The coalition identified three guiding principles and a recommended development of a Toolkit to include practices and tools that may be used to achieve the principles. The purpose of the Call to Action Meeting is to discuss the recommendations and seek feedback from the broader community. Next steps are continued communications to seek feedback and modify the Toolkit.

The following were members of the coalition of advisors:

- Leo T. Furcht, M.D., Coalition Chair and FASEB Past President, Allen Pardee Professor and Head of Lab Medicine and Pathology, Univ. of Minnesota School of Medicine
- Carol Blum, Ph.D., Director, Research Compliance and Administration, Council on Governmental Relations

- Eric G. Campbell, Ph.D., Associate Professor, Institute for Health Policy, Harvard Medical School
- Gail Cassell, Ph.D., Vice President, Scientific Affairs and Distinguished Lilly Research Scholar for Infectious Diseases, Eli Lilly and Company; Representing American Society for Microbiology
- Tony DeCrappeo, President, Council on Governmental Relations
- Susan Ehringhaus, J.D., Associate General Counsel for Regulatory Affairs, Association of American Medical Colleges
- Ezekiel Emanuel, M.D., Ph.D., Director, Dept. of Clinical Bioethics, National Institutes of Health
- Mark S. Frankel, Ph.D., Director, Scientific Freedom, Responsibility and Law Program, American Association for the Advancement of Science
- Joan Goldberg, Executive Director, American Society for Cell Biology
- Todd Margolis, M.D., Ph.D., Chair, Commercial Relationships Committee, Association for Research in Vision and Ophthalmology, Director, FI Proctor Foundation-Ophthalmology, University of California-San Francisco
- Barbara Perry, Senior Counselor of Congressional Affairs, NASULGC and Associate VP and Director of Federal Relations, University of Washington
- Lawrence J. Rhoades, Director, Division of Education and Integrity, Office of Research Integrity
- Norka Ruiz Bravo, Ph.D., Director, Office of Extramural Research, National Institutes of Health
- Janet Shoemaker, Director, Public Affairs Office, American Society for Microbiology
- Nicholas Steneck, Ph.D., Consultant, Office of Research Integrity and University of Michigan
- James A. Severson, Ph.D., Vice Provost of Intellectual Property and Technology Transfer, University of Washington

Guiding principles

The following three guiding principles represent a framework for a national policy guideline: 1) investigators must conduct research activities objectively; 2) investigators must operate with transparency; 3) investigators must be accountable to all stakeholders.



Practices

Recommended practices to help achieve these principles were developed. For investigators, these practices focus on compliance with requirements and voluntary practices to ensure objectivity, transparency, and accountability. For example, investigators are responsible for compliance with requirements and ensuring research objectivity. They have an obligation to trainees and patients. In sponsored research, investigators are responsible for data collection, analysis, and publication with no undue delays. Consulting and entrepreneurial activities should have a defined scope and compensation with scrutiny tailored to degree of risk each type poses (e.g., equity causes greater concern). Investigators must adhere to patent law and disclosure to institution of inventions and co-inventors. Investigators must disclose as required but transparency is enhanced by voluntary disclosure.

Recommendations for institutions and publishers focus on harmonization of policies and practices to avoid confusion and ensure compliance. Specifically, they should work towards more consistent disclosure requirements and replace the term “financial conflicts of interest” with “financial interests” when appropriate.

Professional societies and organizations should embrace their role in promoting research ethics for their members. Finally, industry has a role insuring that collaborating investigators are in compliance.

COI Toolkit

The COI Toolkit highlights recommended practices, tools, and resources developed by FASEB and others that may be used by the community to better navigate financial relationships between academia and industry. It is a freely available, online resource, hosted and maintained by FASEB and will be improved upon over time based on use and feedback from the community. The Toolkit can be accessed at:

<http://opa.faseb.org/pages/Advocacy/coi/Toolkit.htm>

CALL TO ACTION

FASEB aims to have organizations: 1) endorse the concept of a national guideline for the disclosure and management of financial relationships between academia and industry based on the principles of objectivity, transparency, and accountability; 2) implement practices that can be

used to accomplish these principles; and 3) link to the Toolkit from their website, submit materials for inclusion in the Toolkit, and provide ideas on how it might help develop organization’s activities.

SHARED RESPONSIBILITY, INDIVIDUAL INTEGRITY

The scientific community has a shared responsibility to ensure public trust in research. All stakeholders are in this together. We should not allow ourselves to be subject to questions about ethics. Those responsible for the review and oversight of academic-industry relationships should work together to develop more clear and consistent policies and practices. Investigators should be individually accountable for making choices, to comply with policies, and to take responsibility to protect against the risks. In the end, the goal is to enhance public trust in the biomedical research enterprise.

