Conflict of Interest and Medical Innovation: Ensuring Integrity While Facilitating Innovation in Medical Research: Workshop Summary

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Sarah H. Beachy, Adam C. Berger, and Steve Olson, Rapporteurs; Roundtable on Translating Genomic-Based Research for Health; Board on Health Sciences Policy; Institute of Medicine

CONFLICT OF INTEREST AND MEDICAL INNOVATION

Ensuring Integrity While Facilitating Innovation in Medical Research

WORKSHOP SUMMARY

Sarah H. Beachy, Adam C. Berger, and Steve Olson, *Rapporteurs*

Roundtable on Translating Genomic-Based Research for Health

Board on Health Sciences Policy

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Willing is not enough; we must do."
—Goethe

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Although the reviewers listed above have provided many constructive comments and suggestions, they did not see the final draft of the workshop summary before its release. The review of this workshop summary was overseen by **Harold J. Fallon,** Dean Emeritus of the University of Alabama at Birmingham School of Medicine. Appointed by the Institute of Medicine, he was responsible for making certain that an independent examination of this workshop summary was carried out in accordance with institutional procedures and that all review comments were carefully

considered. Responsibility for the final content of this workshop summary rests entirely with the rapporteurs and the institution.

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The Roundtable wishes to express its gratitude to the expert speakers whose presentations helped outline the challenges in as well as the opportunities for facilitating collaboration to foster innovation while ensuring the integrity of medical research. The Roundtable also wishes to thank the members of the planning committee for their work in

developing an excellent workshop agenda. The project director would like to thank project staff who worked diligently to develop both the workshop and the resulting summary.

Contents

Boxes and Figures

BOXES

FIGURES

Abbreviations and Acronyms

AAMC	Association of American Medical Colleges
ASCO	American Society of Clinical Oncology
CDHI	Center for Digital Health Innovation
CMS	Centers for Medicare & Medicaid Services
CMSS	Council of Medical Specialty Societies
CRA	collaborative research agreement
FDA	U.S. Food and Drug Administration
FY	fiscal year
IOM	Institute of Medicine
IRB	institutional review board
NCATS	National Center for Advancing Translational Sciences
NIH	National Institutes of Health
PHS	U.S. Public Health Service
UCSF	University of California, San Francisco

1

Introduction and Overview[1]

Scientific advances such as the sequencing of the human genome have created great promise for improving human health by providing a greater understanding of disease biology and enabling the development of new drugs, diagnostics, and preventive services. However, the translation of research advances into clinical applications has so far been slower than anticipated (DiMasi et al., 2003; IOM, 2014). This is due in part to the complexity of the underlying biology as well as the cost and time it takes to develop a product. Recent estimates suggest, for example, that bringing a new drug to market requires expenditures in excess of $1 billion and a time frame of more than 10 years (Paul et al., 2010).

Pharmaceutical companies are adapting their business models to this new reality for product development by placing increasing emphasis on leveraging alliances, joint development efforts, early-phase research partnerships, and public–private partnerships. These collaborative efforts make it possible to identify new drug targets, enhance the understanding of the underlying basis of disease, discover novel indications for the use of already approved products, and develop biomarkers for disease outcomes or directed drug use. Partnerships can also reduce duplicative efforts and create a much more efficient, robust, and successful system for translating discoveries into health care applications by sharing unique resources and expertise among participants.

[1]The planning committee's role was limited to planning the workshop, and the workshop summary has been prepared by the workshop rapporteurs as a factual summary of what occurred at the workshop. Statements, recommendations, and opinions expressed are those of individual presenters and participants, and are not necessarily endorsed or verified by the Institute of Medicine, and they should not be construed as reflecting any group consensus.

While the potential benefits of collaboration are significant, the fact that the relationships among development partners are often financial means that it is vital to ensure trust by identifying, disclosing, and managing any potential sources of conflict that could create bias in the research being performed together (Brennan et al., 2006). In 2009 the Institute of Medicine (IOM) Committee on Conflicts of Interest in Medical Research, Education, and Practice defined *conflict of interest* as a relationship that may place primary interests (e.g., public well-being or research integrity) at risk of being improperly influenced by the secondary, personal interests of the relationship (e.g., financial, professional, or intellectual gains) (IOM, 2009). For example, a researcher may be focused on a specific area of research and this may influence the judgments the researcher makes.

The committee's 2009 report called for striking a balance between protecting against financial conflicts and advancing the generation of knowledge that benefits society. However, some public and private institutions have adopted strict conflict of interest policies, leading to difficulties in establishing collaborative efforts, to challenges in gaining access to external scientific expertise, and to restricted interactions and communications between industry representatives and health care providers (Zinner et al., 2010). Other institutions have sought to identify and manage conflicts of interest as a way of permitting research to continue while protecting the integrity of the research process and maintaining public trust (Lockhart et al., 2013). Challenges also exist in effectively communicating physician–industry relationships to patients so that the contexts as well as the benefits of these relationships are clear. Publicly available databases have been developed to disclose financial relationships but there is disagreement about the information they should contain and how the data should be presented to patients.

To explore the appropriate balance between identifying and managing conflicts of interest and advancing medical innovation, the Roundtable on Translating Genomic-Based Research for Health hosted a workshop in Washington, DC, on June 5, 2013, titled Conflict of Interest and Medical Innovation: Ensuring Integrity While Facilitating Innovation in Medical Research. The Roundtable has examined a wide variety of issues involved in moving from basic scientific discoveries to clinical applications. Conflicts of interest are critical factors in many of these issues because of the collaborative nature of the translational process, said Sharon Terry, president and chief executive officer of Genetic Alliance. The intersection between conflicts of interest and innovation is

where new ideas are generated, Terry said, and they provide opportunities for growth and advancements in biomedical research. The goal of the workshop was to discuss conflicts of interest in the context of establishing best practices for facilitating innovation in medicine (see Box 1-1).[2] A wide range of stakeholders, including government officials, pharmaceutical company representatives, academic administrators and researchers, health care providers, medical ethicists, patient advocates, and consumers, were invited to present their perspectives and participate in discussions during the workshop.

All individuals and organizations have conflicts, regardless of the kind of work they are doing, said Allen Lichter, chief executive officer of the American Society of Clinical Oncology (ASCO). For that reason, *conflict of interest* can be a misleading term. ASCO has sought to recast its conflict of interest policies as "disclosures of relationships." A relationship may constitute a conflict in one context but not in another. Whether these relationships raise concerns or actual or apparent conflicts requires review of the circumstances surrounding the relationships because the perceived conflict could be a matter of interpretation. As multiple speakers pointed out during the workshop, conflicts of interest are inevitable in the development of medical treatments and devices and should not reflexively be seen as negative. Improvements to the way conflict of interest is communicated with members of the public and patients could be helpful to ensure and maintain the trust of these groups.

BOX 1-1
Workshop Objectives

- To articulate and clarify current conflict of interest policies.
- To examine and discuss the scope and goals of conflict of interest policies.
- To examine the effect of current conflict of interest policies on medical innovation.
- To identify best practices and potential solutions for facilitating innovation under current conflict of interest policy implementation while still ensuring scientific integrity and public trust.

[2]The workshop agenda, speaker biographical sketches, a full statement of task, and a list of registered attendees can be found in Appendixes A–D, respectively.

THEMES OF THE WORKSHOP

Chapter 2 provides an overview of the issues surrounding conflicts of interest from several different perspectives, including those of clinicians, industry representatives, and government regulators. The meaning of conflict of interest is discussed, along with perceptions of the implemented policies, their goals, and impacts. Strategies for industry–academic partnerships and an overview of government conflict of interest disclosure policies are described. Chapter 3 explores the importance of transparency as it relates to disclosure of relationships and collaborative agreements. A discussion of issues that arise when serving on advisory committees and when recruiting consulting experts for government work is also addressed. Chapter 4 examines how public descriptions of conflicts of interest, including reporting on the issue, shape the perceptions of policy makers, patients, and the broader public. This chapter also addresses the importance of communicating the context for conflicts of interest. Chapter 5 offers examples of how academic institutions are managing conflicts while balancing their objectives to encourage medical innovation. This chapter also examines the need for increased public knowledge of conflicts of interest and emphasizes that effective conflict of interest policies support the institution's primary goals of research and medical innovation, which is to improve the lives and health of patients.

2

Conflict of Interest Policies: An Overview

Important Points Highlighted by Individual Speakers

- Achieving a clearer understanding of the phrase *conflict of interest* and of the actual, perceived, and potential conflicts will help stakeholders weigh the benefits and risks of collaborating.
- Conflict of interest policies are a mechanism for preventing and managing undue influence as opposed to reacting to conflicts that may impede collaborative efforts.
- Effective conflict of interest policies are consistent, enforced, and based on evidence, risk, and benefits so that the policies preserve research integrity and facilitate innovation.
- Investment in academic research has been a driver of innovation, but the multiple missions of research institutes provide a challenge to understanding which relationships should be considered a conflict.
- The financial disclosures required by the Physician Payments Sunshine Act will provide useful information and will facilitate transparency and communication, but consideration of the context of the conflict of interest is also necessary to accurately represent the value of those.
- Conflict of interest policies are intended to enhance academic–industry relationships, support the objectivity of research, and maintain public trust by managing conflicts, not by eliminating or avoiding them.

Conflict of interest policies affect the complex relationships among many stakeholders, including those involved in academic–industry partnerships. Individual speakers stated that defining conflict of interest and examining the perceptions and goals of these relationships can alleviate some of the challenges encountered when different stakeholders collaborate. Effective policies that reflect stakeholder interests can also be used to manage conflicts among collaborators.

THE CURRENT LANDSCAPE: DEFINITIONS AND GOALS

Conflict of interest policies need to balance countervailing goals, values, and interests, said Bernard Lo, president of the Greenwall Foundation and chair of the committee that produced *Conflict of Interest in Medical Research, Education, and Practice* (IOM, 2009). "Everything we do in clinical practice involves weighing the benefits of an intervention for a patient versus the burdens and risks. When we do policy work, we also have to think about the benefits of a policy versus its burdens, risks, and costs." Because of this, Lo suggested that voluntary standards developed by professional societies may have advantages over regulations issued by government agencies.

The connotation of the phrase "conflict of interest" itself is a challenge because the phrase seems to suggest that misbehavior has already occurred. It also conflates actual conflicts, potential conflicts, and perceived conflicts, Lo said. The IOM committee observed that all conflicts of interest involve perceptions or appearances because they are specified from the perspective of people who do not have sufficient information with which to assess the actual motives of a decision maker and the effects of those motives on the decisions themselves. Bias can only be detected after the fact, Lo said, which means that distinctions between perceived and actual conflicts can be misleading.

A challenge that exists with describing conflict of interest is that a judgment must be made about what is an "unacceptable risk that primary interests [are] unduly influenced by secondary interests," Lo said. What risks are unacceptable? What is an undue influence? It is common for most reasonable people to disagree over defining the risks and influences, he said.

Policy Goals and Impacts

One result of effective conflict of interest policies is to enable productive relationships while maintaining trust in the system. Only when a relationship is disclosed can it be assessed and managed. Conflict of interest policies identify collaborative relationships that may raise significant concerns about undue influence and bias, Lo observed. By doing so, the policies are intended to prevent undue influence ahead of time rather than to respond to bias after a conflicted relationship is revealed. Another goal of conflict of interest policies is to encourage relationships that foster such aims as developing improved therapies for patients, he said. Collaborations among researchers, physicians, and industry are beneficial for producing new therapies where effective treatments do not now exist to extend and improve the lives of patients. Drug development is a very difficult and expensive process, Lo noted. Developing a single new U.S. Food and Drug Administration (FDA)-approved drug can require screening many thousands of compounds, putting hundreds through preclinical trials, and then conducting clinical trials on promising candidates. If conflict of interest policies hamper the discovery of new drugs that are effective, patients will suffer, he said.

Many different groups influence the policy makers responsible for enacting conflict of interest policies, including the media, professional associations, and advocacy groups. The underlying question, said Gabriela Lavezzari, assistant vice president for scientific affairs at the pharmaceutical industry association P*h*RMA, is how a patient might be affected by these policies.