DISCUSSION

- Comment from participant: One practice that has worked to support disclosure in presentations (research presentation, grand rounds, etc.) is having the second slide always as the “disclosure slide.”
- Question: What is the plan for implementation? Dr. Furcht: The ability to reach the scientific community is the strength of the FASEB effort. But implementation hinges on the institutional community and the ability of scientists and others to work together. Consensus by institutions is needed to improve clarity for investigators. Investigators can make recommendations but institutions have the ability to enforce rules.
- Comment from participant: The Toolkit will be very helpful in educating faculty especially investigators from other countries and key personnel on grants. The term “conflict of interest” raises alarm for many investigators, so changing the terminology to “financial interest” would be helpful.
- Comment from participant: The chemical industry is important because it supplies biomedical science. These issues are the same that chemistry is facing.



- Question: What will be the definition of success (e.g., if professional societies accept and incorporate, avoidance of Congressional action, etc.)? Dr. Furcht: Moving this issue forward to develop better approaches at levels to respond to challenges of academic-industry relationships. Measure of success is advancing human health. COI brings an element of fear of public acceptance of relationships. This is new territory but there is immense opportunity.

- Comment from participant: I have some discomfort with the concept of “uniform national guideline” because there is a need to examine investigators’ and institutions’ accountability within their environment. We should find out if or why the Public Health Service and National Science Foundation guidelines are not working as well as it can and bring people comfortably into compliance.

Biomedical research and the public trust

CONGRESSWOMAN DIANA DeGETTE (D-CO)

Democratic Chief Deputy Whip and
Vice Chair, Energy and Commerce Committee,
U.S. House of Representatives

Representative DeGette is currently serving her 6th term in the U.S. Congress representing the First District of Colorado. She is the Vice Chair of the powerful House Committee on Energy and Commerce, an exclusive congressional committee with vast jurisdiction over health care, trade, business, technology, and consumer protection. She was promoted to the House Democratic leadership as Chief Deputy Whip in 2005. Rep. DeGette is committed to improving health care and expanding medical research. She has become one of Congress’s leading experts on cutting-edge scientific research and is the author of the Stem Cell Research Enhancement Act that would overturn President Bush’s ban on embryonic stem cell research.

PUBLIC TRUST IN BIOMEDICAL RESEARCH

In recent years, the public’s trust of the safety and efficacy of biomedical research has diminished. This trust has been tested in part by high profile cases resulting in harm or death to patients because it appeared that financial interests had higher priority than the public’s health. For example, Vioxx was taken off market when it was discovered scientists had not included critical findings in study results. In the case of Ketek, safety problems were hidden by the manufacturer until revealed by a Food and Drug Administration (FDA) investigation. Sanofi-Aventis (maker of Ketek) should have alerted the FDA but failed to do so. The House Energy and Commerce Subcommittee held hearings on conflict of interest (COI) cases at the National Institutes of Health (NIH).

While such cases of COI may be relatively rare, even the rare cases need to be prevented especially given the decline in recent public trust. Scientists who are entrusted with taxpayer dollars must answer to their institution and protect its integrity.

What they need to remember is that their work provides hope for many Americans who are ill or taking care of a family member with an illness. Even rare cases capture the public’s attention and decreases trust. COI or the appearance of COI can have devastating effects.

NEED FOR STANDARDS

The NIH issue was largely resolved by a revision of intramural ethics guidelines. The community needs to continue to be vigilant. While the NIH rule is not perfect, the public needs these types of measures in place even though some NIH scientists feel that some aspects of them are overly restrictive. When people see that universities have NIH grants, they expect this work is done in the public interest. Government, academic, and industry scientists must work together to protect the public and assure that there is trust in the research base by addressing the issue of financial COI.

A related issue includes FDA legislation passed by the House and Senate last month that contains COI provisions. These bills would discourage



inclusion of individuals with vested interests in a drug review from serving on advisory committees and prohibit voting on any matter in which they have an interest. Later this year, a human subjects research protection bill will be reintroduced that attempts to harmonize the Common Rule and FDA regulations which govern most of the clinical research. It would also mandate that Institutional Review Boards (IRB) members disclose COI.

The goal of these efforts is to ensure the integrity of research by creating more consistent standards. By doing so, it is more likely that ambiguity and confusion can be avoided. It is hoped that Congress will continue to standardize rules and management across agencies. Investigators whose research is funded by multiple agencies would benefit from some standardization of COI policies and procedures.

There has been too much time spent arguing the semantics of various COI rules. We need clear guidance. The onus should rest on industry and academia to work together to create more explicit guidelines. COI guidelines vary by state and by institution. Collaborations across state lines and between institutions make it even more imperative that COI standards exist. Without such standards, we run the risk of further confusing the public about the integrity of research and exacerbating their distrust.

The public is placing ever increasing demands on the health industry to develop technologies to treat diseases and conditions. By pursuing these endeavors, we must not shortchange ethical values and the public's health. The community should continue to address these issues and develop overriding principles.

DISCUSSION

- Comments from participant: Full and adequate funding of FDA is urged so the agency has the resources to do everything to protect the public. Rep. DeGette acknowledged that she and other House Energy and Commerce members are acutely aware at how much the FDA is underfunded but pointed out the current budgetary constraints.
- Question: To what extent is Congress interested in developing legislation regarding extramural researchers COI? Rep. DeGette: It would have been difficult for Congress to legislate the changes to the NIH ethics rules and commended Dr. Zerhouni's steps from within. Similar to the Congressional ethics rules, sometimes it is necessary to go above and beyond expectations to regain public trust.
- Comment from participant: The pendulum must not swing too far in the wrong direction at a time when industry is struggling to provide new therapies. Knowledgeable individuals are needed to do the peer review for FDA and NIH.
- Rep. DeGette commented that institutions, NIH, and FDA have coordinated quite well on research and ethics standards (e.g., Common Rule). However, it might be important to look at the differences between industry procedures and institutional rules regarding management of these relationships.
- Question: Does Congress plan to review the Bayh-Dole Act? Some argue that Congress helped create COI problems because Bayh-Dole creates financial incentives. Rep. DeGette: No changes are expected in the near future, but it needs to be continually examined.



Partnerships in science: academic-industry relationships

ERIC G. CAMPBELL, Ph.D.

Associate Professor, Institute for Health Policy,
Harvard Medical School and
Massachusetts General Hospital

Eric G. Campbell is Associate Professor at the Institute for Health Policy and the Department of Medicine at Massachusetts General Hospital (MGH) and Harvard Medical School. One of his main research interests lies in understanding the effects of academic-industry relationships on the process and outcomes of biomedical research. Dr. Campbell reported he has no relationships of any kind with any firm whose products or services relate to the life science research enterprise. Research funding is provided by NIH and the Greenwall Foundation. His comments do not represent the views of the Institute for Health Policy, MGH, or Harvard Medical School.

Academic-industry relationships (AIRs) are defined as arrangements between academic researchers and institutions and industry in which something of value is exchanged. Examples include research relationships (e.g., grants and contracts), consulting, licensing, equity, training, and gifts (e.g., food and equipment). AIRs are a fundamental part of the modern life science enterprise. They have both benefits and risks. The challenge is to disclose them, ban the ones that are inappropriate, and manage the rest. Policies and procedures related to the disclosure and management of these relationships should maximize the benefits and limit the risks. Failure to do so could have dire consequences for the future of the life science enterprise.

SCOPE OF AIRs IN THE LIFE SCIENCES

Faculty members

Data from 1995 show that 60 percent of faculty served as consultants, 43 percent received research related gifts, 28 percent received research funding from industry, and nine percent owned equity in firm(s) related to area of scientific expertise. In total, 79 percent of faculty researchers had at least one type of AIR related to their research or area of expertise.

Institutional Review Board (IRB) members

A recent survey of IRB members of the largest academic research universities in the U.S. revealed that 36 percent of IRB members had at least one type of AIR. Twenty-six percent received research funding, 17 percent received payments for attending meetings, 14 percent served as consultants, 14 percent served on a speakers bureau, 10 percent

served on a scientific advisory board, seven percent received support for students, and two percent served as an officer or executive.

Forty-three percent of IRB chairs had at least one type of AIR. Twenty-nine percent received research funding, 17 percent received payments for attending meetings, 17 percent served as a consultant, 12 percent served on a speakers bureau, 17 percent served on a scientific advisory board, seven percent received support for students, and one percent served as an officer or executive.

Physicians

A recent survey of physicians showed that 94 percent of physicians had at least one type of AIR. Seventy-eight percent received drug samples, 83 percent received food and beverages, 35 percent received reimbursements for meetings, 18 percent received consulting payments, 15 percent served on speakers bureaus, nine percent served on advisory boards, and three percent received payments for enrolling patients in clinical trials.

BENEFITS AND RISKS OF AIRs

Benefits

Academic-industry relationships provide increased resources and funding for academic research (\$1.5 billion in 1995). They are associated with increased academic productivity. For example, industry-funded scientists publish significantly more articles in high-impact journals. They are associated with increased commercial productivity in the form of patent applications, granted patents, licenses, startups, and products of the market. AIRs provide increased support for students. They provide the opportunity for academic investigators



to participate in application of research. It is thought that the personal financial gain helps to offset the wage differential between industrial and non-industrial sectors that will assist in recruitment and retention of academic scientists and administrators.

Risks

Scientists funded by industry are more likely to delay publication of results, deny other scientists access to their data, and participate in trade secrecy. Scientists with industry ties are more likely to work on projects that have commercial potential. Thus, AIRs may shift focus of academic science away from basic research. Relationships have the potential to bias research. For instance, research has shown that studies funded by industry are significantly more likely to have results that appear to be favorable to industry. AIRs are associated with increased management and negotiation costs. There is increased public skepticism and the perception of being “bought out.” Finally, they have the potential to pose risks to patient safety. For example, approximately 17 to 20 percent of IRB members with AIRs voted on proposals from companies with which they had a relationship.

DISCLOSURE AND MANAGEMENT

Need for more consistent disclosure policies

Disclosure is the first step. It is not a panacea, but it is important. Some form of annual disclosure for faculty is the norm in academia, but disclosures differ greatly between institutions and states. There are elements of policies that could be standardized which would make the process of disclosure easier for investigators. The development of common disclosure policies and procedures that apply to all faculty and administrators in all institutions receiving federal funds would be beneficial. All relationships at the institutional level should be disclosed and managed.