P*h*RMA performed a landscape analysis of key stakeholders in the drug development ecosystem, from academia, industry, professional associations, government agencies, legal experts, health policy analysts, and bio-ethicists, Lavezzari said. The goals of the study were to collect expert views on what constitutes a conflict of interest and to understand how tightened regulations on conflicts of interest have affected stakeholders' work, with a particular focus on their ability to access and share scientific information.

The majority of key stakeholders in the P*h*RMA study identified financial conflicts, followed by personal, professional, and institutional conflicts of interest, when asked to describe the types of conflicts they encounter (see Figure 2-1). Lavezzari agreed with other speakers at the workshop that conflicts can arise from non-financial as well as financial relationships and that sometimes the former can be more powerful than the latter.

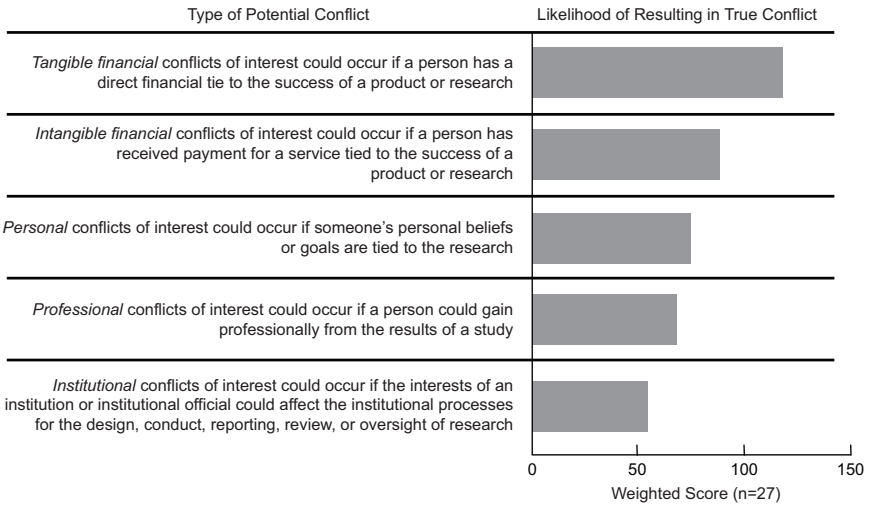

FIGURE 2-1 Types of conflict and the likelihood of a true conflict, as reported by industry and academic researchers.
SOURCE: Gabriela Lavezzari IOM workshop presentation, June 5, 2013.

The analysis also identified five areas where conflict of interest policies and perceptions have the greatest impact, Lavezzari reported (see Box 2-1). More than 75 percent of respondents said that conflict of interest policies had a negative impact on paid speeches, resources invested to monitor policies, time spent on complying with policies, paid consulting with industry, the ability to fill FDA advisory committees, and the time to initiate a collaboration. The survey also revealed that conflict of interest policies have had an impact on industry research activities, said Lavezzari (see Figure 2-2). One individual industry researcher who responded to the survey said that conflict of interest policies have made it challenging for industry to collaborate with academic researchers who are also health care professionals and have authority to prescribe drugs and devices. When research collaborations with industry are reduced, that reduces research productivity, said an individual academic researcher. In addition, conflict of interest policies increase the amount of time spent complying with policies and the resources devoted to monitoring policies. A new industry of full-time employees who work on conflict of interest has been created, said an individual government researcher. It has become a costly and time-consuming specialty which also takes time away from those who have other primary duties.

BOX 2-1
Key Effects of Conflict of Interest Policies

The key effects of conflict of interest policies and the perceptions of conflicts of interest in the P*h*RMA study were summarized by Lavezzari as

- *Impaired collaboration*. Industry and academic partners both agreed that conflict of interest policies increase the time needed to initiate collaborations. Even more worrisome, they reduce the ability and desire to start a collaboration.
- *Increased research burden*. The resources spent monitoring and complying with policies increase the burden on research.
- *Limited FDA access to the best experts*. Even as FDA increasingly focuses on more targeted therapies and personalized medicine, it has less access to the expertise needed to provide regulators with feedback about a drug. With some diseases, relatively few experts exist, and they tend to have relationships with industry. Experts also may be worried about being perceived as having a conflict of interest, or they may not have the time to serve on an advisory committee. A waiver process exists so that FDA still can work with experts who might have conflicts, but as therapies become more targeted, this problem will increase.
- *Decreased physician education*. Conflict of interest policies can result in less funding, fewer events, and less expertise for continuing medical education and physician education, with paid company speeches the area most affected by these policies.
- *Decreased communication*. Having fewer company-sponsored talks or physician talks on behalf of companies can reduce overall levels of communication.

Extreme instances of true conflicts of interest have generated attention and have led to negative perceptions of industry relationships and to stricter policies. Part of the reason, Lo observed, is that there have been some prominent and well-publicized cases in which biased or inaccurate research findings resulted in harm to patients. These cases have involved drugs such as Vioxx®, Paxil®, and Avandia® as well as Infuse, a recombinant human bone morphogenetic protein, which has been used in spine fusions (DOJ, 2008; Krumholz et al., 2013; Palmer, 2010; Thomas and Schmidt, 2012). As a result, many conflict of interest policies tend to aim to eliminate conflicts by avoiding industry–academic relationships. A better approach, Lavezzari said, is to manage conflicts and promote shared access to scientific knowledge. Definitions of conflicts can be standardized and narrowed

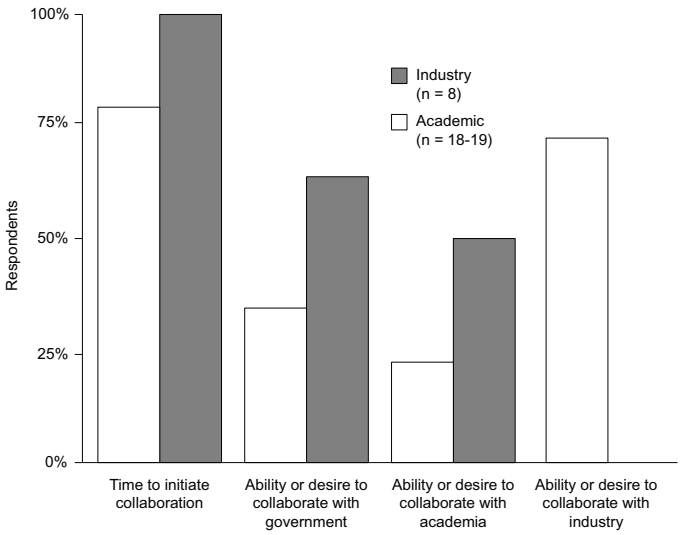

FIGURE 2-2 The impact of conflict of interest policies on industry and academic researchers.
SOURCE: Gabriela Lavezzari IOM workshop presentation, June 5, 2013.

to remove the perception that all relationships constitute conflicts. In this way, perceptions of conflicts can be addressed, best practices can be instituted, and beneficial relationships can be promoted, Lavezzari said.

The underlying implicit assumption in most conflict of interest policies today is that more disclosure is equivalent to more transparency. Transparency in turn is assumed to lead to less undue influence and bias, greater accountability and trustworthiness, and enhanced public trust. But well intentioned conflict of interest policies also can have unintended adverse consequences, Lo said. Disclosures made in different contexts—such as writing a grant, submitting an abstract to a professional meeting, submitting a manuscript to a journal, or serving on an advisory committee—can be inconsistent. Such variations in reporting relationships can cause people to infer that misbehavior has occurred, whereas the inconsistencies may arise instead from inconsistent disclosure requirements, different time periods, variations in what must be disclosed, or different thresholds for the amounts that need to be disclosed. The risk of inconsistencies leading to allegations of misconduct also could deter physicians or researchers from collaborating on valuable activities. Standardized disclosure formats could prevent such inconsistencies, and such formats have been discussed intensively in recent years, Lo said.

Conflict of interest policies have been criticized as an overreaction to egregious cases of research misconduct or other irresponsible research practices, Lo said. From this perspective, such policies cause potential collaborations to be viewed with suspicion when, in fact, they are trying to move research forward. However, other critics argue that the greatest fault of conflict of interest policies is that they are weak, inconsistent, and inadequately enforced. Other unintended adverse consequences include administrative burdens and opportunity costs. Potential collaborators may decline to participate because of the amount of effort required before the collaboration begins.

Conflict of Interest in Medical Research, Education, and Practice (IOM, 2009) emphasized the evaluation of conflict of interest policies. It called for empirical research to be conducted and published in peer-reviewed journals so that future policies can be based on evidence, not just on assertions or conjecture. Conflict of interest policies need to be risk-based, with a focus on the greatest risks to the integrity and rigor of research, Lo said. They also need to be benefit-based, so that they reflect the potential benefits of developing new knowledge and treatments, he said. Finally, the policies need to be evidence-based through the identification of relationships that facilitate innovation or undermine the integrity and rigor of research, Lo said. Disclosure then needs to be performed in a way that facilitates the identification of high-benefit/low-risk relationships and high-risk/low-benefit relationships, he said.

ENHANCING THE ACADEMIA–INDUSTRY RELATIONSHIP

The academia–industry relationship is complex, said Neal Cohen, professor of anesthesia and perioperative care and medicine and vice dean of the School of Medicine at the University of California, San Francisco (UCSF). It encompasses not just academic and industry researchers but also administrators, clinicians, patients, and their families. Each of these groups has its own goals, challenges, and conflicts. "We need to think very carefully about how we build these relationships," he said.

Clinicians care for patients, which can create conflicts involving how they are financially compensated for their expertise, how they manage their patients, how their institutions hold them accountable for providing cost-effective care, and how they relate to their scientific colleagues, graduate students, postdoctoral fellows, and those in industry, said Cohen. In addition, faculty members seek to protect not only their academic freedom but also their autonomy and their control over their research, clin-

ical, and administrative environments. It is a "challenging and competitive environment" that requires creative solutions beyond the traditional ones put in place in recent years, he said.

Academic faculty members get mixed messages about their missions from their institutions, the public, regulators, friends, and family, Cohen observed. Faculty are supposed to create and disseminate new knowledge, secure extramural research supports with indirect cost recovery, commercialize advances, create new businesses, and use new technologies and drugs to benefit patients. Despite this multiplicity of goals, faculty are also expected to avoid conflicts of interest and conflicts of commitment, protect intellectual property, ensure academic freedom, and be transparent with their findings. In this last area, they are told to report on all activities for which there is a potential, real, or perceived conflict. But in many cases, Cohen said, discerning whether there is a conflict is difficult because definitions of potential conflicts vary among individuals. "How do I disclose what I don't recognize as a conflict? This is a big issue."

Lo and Cohen agreed that disclosure requirements can be challenging and confusing. Disclosures can be different for administrators, researchers, and clinicians. In most universities, faculty are encouraged to engage in activities outside the university, and these external relationships create additional complications for disclosures, Cohen said. Furthermore, disclosures or failures to make a disclosure have to be interpreted, which also can be challenging.

All stakeholders—including government agencies, commercial payers, and health plans—have their own unique goals and conflicts that go along with them when they build relationships with other groups. Academic institutions have conflicts borne of their multiple missions, even though they are often held less accountable than individuals, Cohen said. They are supposed to be educating students while also conducting research, which can cause the teaching mission to get lost. Institutions seek to protect and advance their standing on such measures as funding from the National Institutes of Health (NIH) or the *U.S. News & World Report* rankings of college and universities. They aim to protect intellectual property and benefit from royalty and licensing payments while also creating and disseminating new knowledge.

The collaborative research enterprise for institutions has expanded greatly over the past two decades, according to Todd Sherer, associate vice president for research and executive director of the Office of Technology Transfer at Emory University. Reported research funding has in-

creased each year, rising from $12 billion in 1991 to $61 billion in the fiscal year (FY) 2011 survey.[1] The number of new invention disclosures filed by faculty has closely tracked that increase, rising from about 5,000 to nearly 22,000 during that same time period. In 2011 alone, almost 600 new products were introduced to the market, and more than 600 new startups were formed. Almost 4,000 startups were believed to be operational in 2011, employing an estimated 55,000 people. In FY 2011, $2.5 billion in licensing revenue was reported from an estimated $80 billion to $120 billion in product sales. The relationship between industry and clinicians can be extensive and substantial. There are clear financial drivers for institutions to promote innovative research, Sherer said.