Need for more consistent review and management practices

There is also variability in review and management of AIRs. Institutions ban some relationships, but there are no agreed-upon guidelines or rules for what is acceptable and what is not. In general, investigators cannot hold equity in company and conduct clinical trials sponsored by that company. Some institutions have banned gifts

to individual scientists. We need to aggressively manage relationships in accordance with policy by establishing monitoring boards.

Implications for the future

Too often, debates about COI in research are based on anecdote and allegation and not the research in this area. The community needs to stop the “spin” (the extreme opinions on both sides) and meet in the policy middle. Some have proposed banning all relationships. Relationships should be preserved because they can have tremendous benefits, but not all relationships are acceptable either. The extremes are not helpful in terms of developing policy. Institutions should develop and implement policies and procedures that assist faculty members in making good decisions about AIRs. Mechanisms are needed to share experiences so others may learn. We also need to educate the public, elected officials, faculty, and industry representatives.

CONSEQUENCES FOR THE FUTURE OF THE LIFE SCIENCE ENTERPRISE

Failure to effectively manage these relationships will result in continued scandals, compromised academic values, concerns about human subjects protections, increased governmental regulation, failure to capitalize on public investment in life science research, and loss of public support for academic science and industry.

DISCUSSION

- Question: Why were data from life sciences presented and not other disciplines? Dr. Campbell: Data on faculty in life sciences were presented because funding has not been available to study AIRs other disciplines.
- Comment from participant: It is beneficial for advancing science and public health when the best and brightest academic scientists provide consultation to industry. But they should not be expected to work for free. Advice is needed by industry and faculty should be compensated. Broad sweeping bans are not beneficial.
- Comment from participant: Development of new drugs and devices would be hindered if there were no bi-directional flow of knowledge. The



competitive advantage of the U.S. is a result of interactions between academia and industry.

- Comment from participant: In some companies, grant-making is done by medical staff

with no input from marketing and that separation is important.

Managing financial relationships: a technology transfer perspective

JAMES A. SEVERSON, Ph.D.

Vice Provost of Intellectual Property and
Technology Transfer, University of Washington

James A. Severson is Vice Provost of Intellectual Property and Technology Transfer at the University of Washington. He is responsible for UW TechTransfer, the unit of the University that seeks to enhance the public-service mission of the university by creating partnerships that result in investment in the development of commercial products and services from innovations generated at the university. The University of Washington receives more federal research funding than any other public university and has one of the largest operations for commercializing its faculty inventions. He is Past President of the Association of University Technology Managers and is currently a Board Member for the Council on Governmental Relations.

Traditional roles of academic institutions are changing in part due to state initiatives to promote technology transfer and regional economic development. Technology transfer activities create academic-industry relationships (AIRs) for which financial COI need to be addressed. Tools that can help guide and educate researchers about COI are beneficial to identify, review, and manage these relationships.

TECHNOLOGY TRANSFER AND THE CHANGING ROLE OF ACADEMIC INSTITUTIONS

Roles of academia and industry

Traditional roles for government are funding basic research, making tax policy, and providing infrastructure. Universities perform most of the basic research and train students to enter the workforce while industry performs most of the applied research and develops products.

Changing roles of academia are evident by the increase in interdisciplinary research and emphasis on commercialization. A number of states have pursued strategies to enhance competitiveness and job creation that have focused on research and the transfer of discoveries made at research institutes. These state-based programs directly sponsor research, encourage investment in early-stage

companies, encourage collaboration, and provide assistance to early-stage companies. Academic technology transfer operates at the interface of university and industry roles and seeks to move new and useful technologies from academic laboratories into industry product development programs.

A technology-based economy

Elements of a technology-based economy include strong intellectual infrastructure, efficient mechanisms to transfer technology between people and institutions, excellent physical infrastructure, highly skilled technical workforce, sources of capital, and an entrepreneurial culture.

States encourage economic development as a mission of universities. The goals for states are competitiveness and job creation.

Ways that universities partner with industry

Universities partner with industry in a number of ways, such as student training, faculty consulting, research sponsorship, collaborative research and consortia, technology licensing, and exchange of research materials and gifts.

It is a challenge for institutions when companies interact with them as businesses. Academic institutions are much different especially with regard to the freedom institutions give investigators to pursue outside activities. AIRs are unique types of relationships.



ADDRESSING CONFLICTS OF INTEREST

Key theme: Nothing works as well as faculty helping other faculty.

Council on Governmental Relations (COGR)

COGR represents more than 160 research universities and research institutions and provides an interface with federal agencies to clarify regulations and to educate about the burden of regulation on research enterprise. There is a high degree of training and education amongst their members. Past COGR initiatives in this area include development of documents for individual and institutional conflicts such as “21 Questions about Technology Transfer” (found at www.cogr.edu) which addresses issues such as objectivity, technology transfer, and conflicts of interest. The academic community recognizes the importance of addressing AIRs in a responsible manner. COGR has collaborated with FASEB on this issue from the beginning, and COGR endorsed the FASEB project.

Stanford meeting

A meeting of institutional officials (“Stanford meeting”) produced a document, “Nine Points to Consider in Drafting Technology Licenses” that discusses the role of universities in anticipating and helping to manage technology transfer-related conflicts of interest.

Washington’s Ethics in Public Service statute

Insight can be gained from Washington’s “negative” experiment (discouraging AIRs in research). In the 1990’s a broad state-wide ethics act was enacted by the state legislature. As agencies of the state of Washington, this act applied to the state universities and with time it had a chilling effect on the interactions of university faculty with businesses. In 2005, an initiative spearheaded by the state-wide alliance of technology companies and the state universities worked with the governor’s office to pass a revision of the act that allows the universities to use the standards established by the NIH and NSF for their technology transfer activities. The new rules that the law enabled are currently being implemented.

CONCLUSIONS

Academic technology transfer is at a challenging interface that has become an integral part of the research university. It is important to balance the varied expectations of faculty, universities, trustees with those of the local business community and government.

Technology transfer offices help create and manage relationships but not judge them. Technology transfer should provide accurate and timely information so that the institutional officials who review and manage them can do their job. Anything that provides clarity and consistency is important, and the FASEB project is a step in that direction.

DISCUSSION

- Question: What are challenges in improving AIR management? Dr. Severson: One of the biggest challenges is timely and efficient disclosure. At the University of Washington, both significant financial interests and outside work requests are sent to a single individual for review and development of a management plan. But it does not have to be a linear process. For example, we encourage investigators to disclose any financial relationship that they might have in a specific transaction to the institution while the technology transfer staff is negotiating a license that might create a financial conflict. Clarifying and streamlining is important so that beneficial relationships can move forward in a timely fashion. Also, tension arises when there is disagreement on values, which is inevitable because many of these situations are judgments made by people.

- Question: How much help is provided from industry for education of these issues? Dr. Severson: The support and initiative of the Washington Technology Alliance to help change the state Ethics Act is a good example of how the business community can play a role. A task force assembled by the Technology Alliance collected information both in the state and from other states and worked with the research universities to draft a bill that provided universities with additional flexibility in rule-making to cover these situations.



Ensuring objectivity in research

NORKA RUIZ BRAVO, Ph.D.

Deputy Director for Extramural Research,
National Institutes of Health (NIH)

Norka Ruiz Bravo is the NIH Deputy Director for Extramural Research. The Office of Extramural Research is the NIH focal point for the oversight, of tools, policies, guidance and operations needed to administer and manage NIH grants, including the roles and responsibilities of grantee institutions and their compliance with policies and regulations.

Research objectivity is of paramount importance to the NIH, scientists, and to institutions and the public. Conflict of interest (COI), which can compromise research objectivity, is multidimensional and complex. Investigators and institutions proactively seek ways to address these difficult conflict of interest issues and ensure objectivity in research, which is critical to maintain the public's trust.

RESEARCH MUST BE CONDUCTED OBJECTIVELY

It is critical that research decisions are based on scientific evidence and not on inappropriate influences. Only by conducting research with objectivity, integrity, and transparency will we maintain the public's trust. And without the public's trust, significant investments in research will not be supported -- and important biomedical discoveries will not be made. The scientific community must remain mindful of COI issues.

COI IS MULTIDIMENSIONAL AND COMPLEX

COI issues are rarely simple and most often are multidimensional and complex. For example, COI can be actual or apparent, personal or financial, or a combination of two or more of these characteristics. And COI can affect a number of important areas, such as research, education, and clinical practice. To avoid pitfalls, investigators must know the rules that pertain to COI and be cognizant of its many manifestations.

THE RULES

The NIH has regulations and policies that govern relationships between private enterprise and NIH staff, NIH advisors (e.g., peer reviewers, council

members, and other advisors), and NIH grantees and contractors. Ensuring objectivity drives NIH COI policies. Overall however, balance is important. In crafting and implementing COI regulations and policies, NIH has strived to preserve the public good that results from interaction with private enterprise while ensuring that objectivity in research and the public's trust are maintained.

Rules for NIH staff

In general, NIH staff members may not participate in outside consulting with substantially affected organizations (SAOs) such as pharmaceutical companies. With prior approval, however, NIH staff members are allowed to participate in outside activities such as grand rounds lectures and scientific grant review and may receive compensation for academic outside activities (e.g., teaching courses, writing textbooks, reviewing manuscripts and editing journals, and practicing medicine and other health professions). In summary, what the rules for NIH staff mean in plain language is: 1) I may not serve two masters; 2) I may not double dip; and 3) I may speak and I may write within the bounds of the first two rules.

Rules for grantees and contractors

Institutions that receive NIH support must have a written and enforced policy to identify and manage, reduce, or eliminate investigators' financial COIs that could affect research objectivity, and they must report to the NIH when they have identified financial COI. They are not obligated to provide details, but they must make additional information available to the NIH upon request. A common question is whether the NIH should require investigators receiving NIH funds to abide by the NIH internal COI rules. In fact, the NIH internal COI regulations govern federal employees, who



because of their employment status are held to a different standard. These NIH internal COI regulations do not apply to NIH-supported investigators.