If the structure of an institution includes a health care delivery component, it will have commitments to patients, to the families of patients, and to the larger community. Institutions also need to raise funds from philanthropists and others, which may encompass such issues as naming rights. For example, Genentech Hall is the name of one of the buildings on the UCSF campus, but some have objected to the presence of a biotechnology company's name on an academic campus. However, the company named the building and provided $50 million toward funding the research facility as part of a settlement over a patent dispute for the drug, Protropin (Barinaga, 1999). "Does that create conflicts?" asked Cohen. "Are those [conflicts] real or perceived?"

Conflicts of interest also arise from the goals of those in industry. Industry would like to control intellectual property, reduce the high cost of product development and regulatory burdens, and balance the needs of its own researchers for autonomy with the need to commercialize products, Cohen said.

Some people believe that the only way to manage these conflicts is to avoid developing relationships between industry and academics. But Cohen said that this perspective represents a very narrow view of the complex relationship between physicians and patients. Would this perspective mean that physicians should discourage their patients from participating in clinical trials? The fact that many patients seek out physicians who consult with industry for their knowledge and experience should also be considered before calling for the elimination of relationships between academia and industry, Cohen said. A workshop partici-

[1]Association of University Technology Managers U.S. Licensing Activity Survey Highlights, http://www.autm.net/AM/Template.cfm?Section=FY_2011_Licensing_Activity Survey&Template=/CM/ContentDisplay.cfm&ContentID=8731 (accessed December 6, 2013).

pant agreed that there should not be a complete separation of industry and academia but suggested that some separation is needed—for example, that pharmaceutical marketing should be separated from medical education.

Cohen suggested several steps that could enhance academic–industry interactions, minimize risks, and create the right balance between collaboration and competition. Conflicts need to be defined from the perspective of each party, he said, and then they need to be managed so as to protect human subjects and improve medical treatment as much as possible. Transparency is essential, and transparency requires a mechanism to disclose conflicts. While economic relationships are important and easier to measure, other non-financial relationships also need to be understood, he said. Sharon Terry agreed, noting that biases in research could potentially lead a field astray. These other types of non-financial biases need to be taken into account when thinking about their impact on outcomes in research, said Heather Pierce, senior director of science policy and regulatory counsel for the Association of American Medical Colleges (AAMC).

Creating a single template for disclosure using standard definitions is important, but it will be difficult, Cohen admitted, because the purposes of disclosures are very different depending on the circumstance of the relationship. Disclosures cover different topics, concerns, time periods, and obligations. Furthermore, conflicts may be unintended or unrecognized. In addition, disclosures need to be available to all the parties that need to know, including patients. If a clinician has invented a hip prosthesis and is collecting profits from its use and then informs his or her patients that this is the best device to use, many patients would trust that the physician was providing expert advice and would thus elect to use the prosthesis. But the key question is whether the prosthesis is the correct one to use for that particular patient; a different surgeon might recommend a different device. What would be the non-conflicting recommendation? “These are difficult decisions with respect to not only disclosing but interpreting the disclosure in a way that allows patients, families, and the community at large to make the right decisions,” Cohen said.

Addressing bias more explicitly and proactively could address the problem of undue influence, Lo said. Having more robust peer review processes before clinical trials start would produce better research, as would having more explicit standards, guidelines, and checklists for preclinical and clinical studies. The comparative arm should be a reasonable comparison, not just the weakest result in the control arm so that the ex-

perimental arm looks better. Flawed comparisons can make a drug under study look better, but they do not help patients. "Some of the attention we're now spending just on the disclosure of relationships might be better applied to looking at how to characterize and to remove undue influence and bias," Lo said.

Clarifying and perhaps merging the roles and responsibility of conflict of interest advisory groups and institutional review boards (IRBs) will provide these groups with the expertise they need to conduct a scientific evaluation and to understand where the conflicts are and how those conflicts are managed, Cohen said. "Right now they're done in parallel. We need to figure out a way to integrate those more effectively." Individuals who serve on both an IRB and a conflict of interest committee would be helpful for informing policy, said Guy Chisolm, director of the Innovation Management and Conflict of Interest Program at Cleveland Clinic. "This has been a tremendous benefit [for] understanding ourselves as an institution and the possible contradictions or hold-ups [for] investigators," he said.

The reporting requirements of Section 6002 of the Affordable Care Act, often referred to as the Physician Payments Sunshine Act[2] that will go into effect in 2014 have been designed to help patients make informed decisions and to discourage financial relationships that inflate health care costs. Beginning August 1, 2013, manufacturers are to collect and track data on their financial relationships with physicians and teaching hospitals. These data must be reported annually to the Centers for Medicare & Medicaid Services (CMS) beginning March 31, 2014, and CMS will make the data available to the public on a website that will launch by September 30, 2014.

The goal of the Physician Payments Sunshine Act is to promote transparency about relationships by providing consumers with information to make better informed decisions about their health care. But patients are focused on getting good care rather than reducing health care costs, and Cohen questioned whether disclosing financial relationships to patients could affect costs. On the other hand, he said, it is important to have a disclosure process despite the cost of compliance, which has been estimated to be $1 billion over 5 years (Rosenthal and Mello, 2013). Even though disclosure does not necessarily change behaviors, it provides useful

[2]Centers for Medicare & Medicaid Services, Official Website for Open Payments (Physician Payments Sunshine Act): http://www.cms.gov/Regulations-and-Guidance/Legislation/National-Physician-Payment-Transparency-Program/index.html (accessed November 8, 2013).

information. The information, however, has to be put in context because reporting alone can misrepresent the nature and the value of a relationship.

Cohen said that medical schools could do a better job of educating students about the value of relationships with industry and the challenges associated with those relationships. "Until we go back to the basics and talk about what we're trying to accomplish in thinking about industry–academia relationships, and how to most effectively accomplish them, we won't have done our duty," he said.

Creative forms of collaboration can break down the silos between industry and academia while avoiding some of the issues associated with traditional collaborations, Cohen continued. One such example is the Medical Device Innovation Consortium developed by FDA, which facilitates collaborations among academia, industry, and federal partners, said Michelle McMurry-Heath, associate director for science at FDA's Center for Devices and Radiological Health. The Medical Device Innovation Consortium allows for the pooling of financial resources, intellectual property, and ideas so that members can work together to solve regulatory science needs. The idea behind the consortium was to get the hard negotiations out of the way at the institutional level so that the science could be the focus of later work. The "foundation is laid, so now when we have additional research that we do jointly, it should be a smoother path," McMurry-Heath said.

Open innovation research and data networks, screening facilities, compound libraries, and sharing of personnel, can also benefit partners in industry–academia networks, Cohen said (IOM, 2013). Autonomous organizations within academia, such as incubators, can allow for open communication and innovative roles for graduate students, postdoctoral fellows, and faculty members. Such arrangements need to include master agreements, oversight structures, arrangements for distributing credit for discoveries, and agreements for the sharing of financial risks and benefits. For example, one model is to have a strategic planning board that defines goals and identifies potential collaborative partnerships and opportunities; a coordinating committee that identifies and leverages expertise and manages databases; and an advisory board that evaluates strategies, provides oversight, and manages conflicts of interest.

As an example of such an arrangement, Cohen cited the UCSF Center for Digital Health Innovation (CDHI), which leverages the institution's strengths in clinical care, health sciences discovery, education, and innovation by using industry expertise in development, manufacturing, and commercialization. The focus is on developing standards-based,

open platforms for data exchange and on incubating CDHI startups to the point where they are ready for commercialization. For example, the Health eHeart Study is a clinical trial and therapeutic management platform based on social media that allows patients and providers to exchange information. Patient- and device-recorded data and surveys, genetic and blood analysis with specimen banking, and device integration allow for improved health care delivery and the rapid creation of large cohorts for registries and clinical trials. All of the study data must be secured according to the guidelines of the Health Insurance Portability and Accountability Act of 1996.[3] The result is that the study, Cohen said, is similar to the Framingham Heart Study, except that it is able to be carried out on a global scale because of the digital nature of the data collection and analysis.

The key to enhancing product development and facilitating academia–industry relationships, Cohen said, is to maintain a commitment to core values: "core values of the institution, core values of the faculty, core values of industry, and core values of the community." Identifying and managing conflicts can ensure transparency and allow individuals to determine whether conflicts might influence decisions while maintaining the integrity of science and the public trust.

NIH POLICY ON CONFLICTS OF INTEREST

Government regulations are not intended to stifle academia–industry relationships, said Sally Rockey, deputy director for extramural research at NIH. Rather, they are meant to enhance those relationships, support the objectivity of research, and maintain public trust through the appropriate management of conflicts. NIH is "a public agency, and we want the public to trust the research that we're generating," she said.

Not all financial interests are conflicts, but conflicts are inevitable, so they need to be properly managed, Rockey said, agreeing with other speakers. NIH does not seek to manage the financial interests of investigators. Its relationship is with the institution, and it assigns responsibility for dealing with conflicts largely to institutions. It is impractical for NIH to

[3]The Health Insurance Portability and Accountability Act (HIPAA) regulates the privacy of individual health information and sets security standards to protect electronic health information. Health and Human Services, Summary of the HIPAA Security Rule: http://www.hhs.gov/ocr/privacy/hipaa/understanding/srsummary.html (accessed January 13, 2014).

collect information on the financial interests of every single investigator, and it does not perform this role, Rockey said.

Conflict of interest policies in the U.S. Public Health Service (PHS), which includes NIH, were promulgated in 1995 and revised in 2011 (HHS, 2011). NIH worked closely with investigators and institutions to arrive at the final, revised regulations. When NIH began talking about revising the conflict of interest regulations, the number of financial conflict of interest reports submitted to NIH increased dramatically, Rockey said. Relationships were developing, but a large number had not been previously disclosed.

The new regulations establish standards that provide a reasonable expectation that the design, conduct, support, and reporting of research funded under PHS as grants or cooperative agreements will be free from bias resulting from investigator financial conflicts of interest, Rockey said. The term "reasonable expectation" signals that conflicts will arise but that they will be managed to produce objective research. Investigators disclose to the university or to the institution all significant financial interests, including any such interests that pertain to their institutional responsibilities. It is a preventive and proactive strategy, Rockey said.

Institutions need to have and implement a policy, Rockey stated. They must train their investigators and others involved in the research. They must look at financial interests and determine whether the interests constitute a financial conflict of interest. If conflicts occur, they must be managed.

Some institutions have been very strict and restrict relationships with industry, while others lean more toward management. The PHS regulation states that institutions must manage conflicts, but it does not specify how this must be done, said Rockey. If a conflict is identified, the institution must report that conflict to NIH and tell the agency how the conflict is being managed. NIH oversees the institutional policies, but it is not an auditing group. It does some targeted and proactive compliance, but its main job is to oversee the process. With the new requirement that institutions report how they are managing a conflict, NIH can determine whether specific trigger points have been reached and whether it needs to work with an institution.

At times the government's policies can seem somewhat confusing, Rockey acknowledged. The Bayh-Dole Act[4] encourages academia–industry partnerships, while conflict of interest regulations constrain

[4]The University and Small Business Patent Procedures (Bayh-Dole) Act of 1980. Public Law 96-517, 96th Congress. December 12, 1980. 94 Stat. 3015.

those relationships. The same balancing process is evident in NIH's new National Center for Advancing Translational Sciences (NCATS), which was created to catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics. For example, a centerpiece of the NCATS program has been the Discovering New Therapeutic Uses for Existing Molecules program, through which eight companies have made available to academic researchers their libraries of molecules and compounds that have gone through preclinical trials but have not progressed further. The program had model template agreements for intellectual property, but conflicts of interest have been an issue. Again, Rockey said, NIH's approach has been not to eliminate conflicts but to manage them. In fact, by managing the conflicts, investigators and companies have become more interested in participating in the program. The conflict of interest policies "gave people much more peace of mind that we were going to be able to approach this new program and manage whatever conflicts of interest might arise in appropriate ways," said Rockey.

International Relationships and Market Forces

Relationships with industry are much less regulated in other countries. For example, in the Philippines physicians attend continuing education programs with shopping bags to fill up with samples from drug companies, Cohen said. They do it for the most part because they want to give their patients access to drugs that they otherwise could not afford, but their prescription behaviors are clearly dependent on those relationships. "In many of the countries that I've visited, these issues aren't being addressed at all," Cohen said. Yet many future clinical advances will require studying groups of patients much larger than the numbers available in the United States. "We have to look to Asia for those relationships, and then we start dealing with some of the regulatory requirements and restrictions of various companies and the ability to control the intellectual property and potentially be able to build markets. It's incredibly challenging," Cohen said. International relationships are made even more complicated because many sub-recipients of awards are located in countries without rigorous conflict of interest policies. These U.S. researchers are therefore responsible for managing the conflicts of interest and making sure those subcontractors or sub-awardees have conflict of interest policies. This creates a need for universities and other institutions to try to figure out what other countries are doing.

Terry also pointed out that the practice of medicine occurs in a market economy, which means that treatments have to be sustainable. Drugs are available today because of commercial interests, and the market allows access to needed drugs. Individuals need to understand that, and they need to be empowered to engage in their own health care to better understand what decisions might be affected by conflicts of interest. But disclosure policies are not necessarily targeted to the individual patient, Lo said. Most patients will not look at whatever disclosure information is available, but researchers, investigative journalists, policy makers, and others will look for patterns that apply more broadly. Where institutions implement quality improvement measures to improve patient outcomes, "that's the kind of value we're most likely to see," Lo said.

3

Perspectives on Conflict of Interest Policies

Important Points Highlighted by Individual Speakers

- A financial relationship does not of itself indicate a conflict of interest, which is why transparency of relationships with context is important.
- Better mechanisms are needed to detect and measure non-financial relationships that may pose a conflict of interest.
- Improving transparency by clearly defining goals, problems, and responsibilities can be helpful when designing precompetitive collaborations.
- Resolving legal conflict of interest issues within the scope of the collaboration would promote innovation.
- Research needs to drive risk–benefit analyses for collaborations, and legal processes need to be devised to enable partnerships within the framework of conflict of interest policies.
- Innovative ways for accessing expertise are needed to provide prompt knowledge and guidance within current policies.

Each member of a collaboration has not only different interests but also a perspective on that collective effort that is different from the other members of the collaboration. These different perspectives can be a spur to creativity, but they can also create conflicts. Individual speakers at the

workshop examined conflicts of interest in relation to transparency, collaboration, and access to expertise.

POLICY TRANSPARENCY

Conflict of interest policies are designed to reduce incentives that can lead to biased research results and to preserve the public trust, said Pierce. "This is absolutely fundamental to our research enterprise" and to innovation, she said.

Various organizations have conflict of interest policies, including the federal government, state government, research institutions, and professional societies. The policies of these different organizations have overlapping goals—including protecting data and research subjects, accelerating innovation, and achieving better health for all—but they are not identical. The guidance and limits of the policies of a professional society may have different impacts on innovation than disclosure policies reviewed and managed at institutions, Pierce said.

Pierce agreed with other speakers that money is often used as a surrogate in conflict of interest policies for thinking about bias, largely because funding can be measured. But she would not recommend applying the surrogate structure to other types of conflicts. For example, it would be very difficult to write a regulation governing an academician's objective to publish a paper to improve his or her chances of getting tenure. Instead, other mechanisms may be able to detect and allow for the management of conflicts, such as the third-party analysis of data.

Stakeholders need to know that a process exists for reviewing potential conflicts and determining whether there is a risk of bias, Pierce said. Reporters sometimes ask Pierce questions about a discovery of a financial relationship between a physician and a certain company that is worth, say, $10,000. But such a financial interest is not necessarily a conflict of interest, she said, and the "discovery" of such a financial interest does not necessarily connote a problem. Given the approach that some reporters take, she said, it may seem to investigators that they have an uphill battle if they wish to engage in industry collaborations.

Transparency is important, but transparency without context can be problematic. For example, Pierce described a theoretical example of a simple relationship between an investigator and a pharmaceutical company that could lead to the reporting of different financial relationships depending on the timeframe and the party that is asking for the disclo-

sure. In this scenario, the investigator received a $2,500 consulting payment in August 2013. The investigator also served on a scientific advisory board for which she was paid $1,000 in December 2013 and another $1,000 in February 2014. However, because her institution does not require its investigators to report financial interests that total less than $5,000, she does not have to disclose those relationships to the institution. At a continuing medical education seminar in May 2014, she discloses that she has earned $4,500 in the past 12 months from the pharmaceutical company. At a conference in September 2014, her disclosure is $2,000 over the past 12 months. When the Physician Payments Sunshine Act database appears that same month, it may list payments made to the investigator at $5,100 because she has received $4,500 plus the transfer of value of a plane ticket, hotel, and meals. Without the context, the variation in disclosures could be misleading.

Conflict of interest policies may create transparency and public confidence without reducing bias as they are intended to do, observed Lichter. Physicians may withdraw from partnerships because of their fear of possible negative consequences, such as being listed as a scholar who is supported by industry.

A lesson that could be applied to conflict of interest policies may be learned from the regulations that were put in place to limit the duty hours of medical trainees, Lichter said. The supposition was that medical residents were tired from working long hours and that this was leading to mistakes in patient care (IOM, 2008). In 2003 and 2011 work hours were limited by regulations from the Accreditation Council for Graduate Medical Education with the goal of improving patient safety. However, outcomes data have shown that duty-hour limitations have not only failed to improve safety, but they may have worsened it because of more frequent hand-offs among trainees, Lichter said. A better approach would have been to allow some institutions to try different approaches and then study the outcomes.

Without data, policies are based on what people think is reasonable and a good idea, said Lo. Gathering the necessary data will be a challenge, because it will require characterizing, identifying, and analyzing the good and bad consequences of policies. But, Lo said, "it would be a real shame if 10 years from now we're in the exact same place." Evidence and data are needed to form good policies. Sometimes there is not a strong evidence base, Rockey said, and in the case of the NIH financial conflict of interest policy, a proactive strategy for regulations was put in place.

Cohen suggested that in the duty-hour circumstances, patient care problems were caused by lack of supervision rather than sleep deprivation. "We put a solution in place that was for a different problem." In the case of conflict of interest, the problem that needs to be fixed is preventing relationships that compromise the quality and integrity of the science and the public trust. Some individuals and institutions have compromised the public trust, and even if the numbers are small, the problems that have resulted are significant. Asking how these conflicts occurred and how to prevent them in the future does not imply that everyone has a conflict of interest that is compromising their actions. Rather, addressing the issue is meant to enable reasonable and responsible relationships.

AAMC has a conflict of interest metrics project that has been designed to collect data from academic institutions on these issues, Pierce said. One goal of the project is to aggregate the data from institutions and provide it to NIH to facilitate a retrospective review of the impact of its conflict of interest policies. AAMC originally hoped that 25 institutions would sign up for this project, which requires 4 years of data collection and reporting. Already, 76 institutions from across the country have signed up and have provided extensive historical data from before the new rule was implemented, Pierce said.

Pierce said that the questions being asked by the project include: What did you do to prepare for the new rule?, What was the cost of implementing this rule?, Did it require capital investments or infrastructure changes?, Did you hire new people?, What is the impact on your faculty?, What were you looking at before?, How many financial interests did you collect?, How many were determined to be significant financial conflicts of interest and reported to NIH or another funding entity?, and Are you finding and reporting conflicts of interest related to travel?

AAMC is starting to analyze the background data and intends to provide data updates as the project proceeds, Pierce said. Early analysis of data from before the rule compliance deadline will look at implementation costs, conflict of interest review processes and infrastructure, and non-financial impacts on institutions and faculty.

Finally, Pierce stated, as did other workshop presenters, that the community is good at communicating the risks of conflicts of interest but that it has not done as good a job of identifying and communicating the benefits of collaboration among academia, government, and industry. "If we are not pulling together the best resources from our academic scientists, from our industry-trained scientists, and pulling together the resources that each can bring to the equation," Pierce said, "we're missing

out, and not just in small ways but in profound ways that affect discovery in health."

COLLABORATION WITHIN CONFLICT OF INTEREST BOUNDARIES

The mission of NCATS at NIH is to develop innovative methods and "technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions."[1] The fact that resources are limited means that achieving that grand mission requires collaboration, which in turn requires the management of conflicts, said Krishna Balakrishnan, senior technology manager in the Office of Strategic Alliances at NCATS.

Collaborations should start at the home institution, said Balakrishnan. All NCATS projects have multiple, cross-disciplinary leaders working collectively as a team, with everyone from the laboratory research personnel to the principal investigators participating in the planning as well as the implementation of the projects. NCATS also works collaboratively with many of the other institutes and centers at NIH. Collaboration is "in the DNA" of those who work at NCATS, Balakrishnan said.

The Therapeutics for Rare and Neglected Diseases program, which supports drug development collaborations between NCATS and extramural partners with expertise in disease areas or drug targets, is an example of a successful NCATS collaboration, Balakrishnan said. Most pharmaceutical and biotech companies would not usually develop these drugs because of the low financial incentives. However, in the past 3 years, the program has undertaken 15 projects, of which 4 have produced investigational drugs taken into human trials. In a program with Genzyme, the University of Cincinnati has explored the repurposing of granulocyte macrophage-colony stimulating factor (GM-CSF) for pulmonary alveolar proteinosis, a very rare disease. In this case, Genzyme supplies the drug at no cost, and the university provides the disease expertise to develop an inhaler-based formulation of GM-CSF and to complete a toxicology study prior to studying its use in clinical trials.

The Discovering New Therapeutic Uses for Existing Molecules program, which Rockey mentioned, seeks to repurpose existing compounds

[1]National Center for Advancing Translational Sciences. Re-engineering Translational Sciences, http://www.ncats.nih.gov/research/reengineering/reengineering.html (accessed December 31, 2013).

using innovative ideas from researchers. Collaborations are formalized between researchers and industry through collaborative research agreements (CRAs), while memorandums of understanding are used to standardize relationships between industry and NIH. The program also uses confidential disclosure agreements and CRAs between pharmaceutical company partners and applicants, Balakrishnan said. Industry provides the compounds, and they are crowd-sourced to investigators for ideas about how to find new uses for them. The templates are available for the agreements after a relationship is established so that putting new agreements together is not as time consuming. Much of the information, including the CRAs, is available publicly.

Failure of drugs in Phases II and III of clinical trials is often due to drug toxicity and a lack of efficacy, Balakrishnan said. NCATS is trying to address these issues by collaboratively developing a tissue chip, which is an in vitro platform that uses human tissues instead of whole animals to predict drug efficacy, pharmacokinetics, and safety. The intention is to create a modular, reconfigurable platform to produce physiologically relevant, genetically diverse, and pathologically meaningful results. "The problem is massive, because it's not only a biology problem—it's an engineering problem, a bioinformatics problem, and a fluidics problem," Balakrishnan said. The collaboration includes FDA and the Defense Advanced Research Projects Agency and has resulted in requests for applications from academic researchers to develop such chips.

NCATS has developed a set of principles (see Box 3-1) to govern how it approaches collaborations, Balakrishnan said, and these suggested rules could be helpful for other types of collaborations as well. It is important to define problems clearly by setting agreed-upon directions, goals, and responsibilities, he said. In doing so, collaborators are encouraged to look for ways in which there are synergies between complementary

BOX 3-1
NCATS Guidelines for Collaborations

- Complement, rather than compete with, the work of others.
- Revolutionize the process of translation by promoting innovative research.
- Expand the precompetitive space.
- Support and augment regulatory science and its application.
- Galvanize and support new partnerships.

SOURCE: Krishna Balakrishnan, IOM workshop presentation, June 5, 2013.

assets of the partners involved. In collaborations with industry, the science drives the collaboration, Balakrishnan said. Projects focus on new technologies, enabling tools, and dissemination and on de-risking novel therapeutic approaches for industry adoption. Collaborations are typically selected through a solicitation process that is open to anyone. The peer review committees that consider solicitations have members not only from NCATS but also from the venture capital industry, the biotechnology industry, academia, and other sectors. NCATS has also worked to establish itself as an honest broker by being transparent in its work and by designing projects in the precompetitive space so that there is sharing in successes. Lastly, Balakrishnan mentioned the importance of recognizing when a project needs to come to a conclusion and to disengage from the collaboration when it is appropriate. If this is accomplished in a professional manner, then there should be opportunities for the collaborators to work together on future projects. NIH policies, rules, and regulations are strictly enforced and communicated to the collaborators up front. NCATS forms collaborations within the boundaries of conflicts of interest. These policies should serve science rather than penalize it, Balakrishnan said.