INVESTIGATORS AND INSTITUTIONS SEEK WAYS TO MAINTAIN OBJECTIVITY AND PUBLIC TRUST

NIH-supported investigators and institutions are committed to ensuring objectivity in research and proactively seek ways to maintain the public's trust. The FASEB meeting and COI Toolkit are examples of the biomedical community's activities in this important area. This FASEB-led effort is particularly noteworthy because it is directed to the investigators, to whom the policies apply directly and whose behavior is the prime indicator of the success of the policies. The NIH is pleased to join FASEB and other organizations that are highlighting the importance of maintaining objectivity in research and providing guidance to their respective communities.

DISCUSSION

- Question: Can you tell us about the effort by the Research Business Models (RBM) Subcommittee of the National Science and Technology Council's Committee on Science to create greater consistency across federal agencies' COI policies? Dr. Ruiz Bravo: Colien Hefferan from the US Department of Agriculture and I co-chair this group. Only the NIH and the NSF

currently have COI requirements for research grants, and these differ slightly. They might serve as a model for all agencies. We anticipate that RBM will have a draft policy available for comment within a few months.

- Comment from participant: Regarding the description of the intramural regulations, it was suggested that NIH does not have a "higher" standard than the extramural community, but a "different" standard.

- Question: What COI rules do NIH trainees and fellows follow? Dr. Ruiz Bravo: The COI rules apply to NIH extramural trainees if they meet the definition of investigator.

- Question: Should NIH have a role in harmonizing institutional policies? Dr. Ruiz Bravo: Given the diversity of organizational and administrative structures among institutions, it would be ill-advised for the government to prescribe a lot of operational detail. COI is not a "cookie cutter" issue. But the community should agree on core principles that all could adhere to; and NIH would be happy to participate in that effort.

- Question: Regarding recent changes in rules for Food and Drug Administration (FDA) advisory panels, might a similar provision be applied to NIH? Dr. Ruiz Bravo: The FDA rules apply to FDA, which is a regulatory agency; NIH is not a regulatory agency.

AAMC focus on conflicts of interest: four areas of emphasis

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It is important to recognize the importance of public perception of medical research. The current public attention of COI in biomedical research

focuses on how effectively and consistently conflicts of interest (COI) are managed. The task for the community is finding the right balance,



remembering that appearances matter, as does focusing on fundamental values of research integrity, protection of human subjects, and maintenance of the public trust.

AAMC AND FASEB THEMES

FASEB themes in addressing issues of COI are very similar to those that the Association of American Medical Colleges (AAMC) has developed in its work on COI in human subjects research. The underlying ethical values are the integrity of research and maintenance of public trust.

Key FASEB themes

- Concern that *lack of clarity and consistency* may cause confusion and noncompliance by investigators
- Promotion of *national guidelines for disclosure and management* of financial relationships between academia and industry
- Promotion of *better tools for implementation of policies*

Key AAMC themes

- Concern that *lack of clarity and consistency* causes not only internal issues but also confusion and distrust in the public
- Promotion of *national guidelines for disclosure and management* of financial relationships between academia and industry
- Promotion of *better tools for implementation of policies*

AAMC SURVEY ON COI POLICIES

A 2004 AAMC survey on COI policies of academic medical centers (AMCs) revealed that there is inconsistency in key policy characteristics. For example, regarding disclosure thresholds of financial interests, 68 percent of policies adopt Public Health Service standard of \$10,000, 27 percent adopt a disclosure standard lower than \$10,000, and one percent adopt the Food and Drug Administration disclosure standard of \$25,000. There is also variability in the types of interests or relationships that need to be disclosed to the AMC.

CURRENT AAMC INITIATIVES

COI in clinical research

A joint Association of American Universities (AAU)-AAMC Workshop was held in September 2005 during which two key issues were identified: 1) lack of consistency in policies and practices and 2) mixed messages to faculty members from imperatives of economic development/technology transfer and insistence on principled university/industry relationships. This workshop resulted in a call for more detailed guidance and more focus on risks and benefits.

An AAMC-AAU Advisory Committee on COI in Clinical Research Co-chaired by President Mark Wrighton of Washington University in St. Louis and Robert Rich, Vice President and Dean of the University of Alabama at Birmingham College of Medicine was appointed in November 2006.

- The effort will build on the 2001 AAU and AAMC guidelines on individual and institutional COI. The committee will work to define key issues in identifying and managing COI in clinical research and to propose refinements and clarifications of the associations' earlier policy recommendations. The committee will develop more guidance on individual COI policies regarding reporting and disclosure, institutional variations, and what constitutes "compelling circumstances" or situations in which a conflicted investigator might be permitted to conduct human subjects research. There will also be guidance for institutional COI policies.
- The committee will provide active assistance in implementation of their recommendations. Implementation will consist of detailed guidance, model management and monitoring plans, case studies to provide template for analysis and examples of how a template would work with real facts.

Industry funding of medical education activities

Education activities include meals, drug samples, Continuing Medical Education sponsorships, gifts to faculty/trainees, site access by representatives, travel opportunities for faculty members, fellowships, speakers bureaus, and ghost writing.

The AAMC Task Force on Industry Funding of Medical Education will evaluate the benefits and pitfalls and forge consensus principles to guide



medical schools and teaching hospitals in developing policies and procedures for managing various forms of industry support of medical education.

There are three working groups: 1) Benefits and Pitfalls, 2) Unmet Needs and Opportunities, and 3) Professionalism (hidden curriculum and effects on training). Additional issues addressed include site access by drug representatives, scholarships/fellowships/other funds for students and trainees, purchasing, and off-site activities by faculty. The AAMC Task Force report is expected late 2007 or early 2008.

AAMC Forum on COI in Academe

This group was established independently in 2002, and an affiliation with AAMC was formalized in 2006. Membership includes research deans, faculty chairs of COI committees, and COI professionals. Key themes discussed by this group at national meetings include best practices, implementation tools, and education.

Symposium on the Emerging Science of Influence and Reciprocity

This symposium held June 12, 2007 in Washington, D.C. was sponsored by AAMC and Baylor College of Medicine. Speakers included Mike Friedlander and Read Montague (Baylor College of Medicine), Dan Ariely (Massachusetts Institute of Technology), George Lowenstein (Carnegie Mellon University), and Max Bazerman (Harvard University). The individuals approached the issues of influence and reciprocity from a variety of perspectives, including neurobiology, social psychology, and behavioral economics.

Speakers presented data that showed even small favors can influence choice and brain response in measurable ways and self-interest can bias people in unconscious ways, causing them to seek information selectively and process information in a biased way. People are unaware of effects of self-interest and people act unethically beyond their own awareness. Education should focus on the “commonality of unintentional corruption.” A monograph of the proceedings will be available Fall 2007.

CONCLUSION

The AAMC and AAU leadership is committed to promoting greater consistency in policies and practices across institutions. But individual differences should be respected and valued. In typical cases, institutional differences may sometimes make a difference in outcome, but should not often make a difference. At the same time, there is also need for consistency (not “identity”) in some areas of policies and practices.

DISCUSSION

- Question: Are there challenges as a result of how various schools within a university approach COI? Dr. Ehringhaus: The public is focused on the biomedical research enterprise, and we should also focus on that right now. The degree of Federal involvement in non-biomedical research is different and academic-industry relationships are quite different across disciplines.



Conflict of interest in medical research: facts and friction

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Catherine DeAngelis is Editor-in-Chief of JAMA and Scientific Publications and Multimedia Applications and Professor of Pediatrics at Johns Hopkins University School of Medicine. At JAMA, she enforces what is arguably the most stringent and comprehensive policy of any medical journal regarding author disclosure of potential conflicts of interest. Dr. DeAngelis reports that she has no financial relationships with industry.

SCRUTINY OF FINANCIAL INTERESTS IN BIOMEDICAL RESEARCH

Definitions

One definition of conflict of interest (COI) is: “Conflict between the private interests and the official responsibilities of a person in a position of trust” (Merriam-Webster’s Collegiate Dictionary). Financial COI includes any paid affiliation or financial involvement with any entity with an interest in the subject of or materials in the study. Interests include payment or remuneration (not only in dollars), material or financial interest, affiliations, consultancies, competing interests and encompasses current, recent, remote, and future interests.

Increased scrutiny

Academic-industry relationships are pervasive, increasing (or increasingly discussed and reported), and undergoing intense scrutiny. The public is skeptical. Whether or not warranted, the total result arouses public concerns and threatens the credibility of biomedical research. There have been high profile lapses of business ethics, transformation of the research enterprise and privatization of biomedical research. Whether or not warranted, the total result arouses public concerns and threatens the credibility of biomedical research.

The numbers of articles on COI cited annually in Medline has increased. Data from 1974 – 2005 show that there were very few articles cited until 1990 when they grew rapidly to approximately 500 articles cited in 2005.

WHY DOES IT MATTER?

Industry as lobby and funder of research

Drug companies are the leader of the lobby push. 1999-2000 political spending, led by the drug market, totaled \$197 million.

Data on funding of biomedical research by source show that companies are the largest sponsor of research. In 2003, approximately 60-65% funding for biomedical research was provided by industry. For clinical research, it is over 90%. This makes sense in that those who profit from research are the ones that fund it.

Clinical trials registry

The International Committee of Medical Journal Editors was concerned about availability of clinical trial results and published a statement on clinical trials registration. This policy stated that authors of manuscripts describing the results of clinical trials must register the trial on a public database. It is not true that clinical trial results are not made public because they are negative.

Effects on research and publication

Financial interests and relationships can bias *what* authors publish and affect *when, how*, and in some cases, *if* research is published.

- There is an association between industry sponsorship and pro-industry conclusions. It is 3.5 times more likely a study will yield a positive result about a product if that study is funded by industry. Relationships can influence practice guidelines.
- Publication has been delayed to allow for patent application, protect scientific lead, slow dissemination of undesired results, and resolve intellectual property ownership disputes.