SERVING ON ADVISORY COMMITTEES

Federal advisory committees provide formal recommendations on policy to federal agencies, said McMurry-Heath. The committees are composed of individuals who have expertise in the subject matter, but there are limitations on who can serve based on conflict of interest policies. FDA provides as much transparency as possible, but the agency needs to follow the regulations that were approved by Congress, said Jill Hartzler Warner, acting associate commissioner of special medical programs at FDA.

The decision on whether an expert can serve on an FDA advisory board is made by a team of lawyers who advise FDA, said Henry Brem, chairman of the Department of Neurosurgery at Johns Hopkins University School of Medicine. When volunteering to serve on an FDA advisory panel for neurosurgical devices, he had no financial interests in the companies working on the devices, but he needed to disclose significant amounts of information about himself and his immediate family during the conflict of interest reviews. He was ultimately disqualified, not because of a financial conflict, but for an academic conflict because a

treatment he had developed could potentially compete with a treatment he would be considering in the advisory committee. The decisions are being made through a risk–benefit analysis, Cohen said, but the risks and benefits are being assessed by lawyers who are not involved with the dialogue about the goals of participation. "The lawyers should be providing advice and counsel to the leadership in making the decisions, but often their advice and counsel are taken as dogma because institutions, whether they're industrial or academic institutions, are very risk-adverse," Cohen said. Decision makers are needed who take into account the risk but who acknowledge that disclosing the risk and being aware of it could provide the balance that is needed to move forward with something that would benefit patients and society, he said. The reasoning behind these decisions, Lo added, should be transparent to other stakeholders.

Decisions need to be made by balancing risk with what may benefit patients. At NCATS, researchers drive the process of conducting risk–benefit analyses, and lawyers are involved at a later stage of the process once the outlines of a collaboration have been determined, Balakrishnan said. "Once they have come to some sort of an agreement, the lawyers try to figure out how to make it happen."

NETWORK OF EXPERTS

In addition to receiving guidance from experts serving as special government employees on review panels or advisory committees, FDA wanted to have a way to access expertise more quickly and flexibly, McMurry-Heath said. FDA achieved this by collaborating with scientific and clinical professional societies to create a Network of Experts to provide "rapid access to scientific, engineering, and medical expertise when it is needed to supplement existing knowledge and expertise."[2] When a specific scientific question arises, FDA can put out a call to the organizations in the network to find experts who can answer the question. The organizations then provide the names of relevant experts. These individuals are further screened for conflict of interest, and they fill out individual conflict of interest forms and, if needed, confidential disclosure agreements. They then can work with FDA either one on one or in group calls.

[2]Center for Devices and Radiological Health Network of Experts. http://www.fda.gov/aboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/ucm289534.htm (accessed December 9, 2013).

The conflict of interest forms can be filled out rapidly, and the turnaround from the call to completed conflict of interest forms is 7 days. To achieve this so rapidly, the conflict of interest form is streamlined, McMurry-Heath said. The longest such form is one page and should take no more than 1 hour to complete. Which type of form the experts are asked to complete is based on three categories that outline the potential risk of the question being asked. Category A is for questions of limited risk. Category B is for questions of moderate risk, such as those involving a specific product line or a medical indication. Category C is for high-risk products with full conflicts of interest that need vetting. "This allows us to get experts to our scientists and reviewers within 4 to 6 weeks, which in a government timeframe is very quick," McMurry-Heath said.

FDA has already enrolled 25 scientific and professional societies within its network, and it has invitations out to an additional 75. "We're trying to cover the landscape so that we have access to any type of expertise that's needed," McMurry-Heath said.

4

Public Perceptions of Conflict of Interest

Important Points Highlighted by Individual Speakers

- Decades of important medical progress has been achieved through physician–industry collaborations.
- The goal of communicating conflict of interest with the public is to promote innovation and meet patient needs while simultaneously gaining and maintaining public trust.
- One objective for patients is to understand the goals, context, and benefits of physician–industry collaborations and the extent of those relationships as it relates to their care.
- A central, publicly available database provides patients with access to more information about the relationships between their physicians and industry that they can use to inform decisions about their care.
- Freely available databases will provide necessary transparency about financial relationships, but it is important that the context of those relationships and their value is also conveyed in order to avoid negative presumptions that might be made about collaborations.
- Communicating to patients the nature of the relationships and the benefits of those relationships is just as important as sharing information about the risks of physician–industry collaborations.
- The establishment of a single standard for disclosing relationships would provide a mechanism for encompassing both physician and non-physician conflict of interest.

Policy makers and the public obtain information about conflicts of interest from many sources, including the media, websites, health care providers, and other people with whom they interact. The media has an important role in informing the public, and, in doing so, a fuller picture of conflicts of interest should be portrayed, said Hartzler Warner. A better understanding is needed of what type of information is of interest to the public and which elements members of the public need to know about in order to obtain a better understanding about why collaborations are desirable.

COMMUNICATING CONFLICT OF INTEREST

Often when members of the public learn about collaborations between a physician and a health care company, they infer that the relationship has negative consequences. But physician–industry collaborations have produced three-quarters of a century of medical progress, said Mary Grealy, president of the Healthcare Leadership Council. Penicillin, heart and lung bypass machines, statins, deep brain stimulation, and many other advances resulted from physicians, researchers, and manufacturers sharing their expertise. "It's not a coincidence that we are a healthier nation today because of companies and physicians collaborating on innovations for the betterment of society. . . . As we look at the conflict of interest problems and the remedies that can and should be taken against the truly bad actors and bad actions, we need to keep this documentation of health care progress in mind," Grealy said.

Relationships between physicians and industry have received a good deal of scrutiny in recent years from the media and from policy makers. As a result, far more people are aware of payments between physicians and medical innovation companies than in the past, and this awareness will increase dramatically with the implementation of the Physician Payments Sunshine Act. However, the public may not be more aware of the purposes of those relationships, Grealy said. "The goals of the Physician Payments Sunshine Act are laudable," she said, "the public does have a compelling reason to know about these relationships. But the effectiveness of the Physician Payments Sunshine Act will be in the details. Will [the public] simply see columns of names and numbers without background, context, or meaning? Or will they understand the degree to which their lives and their health are affected by these exchanges or by these collaborations?"

Providing raw numbers without context can have a number of unfortunate repercussions, Grealy said. It can create negative presumptions and cynicism over relationships that serve the interest of society. It could lead more physicians to avoid clinical trials, educational conferences, scientific advisory board meetings, and other opportunities that could benefit their patients. It could have a detrimental effect on the dissemination of medical knowledge if it results in less participation in conferences and seminars in which pharmaceutical or medical device companies are involved. "In a worst-case scenario, it could [be misleading] as people pore over the Physician Payments Sunshine Act database to identify which physicians have received the most dollars, even if those dollars are compensating them fairly for their expertise on a project that will advance modern medicine," Grealy observed.

In 2010 the Healthcare Leadership Council created the National Dialogue for Healthcare Innovation as a forum for diverse voices to address issues of conflict of interest and progress in health care, Grealy said. The initiative was designed to bring industry, health care providers, academics, government officials, and patients to the same table to share their views and to work on how to continue to innovate while earning the trust of the public. The dialogue reached consensus on four points: that innovation is critical and collaboration is necessary for innovation, that work is needed to enhance trust in collaborations, that maintaining public trust and transparency is important for collaborations and innovation, and that solving challenges related to collaboration are an economic necessity for the United States, said Grealy. Four key principles to guide collaborations were agreed upon, and the group also pointed to the need for strong internal self-regulation in addition to federal regulation (see Box 4-1).

BOX 4-1
Summary of Keys to Principled Collaboration as Developed by the National Dialogue for Healthcare Innovation

- Collaboration must always be first and foremost for the benefit of patients.
- Researcher and health care autonomy and independence must be protected.
- There must be reasonable access to meaningful and relevant information about how physicians, researchers, and companies engage in collaborative relationships.
- All participants across the health care system must be accountable for their actions.

SOURCE: Mary Grealy, IOM workshop presentation, June 5, 2013.

MEDIA PORTRAYALS OF CONFLICT OF INTEREST

What do drug companies pay health professionals, and what do they get in return? What do doctors prescribe, and how do they compare with their peers? For the past several years these are the questions that Charles Ornstein, a senior reporter for ProPublica, and his colleagues have examined.

In 2010, ProPublica, an independent nonprofit news organization, launched a project called Dollars for Docs, which compiles publicly available data from pharmaceutical companies about their payments to health professionals into a single easy-to-search freely available database. The database started with 7 companies; it now includes 15 companies, representing about 47 percent of the U.S. pharmaceutical sales market and about $2 billion in disclosed payments. Furthermore, the Physician Payments Sunshine Act will require nearly all companies to report such information, which will allow the Dollars for Docs database to be even more robust, Ornstein said.

The database distinguishes the types of interactions that physicians have with industry, Ornstein said. For example, it distinguishes grants for research from fees for speaking and consulting. For research, it notes that the amount shown does not reflect the actual compensation received by the physician listed as the principal investigator. It includes the company's definition of the activity it is supporting and the context and value the company ascribes to that activity.

ProPublica has used the database to write stories on who is getting the payments and the apparent objectives of the payments. For example, companies typically claim that they support experts who are leaders in their profession. But one story demonstrated that among the doctors who were the highest paid, some did not have board specialty certification, many were not associated with academic medical centers, many had not published academic research papers, and some had disciplinary records such as losing their state medical licenses (Ornstein et al., 2010). As a result of that story, the industry has changed how it checks state disciplinary databases to look at the credentials of people employed as speakers or consultants, said Ornstein.

The impact of funding on professional societies was the subject of another ProPublica story (Ornstein and Weber, 2011). It focused on the Heart Rhythm Society, which received about 50 percent of its funding from the pharmaceutical and medical device industry, Ornstein said. The tip sheets to patients from the society left out pertinent information regarding the drugs and devices that people who have heart rhythm irregu-

larities may consider, Ornstein said. "It was not a balanced perspective and, in fact, was tilted in favor of industry."

Ornstein acknowledged that payments for research or consulting activities designed to produce innovations in science differ from those for outreach or marketing. But, he added, "a lot of doctors receive the bulk of their money for giving paid promotional talks on behalf of companies." For example, one physician was recently the first to exceed $1 million in speaking and consulting fees over the past 4 years, even though not all of the companies in the database have disclosed for that entire period and not all companies are in the database.

The website provides lists of the notable drugs made by each company as well as links to an NIH website providing impartial information about those drugs. In addition, the page provides a checklist of questions that patients might want to ask their doctors, including: What are the specific circumstances of this payment?, What is your current relationship with this company?, What drugs have you prescribed me that are manufactured by companies you've taken payments from?, Are there non-drug alternatives that I may want to consider first?, and Are there less expensive generic alternatives to the drugs you have prescribed? The idea is to neither support nor disparage relationships between physicians and companies, Ornstein said. Rather, it is "to allow [patients] to have more informed decisions with their clinicians."

Not all patients are interested in this information, Ornstein said, but some are, and "each patient needs to make a decision for him or her[self] about how interested he or she is in this information and whether or not it's worth a conversation with their physician about it." Some patients may decide to choose another doctor, while other patients trust their physicians to make the decisions that are appropriate for them. "We're not trying to undermine that trust," he said.

PROVIDING CONTEXT FOR CONFLICT OF INTEREST

The public receives a lot of information about innovation and collaboration, Ornstein said. In fact, "the amount of information they are getting about medical journal articles and presentations at conferences far overwhelms information about conflicts of interest." What is needed, he said, is follow-up on the promises of studies to determine whether advances have resulted. However, Grealy said that when members of the public learn of conflicts of interest, they do not hear about the value of

the collaborations at the same time. Patients need to know the context of the relationship between collaborators, specifically the purpose of the relationship and what would be considered fair compensation for the value that comes from that relationship, she said. Characterizing all educational programs as marketing and targeting them for elimination is not a balanced approach.

The ProPublica site does distinguish research payments from payments for presentations, Ornstein said. "Research collaboration is vital to innovation. Where it breaks down is on the issues of speaking and consulting. That's what we've chosen to focus on—the areas where there is less uniformity of perspective."

While the work of ProPublica is important, there is concern that the presentation of the conflict of interest data may diminish the significance of the role of these collaborations for supporting research, said Paul Billings, chief medical officer at Life Technologies. For example, the stories about individual physicians who had received large compensations for their presentations did not contain much detail about why they earned their money, and "they have a right to [their] privacy," he said.

Ornstein countered that ProPublica had repeatedly tried to contact the individuals and the companies about whom reporters have written, but obtaining responses has been challenging. More information is needed from these parties to provide the necessary context for their compensation, he said. Additionally, the information provided by companies contains many inaccuracies, but because the information is now more readily available in one place, companies are taking pains to make sure that it is accurate, Ornstein said. A process will need to be established to maintain the accuracy of the data, correct mistakes, and provide context for the information, Grealy said.

Industry websites as well as ProPublica's website are used by the Cleveland Clinic to verify physician disclosures to the institution, said Chisolm. If any discrepancy is more than a small amount, the physician will receive an e-mail asking the physician to look into the difference, with the institution volunteering to get in touch with the company if the information is wrong. For that reason, Chisolm and his institution are strong advocates of transparency and disclosure.[1]

However, Chisolm said, the media could do much more to educate the public about the nature of and the benefits to society of interacting with industry, as opposed to focusing on egregious missteps by industry

[1]Cleveland Clinic: Integrity and Innovations. http://my.clevelandclinic.org/about-cleveland-clinic/overview/who-we-are/integrity-innovations.aspx (accessed January 9, 2014).

and academia. For example, the name Dollars for Docs carries certain negative connotations, and some things are emphasized while others are de-emphasized on the site, such as the funds going for research. "Maybe there could be a less disingenuous way of portraying that," he said. The checklists of questions for patients to ask their doctors on the ProPublica website may be better received if the questions came from a professional society rather than from the media, said Lavezzari. The way that the conflict of interest information and the questions are presented drives the reader to draw conclusions before he or she has all of the information. Grealy said that ProPublica has done a "nice job of trying to provide some context," but whether the information provided and the way in which it is provided are appropriate is debatable.

The pharmaceutical industry has been critical of Dollars for Docs, but it does not have easy-to-use websites to provide more of this context, Ornstein said. Consulting can encompass a very wide range of activities, from marketing to service on drug safety boards. "Those both would be lumped in under consulting, but they're two totally different things," he said. Having more information about the role of the physician would be helpful. Some pharmaceutical companies are even using the data to push back against physicians who are making money from other companies, Ornstein said. "The industry, which before only had access to its own information, now has access to a competitive body of information that will help them do their jobs better."

Conflict of Interest in Prescribing Practices

Conflict of interest issues extend past collaborations involving physicians. Because non-physicians will be increasingly prescribing medications as health care reform proceeds, such non-physicians will need to be included in any effort to monitor conflicts of interest, a workshop participant observed. One project at ProPublica that is doing just that collects data about prescriptions that health providers across the country have written in the Medicare Part D program. The resulting database, which has records of prescriptions written to the program's 35 million Americans, can be used by members of the public to look up their physicians or other health providers to see what they are prescribing. Financial disclosures are not the only important conflicts of interest to be aware of, Ornstein said; patients should also know if providers are "prescribing drugs in a way that's reasonable, in a way that's consistent with the accepted standards in their field. Patients right now don't have the resources or tools at their disposal to know whether or not that's the case."

A single standard for disclosures for physicians and non-physicians could create a reasonable framework for those who might have a conflict of interest, Grealy said. A single standard also could reduce the amount of resources that go into compliance and thus leave more resources for patient care, research, and other useful activities. Meaningful information needs to be collected in a useful and efficient way, Grealy said. Many companies supported the Physician Payments Sunshine Act because different states were passing their own disclosure legislation with different rules, whereas the Physician Payments Sunshine Act will impose a nationwide standard, Ornstein said. The question then becomes whether institutions and agencies will follow suit and use the same standard or continue to use different standards for non-physicians.

5

Managing Conflict and Facilitating Innovation

Important Points Highlighted by Individual Speakers

- Collaboration with industry is an integral part of the translation process and should be viewed as a positive component of innovation.
- Education of and commitment from faculty at academic research institutions about conflict of interest is necessary for fostering medical innovation.
- Conflict of interest policies at research institutions should be flexible and tailored to specific relationships because a single organizational policy may not capture the complexities of collaborations with industry.
- Simple, routine disclosures and agreements should be considered in an effort to reduce the potential resource burden for complying with conflict of interest guidelines.
- Greater alignment of incentives with research goals could reduce conflict of interest challenges.
- New models for managing conflict of interest policies could be tested in the precompetitive space to determine if they align with institutional goals.
- Improved methods for determining who needs to be informed about which types of relationships are needed in order to effectively communicate with the public about conflict of interest.

Individual workshop presenters described best practices for managing conflict of interest at institutions that are dedicated to performing innovative medical research. The dissemination and implementation of best practices offers ways to facilitate collaboration and medical innovation within the existing conflict of interest policy framework. Throughout the workshop, individual speakers who represented patient advocates, regulators, academic researchers, and industry stakeholder groups discussed alignment of incentives in the broader research ecosystem, increasing public knowledge about conflict of interest policies, and the need to keep patients as a priority (see Box 5-1).

BOX 5-1
Themes of the Workshop

Terry summarized the major themes identified by individual speakers during the workshop in order to provide an overview of the topics discussed and of the potential solutions for dealing with the challenges related to conflict of interest policies:

- Managing financial and non-financial academia–industry relationships is key to fostering productive and transparent collaborations. (Brem, Lavezzari, Pierce, Terry)
- Conflicts of interest are inevitable in the collaborative translation process, and they need to be managed rather than avoided. (Cohen, Lavezzari, Lo)
- In the absence of a strong evidence base for developing policies, using a preventive regulatory approach to conflict of interest is a possible solution for ensuring that quality, integrity, and trust are not compromised. (Rockey)
- One approach to establishing conflict of interest policies that create effective solutions to undue influence is to allow several institutions to try different approaches and then evaluate the outcomes of the implemented policies. (Lichter)
- The use of confidential disclosure agreements and the development of templates for collaborative research agreements can ease some of the challenges encountered when initiating academia–industry collaborations. (Balakrishnan)
- Conveying the benefits of physician–industry relationships and their positive effects on medical innovation in addition to the risks of these relationships would provide more balanced information for patients. (Chisolm, Grealy, Lo)
- A current and accurate central, public database with explanations of industry payments to physicians would offer patients a resource to consult when making health care decisions. (Ornstein)

- Information about the context of a relationship in addition to payment information for physician–industry collaborations is needed so that the value of partnerships is understood and so that advantageous collaborations are not avoided because of negative connotations. (Grealy, Pierce)
- A centralized disclosure system for potential conflicts of interest would reduce the time spent on completing individual forms and would provide a standard format and a more efficient process for reporting. (Lichter)
- Aligning conflict of interest policies with established innovation goals would encourage academia–industry collaborations. (Sherer)
- Implementation of the Physician Payments Sunshine Act presents a mechanism for improving communication about physician–industry relationships and offers an opportunity for increasing public awareness about the risks and benefits of conflict of interest policies. (Chisolm)
- Best practices need to be defined to create more efficient conflict of interest policies to enable the younger generation of researchers to participate in collaborations. (Lavezzari)
- Keeping the needs of patients front and center can facilitate the management of conflicts of interest so that medical advances can proceed. (Anderson, Lichter, Terry)

MANAGING CONFLICTS OF INTEREST AND BALANCING INNOVATION AT INSTITUTIONS

According to Chisolm, commercialization of medical innovations can improve the lives of patients, generate revenue, and support the economic revival of cities. These goals are supported through an aggressive commercialization arm and an effort to recruit, retain, and reward an innovative staff at the Cleveland Clinic, said Chisolm. Over the past decade it has secured hundreds of patents and product licenses and has been a platform for the launch of 55 companies.

Johns Hopkins University also has a tremendous drive to improve medicine and also has an innovative and entrepreneurial spirit, said Brem. His own involvement in the development of Gliadel®, a treatment for high-grade malignant glioma, is an example of the sort of innovation that can be found at Johns Hopkins (Attenello et al., 2008). His research group was funded by NIH as a National Cooperative Drug Discovery Group, which required that industry be a collaborator. Through a partnership with Nova Pharmaceuticals, the Johns Hopkins group took the drug through Phase III clinical trials to receive FDA approval. Initially Medicare did not pay for the drug, but advocacy by patient groups and others

helped to change that decision. Through medical advances such as the development of Gliadel, the median survival time for patients with glioblastomas has been improved (Chaichana et al., 2013). "In the end, patients worldwide are benefiting," Brem said.

Today, Johns Hopkins University is working with the Coulter Foundation to set up innovative groups of biomedical engineers working with clinicians to build companies to deliver products to patients. The university's Brain Science Institute supports the translation of therapies for brain diseases through an interdisciplinary research team. "I'm hopeful that people are building on these precedents and that there are ways to move forward despite the obstacles," Brem said. The university has a legal team dedicated to protecting the reputation of the university and the safety of patients. But lawyers tend to be cautious and it can make progress challenging, he said.

"Collaborations with industry, whether those collaborations are vending relationships, scientific relationships, licensing, or philanthropy, are all essential to the goal of amplification of innovation," said Billings. Collaboration with industry that takes the form of education or marketing is an important part of the translation and application process and is not necessarily bad. "The marketplace and capitalism are not antithetical to evidence-based medicine or to good clinical practice," he said. The rationality of the scientific process is a safety net for science, protecting against uncorrected error or bias, he added.

An innovation-rich agenda requires managing conflicts of interest, and commitment from faculty is needed, Chisolm said. Considerable resources have been devoted to a conflict of interest program at the Cleveland Clinic to work with investigators so that they can innovate within the context of an ethical environment. During weekly meetings, program staff members review every funded grant and the disclosures from investigators of industry affiliations. They then contact investigators to begin a dialogue about conflict of interest regulations and principles. By educating investigators about reporting requirements, the program takes on some of the burden of compliance for faculty members. The institution has good relationships with all of its investigators who have been involved in the management of conflicts of interest, Chisolm said. "The investigators want to publish data that they can claim is free of bias," he noted.

Specific management tools are used for conflict of interest, said Chisolm. Disclosure is required in any presentations or publications, and all colleagues on a research project are also made aware. To remove the po-

tential for bias, in some cases the management may call for data to be reanalyzed by another group that does not report to the investigator with the conflict of interest, Chisolm said. And some plans call for investigators to have read-only access to data or other restrictions in its collection and analysis. Data can be independently audited in any program, and another physician may be put in charge of the final approval of subject selection and consent. External data safety and management provisions may apply, along with purchasing restrictions.

Chisolm noted that institution-wide approaches are not always feasible. For example, management of conflicts can be tailored to the individual case. "It's time consuming," he said, "but I think in the end it's better, because in conflict management one size doesn't fit all. If you're flexible enough to take these on individually, you can stop yourself from inhibiting innovation and the furthering of research findings."

Both Pierce and Sherer agreed that arrangements between an institution and a company can take many forms and that it can be difficult to manage these arrangements as part of the conflict of interest policies at most institutions. Some situations are similar to managing conflicts in individual grants, though multiple projects are involved. In other cases the collaborations are more open-ended and may be more difficult to manage. Especially where people move back and forth between academia and industry, conflicts can be troublesome. Examples of successful collaborations that have avoided conflicts can provide models from which others can learn.

Conflict of Interest Challenges at Institutions

The NIH conflict of interest regulations support the Cleveland Clinic by having the institution, rather than the investigator, decide whether a financial conflict of interest exists. The institution also is in favor of public disclosure and has been pursuing this policy on its own. However, some aspects of NIH's regulations have required extra work and resources for uncertain benefits, Chisolm said. For example, reducing the threshold for significant potential interests from $10,000 to $5,000 tripled the institution's workload for scrutinizing disclosures. In addition, the institution has had to monitor industry-sponsored travel, "which has [had] very little bang for the buck," Chisolm said.