- Publication of unfavorable results is delayed or suppressed by legal means (e.g., Olliveri, Dong, and Kahn cases).
- There have been cases of deliberate lying about data (e.g., Celecoxib case).
- Sponsors have terminated research for commercial reasons (e.g., Convince Trial) resulting in loss of a product that could improve health.
- There have been cases of manipulation of data analysis (e.g., Muraglitazar - a study drug to lower lipids and blood sugar), and hiding bad news (e.g., Vigor), and fabrication (e.g., embryonic stem cell).

CONCLUSION

Financial interests are ubiquitous. Investigators and for-profit companies must work together to make progress that improves human health. They involve researchers, authors, reviewers, and editors. Policies on disclosure must ensure transparent reporting. Managing conflicts of interest appropriately is essential to ensure the public's trust. Biomedical researchers must remember that

the goal of research is better patient care and that at some point we will affect patients.

DISCUSSION

- Question: Are there problems relating to the variability of journal disclosure policies? Does this create a situation in which authors can “shop” manuscripts? Dr. DeAngelis: There is a lack of standardization on journal disclosure policies and there is often not enough information given to the reader. It is difficult for journal editors to agree on specific aspects of journal policies regarding disclosure. When *JAMA* implemented the second statistics review policy, the number of submitted manuscripts on randomized clinical trials did not decrease. There are also high standards for advertisements. This indicates that if the standards are raised, people will jump higher to meet them.
- Question: Do all the *JAMA* journals including the Archives journals have the same COI rules? Dr. DeAngelis: Yes.

General discussion and conclusions

GENERAL DISCUSSION

Dr. Furcht opened the floor for a general discussion and reaction to the “Call to Action” for a national guideline for the disclosure and management of financial relationships between academic and industry in biomedical research.

- Comment from participant: There really is great difficulty for transparency and disclosure because of the desire to avoid release of study results before they are fully analyzed.
- Dr. Furcht: Activities of AAMC, AAU, FASEB and others indicate there is in fact a need for greater consistency beyond the PHS/NSF regulation.
- Comment from participant: From investigators point of view, investigators would like to have greater consistency because it would help improve clarity. When collaborating with colleagues, having common rules would help investigators reinforce one another. Dr. Furcht: FASEB approved this goal, but there is some need

for local autonomy from an institutional perspective. One size does not fit all but would “small,” “medium,” and “large” be appropriate? The scientists can call for this but it is up to the institutions to refine and adopt this.

- Comment from participant: There is a need for set of principles and common language (and definitions as much as possible) that can serve as a “floor” for use by societies and institutions because they need to make decisions about whether or not individuals can participate in some activities. The FASEB principles – objectivity, transparency, and accountability – could be principles the community could all agree upon and adopt. More specific practices are in the COI Toolkit. How we move those towards local interpretation in terms of practice and management is the key issue.
- Comment from participant: The Federal Demonstration Partnership released a “faculty administrative burden” survey and the issue of COI is important in instances of research that crosses boundaries and can be barriers to research and



education. The Toolkit can be important for faculty education. Institutions could use during educational sessions and for COI committees.

- Comment from participant: Development of COI guidelines for societies is an ongoing process. Principles can serve as the standards. Given the need for different tools for different organizations, it might be useful to develop “best practices” for different groups, particularly professional societies. FASEB might consider advocating that each professional society should have COI guidelines and they could use these for educational programs and other activities. At the university level, there is a need for professional standards for individuals. These are two areas in which the collective group could work towards. The next generation of investigators also needs to have tools and standards so that the desired practices can emerge.

- Comment from participant: One challenge is the portrayal of the extremes on this issue. There is a need to engage investigators in a more neutral way. Investigators are presented with choices. For example, if investigators choose to engage in research via a public-private partnership, they must take on the responsibilities related to that choice. With every choice, there are responsibilities.

- Comment from participant: It is important and useful to continue to share information about what is working and what is not working (roadblocks) so that we do not have to reinvent the wheel.

- Comment from participant: This project could be beneficial to COI committee members specifically related to dealing with push back from

scientists about rules. A consistent set of themes would help.

- Comment from participant: In teaching investigators how to deal with students and the potential for COI to impede training, this effort is useful and is one of the highlighted areas in the

- FASEB work on this issue. Mentors have an important responsibility for trainees which should take a priority over financial interests.

- Comment from participant: One society representative described their experience in implementing COI rules for society Board members and staff. All of the volunteers had done extensive disclosures for institutions, but we had to start over new for every activity and they did not like it. Perhaps over time, it will be more standard and everyone will have to accept it as standard practice.

- Comment from participant: Another issue to consider is the challenges of financial relationships between societies and industry (particularly at scientific meetings).

- Comment from participant: Faculty members have rights and responsibilities. Many times, enforcement of rules is an issue rather than a need for new rules. We should move forward positive way despite media portrayal of medical research.

CLOSING REMARKS AND CONCLUSIONS

Dr. Furcht concluded the meeting by thanking the speakers, participants, and National Academies for use of the space. This is a process and there will be additional follow up with requests for continued participation by interested parties.

This document can be accessed on the web at:
<http://opa.faseb.org/pdf/July17CalltoActionSummary.pdf>

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