Purchasing equipment at a university may be subject to conflicts, and even though these purchases can be on a much larger scale than purchases for individual researchers, these potential conflicts tend to receive less atten-

tion than do the conflicts involving individual researchers, Brem said. This can breed cynicism among individual researchers, who feel that they are being held to a very high standard and being subjected to intense scrutiny.

The AAMC came out with institutional conflict guidelines several years ago, but often the data do not exist to identify conflicts, Chisolm said. For example, conflicts between an institution's investment decisions and its commercialization activities need to be avoided or managed, as do potential conflicts between those activities and research or between royalty streams and institutional activities, he said.

It is possible that conflict of interest policies are chasing away innovative people with great ideas who refuse to participate because it is too difficult, Brem said. Young investigators could conclude that they do not have the time or energy for completing disclosures and they do not want to risk creating a poor impression while striving to be promoted academically. But such concerns may be misplaced, he said. When a three-paragraph addition to a consent form was inserted to explain Brem's role in the development of a treatment, patients welcomed that information because they interpreted it as meaning that their physician was an expert.

Lavezzari said that rather than dealing with single issues in isolation, best practices for policies should be defined and taught to researchers so that the broader system can be improved. It is unlikely that any single conflict of interest policy will work for every situation, she said. A more granular approach will be needed to describe relationships among collaborators. Margaret Anderson, executive director of FasterCures, agreed with Lavezzari that not all situations are the same and that solutions need to be devised to better account for the variety of types of conflict of interest that arise.

Potential Solutions for Conflict of Interest Policies

The Council of Medical Specialty Societies (CMSS),[1] which is an organization composed of 39 leading medical societies, has developed a code of conduct[2] for interacting with industry for use by its medical society members, and additional organizations have been signing on. The code mandates that each signer post details about the support it receives from health care companies, and, in doing so, it sets a standard of integrity. "We agonized for 15 years whether to put this [list of support] up, be-

[1]ASCO is member society and a signer to the CMSS Code for Interactions with Companies and Allen Lichter is the president-elect of CMSS.

[2]CMSS Code for Interactions with Companies. http://www.cmss.org/codeforinteractions.aspx (accessed January 9, 2014).

cause we thought it would be so controversial," said Lichter, but after being available for 3 years, it has not received such a response.

CMSS also has strict policies on disclosures of relationships with companies, and it also has a new disclosure management system that combines previously separate systems for meetings and publications. Investigators now can disclose everything on a single site rather than disclosing items on separate sites, Lichter said.

The obvious question is whether a harmonized and centralized disclosure system could be established for everybody. A recent discussion paper developed at the IOM has observed that it could be done (Lichter and McKinney, 2012; Lichter et al., 2012). Creating such a system would not be easy, Lichter concluded, but "it will make the world a better place for researchers."

McMurry-Heath said that the simple needs to be kept simple. Brem agreed that disclosure forms should take no longer than 1 hour to fill out. "These things should be automatic and simple, and there should be one central repository where this is done on a routine ongoing basis," he said. McMurry-Heath added, "If we can find ways to streamline the most simple of agreements [and] disclosures so that we can get those out of the way, we can focus our attention on the things that are more complex and more challenging. [That] would make a lot of this process less burdensome and therefore more attractive for more people."

ALIGNING INCENTIVES IN THE RESEARCH ECOSYSTEM

Terry observed that many of the issues surrounding conflicts of interest arise because incentives are not aligned with goals and that where incentives are aligned with goals, fewer problems arise. Lines are blurring between clinical care and research, between single laboratories and team science, and across borders, which provides an opportunity to focus on research goals rather than a specific section of regulations, Pierce said. If current policies do not fit well with an emerging model, then the policies need to be rethought.

Once objectives for innovation are established, institutional conflict of interest policies need to be aligned with those goals. For example, the reward system for tenure and promotion at most universities still discourages faculty members from working with industry, Sherer said. Faculty members therefore may use conflict of interest policies as a reason for not collaborating.

Anderson emphasized the importance of instituting broadly based, systemic changes to manage conflicts. "If we tackle this institution by

institution, university by university, company by company, I don't see us getting there," she said. New management models for balancing conflict of interest and innovation have arisen in part because of a shortage of resources, and this period of experimentation may help develop creative ways to align incentives and accelerate progress, she said. One area for testing these models could be in the pre-competitive space for collaborating on projects. Sherer suggested that including metrics related to technology transfer in tenure and promotion considerations would encourage partnerships with industry, as would leave policies that permit faculty members to join a startup company.

Increasing Public Knowledge About Conflict of Interest

Clarification, simplification, and harmonization of conflict of interest rules could help foster the measurement of public knowledge about the value of relationships to research and the positive outcomes resulting from these relationships, Billings said. The value of collaboration needs to be documented so as not to let conflicts needlessly prevent medical advances. "All of the drugs that I use in my clinical practice, all of the technologies I apply to my patients, have come out of industry–academic collaborations," said Cohen. "That relationship is absolutely critical to making advances."

The public dissemination of information about industry payments to physicians required by the Physician Payments Sunshine Act will provide much-needed changes for conflicts of interest policies, several workshop participants stated. Chisolm observed that information disseminated by the Physician Payments Sunshine Act is going to generate questions, but these questions provide an opportunity for public education about the nature, benefits, and risks of industry partnerships with academia. Lichter predicted that disseminated disclosure information would not be damaging. In one case he described, when a local newspaper published the salaries of faculty members, the repercussions were minor, despite fears that the information would be misused. Unless there are problems with an interaction that is revealed through the Physician Payments Sunshine Act, Lichter said, individuals should have nothing to fear from having their relationship made public. "If you're ashamed of it, don't do it," Brem said.

Providing the public and policy makers with information about relationships requires thinking about what people need to know to arrive at a decision, McMurry-Heath said. Lichter stated that more research is need-

ed about the views that patients, families, and the broader public hold about these kinds of relationships. Some relationship information will be relevant, while other information will not matter. "We need to think about who needs information about those relationships, in what context they need them, and how we can deliver it to them most readily so that they start to utilize the information that's available," McMurry-Heath said.

PUTTING PATIENTS AT THE CENTER OF CARE

Patients have a specific interest in biomedical research, and that interest is obtaining faster and more effective treatments, Anderson observed. She suggested that the needs of patients should be kept front and center in discussions of conflicts of interest. "If you do that, everything becomes easier—[determining] who you need to talk to, learn from, and share best practices with." Conflicts of interest look very different to a patient who has just been diagnosed with a life-threatening disease, she said. Patients may also view relationships differently depending on the extent of the compensation, Chisolm said. Bringing patients into this conversation is critical, Pierce agreed, because a focus on the needs of patients can help reveal what the important issues are and how best to address those issues. A large body of evidence indicates that physicians are influenced by financial incentives, Lichter said. The challenge is to set up systems where those incentives become less prominent and where the needs of patients become the overriding concern.

FDA still has difficulties incorporating patient advocates and industry representatives into advisory panels that are considering a specific product, McMurry-Heath acknowledged. Advocates may be nonvoting members of panels, but their voices need to be better incorporated into the decision-making process, she said. Recent legislation directed FDA to incorporate patient voices into its regulatory decision making, and the agency has an initiative designed to explore methodologies for measuring patient preferences.

Patients should have a better understanding of what academic medical centers do to identify, pursue, analyze, and restrict the activities of physicians and scientists because of their financial interests, Chisolm said. The medical community needs to do a much better job of informing patients what is done to eliminate bias and to maintain the integrity of research, he said. Patients should be able to make their own decisions

about whether to let a conflict influence the care they receive, Brem said. For example, a patient may prefer to get a drug from a physician who helped to develop that drug because that physician is likely to be an expert on that particular therapeutic.

The critical issue is what is important to the patient, Cohen said. "What are we trying to accomplish, and then how can we together accomplish that goal?" Conflicts need to be disclosed if they are relevant to the underlying goal for patients, but if they are not, conflicts may not be part of the dialogue, he said. There is not an effective mechanism for addressing conflict of issues as they pertain to patients.

Forming collaborations that foster innovation is one way to achieve the objective of meeting the needs of patients, Billings said. Cohen observed that personalized or precision medicine may mean bringing multiple drugs to market for smaller populations, which will require new approaches to measuring the effects of treatments on patients. Terry added that such data could also be used to measure the benefit or harm to a patient of a particular relationship. Lo agreed that the benefits of relationships should be emphasized in addition to identifying potential harms.

Terry noted that a number of themes emerged during the workshop (see Box 5-1). "I have the largest conflict of interest of anybody in the room because I represent my family who lives with genetic disease and also all the families that do live with disease. We're not afraid of that conflict because at the end of the day, that's why we're all here," said Terry. It is crucial, Anderson said, "to be sure that we are not protecting ourselves at the expense of accelerated delivery" because patients are waiting for treatments and physicians want to offer effective therapies.

Everyone at the workshop, whether representing government, industry, or academia, also represents a patient who needs care, Terry said, and all of them therefore have an interest in improving patients' lives through the management of productive relationships that allow collaborations to move forward. "The urgency we feel when we're sick or when our parents are sick or when our children are sick, is the urgency we need to bring forward into all these conversations and actions."

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A

Workshop Agenda

Conflict of Interest and Medical Innovation: Ensuring Integrity While Facilitating Innovation in Medical Research: A Workshop

June 5, 2013

National Academy of Sciences Building
2101 Constitution Avenue, NW
Washington, DC 20418

Workshop Objectives:

- To articulate and clarify current conflict of interest policies.
- To examine and discuss the scope and goals of conflict of interest policies.
- To examine the effect of current conflict of interest policies on medical innovation.
- To identify best practices and potential solutions for facilitating innovation under current conflict of interest policy implementation while still ensuring scientific integrity and public trust.

8:30–8:45 A.M. **Welcoming Remarks and Charge to Workshop Speakers and Participants**

Sharon F. Terry, Roundtable Co-Chair and Workshop Chair
President and Chief Executive Officer
Genetic Alliance

8:45–10:45 **SESSION I: CURRENT LANDSCAPE FOR MEDICAL INNOVATION**

Moderator:
Allen S. Lichter
Chief Executive Officer
American Society of Clinical Oncology

8:45–9:15 **Conflict of Interest and Medical Innovation**

Bernard Lo
President
Greenwall Foundation

9:15–9:45 **Enhancing the Development of Novel Medical Products and Clinical Applications**

Neal H. Cohen
Vice Dean, School of Medicine
Professor of Anesthesia and Perioperative Care and Medicine
Director, International Medical Services
University of California, San Francisco

9:45–10:15 **Developing Policies for Conflict of Interest**

Sally J. Rockey
Deputy Director for Extramural Research
National Institutes of Health

10:15–10:45 **Discussion with Speaker and Attendees**

10:45–11:00 **BREAK**

11:00 A.M.–12:25 P.M. **SESSION II: IMPACT OF CONFLICT OF INTEREST POLICIES ON INNOVATION**

Moderator:
Bernard Lo
President, Greenwall Foundation

11:00–11:15 **Industry Perspectives**

Gabriela Lavezzari
Assistant Vice President, Scientific Affairs
PhRMA

11:15–11:30 **Academic Perspective**

Heather H. Pierce
Senior Director, Science Policy and Regulatory Counsel
AAMC

11:30–11:45 **Government Perspective**

Krishna Balakrishnan
Senior Technology Manager, Office of Strategic Alliances
National Center for Advancing Translational Sciences

11:45 A.M.–12:25 P.M. **Discussion with Speakers and Attendees**

12:25–1:10 **WORKING LUNCH**

1:10–2:10 **SESSION III: PUBLIC PERCEPTIONS OF CONFLICT OF INTEREST**

Moderator:
Jill Hartzler Warner
Acting Associate Commissioner for Special Medical Programs
Food and Drug Administration

1:10–1:30 **Serving Public Interest and Facilitating Innovation: Portrayals of Conflict of Interest**

Charles Ornstein
Senior Reporter
ProPublica

1:30–1:50 **Innovation in the Interest of Society**

Mary R. Grealy
President
Healthcare Leadership Council

1:50–2:10 **Discussion with Speakers and Attendees**

2:10–3:50 **SESSION IV: BEST PRACTICES TO FACILITATE INNOVATION**

Moderator:
Dorit Zuk
Science Policy Advisor to the Deputy Director for Extramural Research
National Institutes of Health

2:10–2:15 **FDA**

Michelle T. McMurry-Heath
Associate Director for Science
Center for Devices and Radiological Health
Food and Drug Administration

2:15–2:20 **Tech Transfer**

Todd Sherer
Associate Vice President for Research
Executive Director, Office of Technology Transfer
Emory University

2:20–2:25 **Industry**

Paul Billings
Chief Medical Officer
Life Technologies Corporation

2:25–2:30 **Academia**

Guy M. Chisolm III
Director, Innovation Management and Conflict of Interest Program
Cleveland Clinic

2:30–2:35 **Public/Consumer/Advocate**

Margaret Anderson
Executive Director
FasterCures

2:35–2:40 **Providers**

Henry Brem
Harvey Cushing Professor
Chairman, Department of Neurosurgery
Professor of Neurosurgery, Ophthalmology, Oncology and Biomedical Engineering
Johns Hopkins University School of Medicine

2:40–2:45 **Medical Professional Society**

Allen S. Lichter
Chief Executive Officer
American Society of Clinical Oncology

2:45–3:50 **Roundtable Discussion with Speakers and Attendees**

3:50–4:05 **BREAK**

4:05–5:00 **SESSION V: CONVERGENCE ON CONFLICT OF INTEREST**

Moderator:
Sharon Terry
President and Chief Executive Officer
Genetic Alliance

4:05–4:50 **Panel Discussion**

Panelists:

Margaret Anderson
Executive Director
FasterCures

Gabriela Lavezzari
Assistant Vice President, Scientific Affairs
PhRMA

Allen S. Lichter
Chief Executive Officer
American Society of Clinical Oncology

Bernard Lo
President
Greenwall Foundation

Michelle T. McMurry-Heath
Associate Director for Science
Center for Devices and Radiological Health
Food and Drug Administration

Heather Pierce
Senior Director, Science Policy and Regulatory Counsel
Association of American Medical Colleges

4:50–5:00 **SESSION VI: CONCLUSION**

4:50–5:00 **CONCLUDING REMARKS**

Sharon F. Terry, Roundtable Co-Chair and Workshop Chair
President and Chief Executive Officer
Genetic Alliance

5:00 **ADJOURN**

B

Speaker Biographical Sketches

Margaret Anderson, M.S., is executive director of FasterCures/The Center for Accelerating Medical Solutions, where she defines the organization's strategic priorities and positions on key issues, develops its programmatic portfolio, and manages its operations. Prior to her appointment as executive director, she was FasterCures' chief operating officer for 5 years. She has extensive experience in managing biomedical and public health initiatives and facilitating multisector collaborations.

In 2011 the Clinical Research Forum recognized Anderson with an award for leadership in public advocacy, a testament to the positive impact of her leadership and FasterCures' vital role in improving the medical research system. She is a founding board member and past-president of the Alliance for a Stronger U.S. Food and Drug Administration (FDA), co-chairs the eHealth Initiative's Council on Data and Research, is on the board of the National Health Council, and is a member of the National Center for Advancing Translational Sciences Advisory Council, the Cures Acceleration Network Review Board, the National Health Council Board of Directors, United for Medical Research Steering Committee, and the Institute of Medicine's Forum on Drug Discovery, Development and Translation. She served as a board member of the Council for American Medical Innovation and the Coalition for the Advancement of Medical Research.

Ms. Anderson joined FasterCures after 5 years at the Academy for Educational Development (AED) in Washington, DC. At AED she was the deputy director and a team leader in the Center on AIDS & Community Health. Her responsibilities included financial and budget oversight; management of a team, projects, and staff; and strategic planning. She managed a portfolio that consisted of grants and contracts from the Cen-

ters for Disease Control and Prevention, the Ford Foundation, and the Annie E. Casey Foundation.

Between 1995 and 1998 Ms. Anderson was program director for the Society for Women's Health Research. At the society she managed grant-funded programs, including the startup planning for the multiyear campaign Some Things Only a Woman Can Do to increase women's awareness of and participation in clinical trials, the Get Real: Straight Talk About Women's Health campaign for college campuses to improve young women's health, the Vive La Difference video and facilitator's guide to provide information about sex-based biology, and the annual Scientific Advisory Meeting.

Prior to joining the society Ms. Anderson was a health science analyst at the American Public Health Association (APHA) from 1992 to 1995, where she managed a programmatic portfolio on HIV/AIDS and other sexually transmitted diseases, infectious diseases, women's health, and public health infrastructure issues. At APHA she staffed the AIDS Working Group, the Science Board, and the Long Term Care Task Force and wrote a series of reports on emerging HIV/AIDS issues.

From 1987 to 1991 Anderson was an analyst and project director at the Congressional Office of Technology Assessment. As a staff member in the Biological Applications Program, she contributed to studies on the societal implications of genetic testing. She directed reports on genetic and medical testing in the workplace and contributed to reports on forensic uses of DNA testing, cystic fibrosis screening, and U.S. investment in biotechnology.

Ms. Anderson holds a bachelor's degree from the University of Maryland and a master's degree in science, technology, and public policy from George Washington University's Elliott School of International Affairs.

Krishna (Balki) Balakrishnan, Ph.D., M.B.A., serves as the senior technology manager at the National Center for Advancing Translational Sciences (NCATS), a part of the National Institutes of Health (NIH) that is committed to pushing the frontiers of drug discovery and development through collaborative means. Scientists at NCATS explore novel ways to incorporate the findings of the human genome into chemical starting points for disease intervention. A vast majority of these scientific projects are collaborative in nature, and Dr. Balakrishnan is actively involved in all aspects of developing these strategic alliances. Just prior to joining NCATS, Dr. Balakrishnan served as executive director at the Foundation for Advanced Education in the Sciences, a nonprofit founda-

tion affiliated with NIH. Dr. Balakrishnan's earlier positions at NIH included marketing group leader at the NIH Office of Technology Transfer and senior technology development manager at the National Heart, Lung, and Blood Institute.

At the NIH Office of Technology Transfer, Dr. Balakrishnan oversaw all marketing activities. During his tenure, he promoted and widely expanded NIH's institutional brand, sharply increasing the number of licenses issued and also the total licensing revenues. He was responsible for initiating market research studies, for making program evaluations, and for publicizing and marketing the NIH brand widely. In 2005 he obtained NIH evaluation funding, which enabled him to examine in depth the role of NIH inventors in technology transfer. For his commitment and contributions toward training postdocs for alternate careers in science, Dr. Balakrishnan was awarded the prestigious NIH Director's Mentoring Award.

Prior to working at NIH, Dr. Balakrishnan was vice president of technology and business development and vice president of research and development at a division of Covance, formerly Berkeley Antibody Company. At Covance he led, at different times, the company's new product development, technology licensing, manufacturing, and research and development activities. This deep industry experience in all aspects of biological product development and the wide perspectives gained by working in both for-profit and nonprofit organizations has provided Dr. Balakrishnan with the flexibility and creativity needed to negotiate complex agreements.

Dr. Balakrishnan earned a Ph.D. in biophysical chemistry from Stanford University and an M.B.A. from the University of California, Berkeley. He completed the management cadre leadership development program at NIH and has won a number of performance awards. He is the co-inventor on two U.S. patents and has published and presented globally on various technology transfer aspects and topics. He also serves on various professional boards, panels, and advisory committees.

Paul R. Billings, M.D., Ph.D., is a board-certified internist and clinical geneticist who serves as chief medical officer of Life Technologies Corporation, a new position aimed at improving patient care through expanding the use of medically relevant genomic technologies in clinical settings. Dr. Billings brings extensive expertise and health care experience in the areas of genomics and molecular medicine. Most recently he served as director and chief scientific officer of the Genomic Medicine Institute at El Camino Hospital, the largest community hospital in the

Silicon Valley. He was a member of the U.S. Department of Health and Human Services' Secretary's Advisory Committee on Genetics, Health, and Society. He currently serves on the Scientific Advisory Board of the Food and Drug Administration and the Genomic Medicine Advisory Committee at the Department of Veterans Affairs. Dr. Billings has had a distinguished career as a physician and researcher. He has been a founder or chief executive officer of companies involved in genetic and diagnostic medicine, including GeneSage, Omicia, and CELLective Dx Corporation.

Henry Brem, M.D., has developed new tools and techniques that have changed the field of neurosurgery. Dr. Brem carried out the pivotal clinical study that introduced navigational imaging into the neurosurgical suite. His work led to the U.S. Food and Drug Administration's approval of the first image-guidance computer system for intraoperative localization of tumors. Furthermore, he has changed the surgical armamentarium against brain tumors by inventing and developing Gliadel® wafers to intraoperatively deliver chemotherapy to brain tumors. His work has shown that surgeons can deliver potent therapies directly at the tumor site.

Dr. Brem is the Harvey Cushing Professor of Neurosurgery, Oncology, Biomedical Engineering, and Ophthalmology and chairman of neurosurgery at Johns Hopkins as well as chief of neurosurgery. He received his undergraduate degree from New York University and his medical degree from Harvard University, and he trained in neurosurgery at Columbia. He has built one of the largest brain tumor research and treatment centers in the world. He reinstituted the Hunterian Neurosurgery Laboratory (originally founded by Cushing) and has trained numerous researchers in brain research, particularly in intraoperative imaging, angiogenesis, immunotherapy, stem cell therapy, and targeted brain therapy. Since 2000 he has led the number-one-ranked Johns Hopkins Neurosurgery Department with a wide range of research, clinical, and teaching innovations.

Dr. Brem's teaching was recognized by the Hopkins Professors Award for Excellence in Teaching in 1996. In 1998 he was elected to the Institute of Medicine of the National Academy of Sciences. In 2000 he was awarded the Grass Award by the Society of Neurological Surgeons for meritorious research. Under Dr. Brem's leadership, *U.S. News & World Report* named Johns Hopkins Hospital as having the top ranked neurosurgery and neurology departments for 2010–2012. His trainees are leading brain tumor centers and neurosurgery departments throughout the world.

Guy M. Chisolm III, Ph.D., is a professor in the Department of Cellular and Molecular Medicine and vice chair of the Lerner Research Institute at Cleveland Clinic. He has previously served on Cleveland Clinic's board of governors and board of trustees. He received a B.S. from the University of Pennsylvania, a Ph.D. from the University of Virginia, and postdoctoral research training from the Karolinska Institute (Stockholm) and the Massachusetts Institute of Technology.

Dr. Chisolm has published more than 100 articles on vascular cell biology and atherosclerosis. His research funding has come from the National Institutes of Health (NIH) (predominantly), the American Heart Association (AHA), and industry. He received the Research Merit Award from the AHA's Ohio Valley Affiliate (2001) and a Special Recognition Award for Vascular Biology Research from the AHA's (national) Council on Arteriosclerosis, Thrombosis and Vascular Biology (2006). He has served on journal editorial boards and as member or chair of multiple grant review study sections for NIH and AHA.

Dr. Chisolm is heavily involved in the Cleveland Clinic Lerner College of Medicine (CCLCM) of Case Western Reserve University (CWRU). He is director of the school's basic science curriculum and sits on admissions, faculty appointments, student promotion, and GI curriculum committees. He received the 2007 Lerner Research Institute Award for Excellence in Education and the 2009 CCLCM Distinguished Faculty Award.

Dr. Chisolm is director of Cleveland Clinic's Innovation Management and Conflict of Interest (IM&CoI) Program, chairman of the IM&CoI Committee, and a member of the Clinic's board of trustees conflict of interest committee, and he helped craft the clinic's current conflict of interest policies. He led the organizational committee for a national summit, A Dialogue on Biomedical Conflicts of Interest and Innovation Management, held at Cleveland Clinic on September 6, 2013. He is also a member of CWRU's conflict of interest committee and served on CWRU's President's Committee on Conflict of Interest Policy Development. He is a member of the University of Michigan's Committee on Institutional Conflict of Interest in Clinical Trials.

He is on the steering committee for the Association of American Medical Colleges (AAMC) Forum on Conflict of Interest in Academe (FOCIA), hosted its annual national meeting, and served on planning committees for their subsequent annual meetings He served on the joint AAMC–AAU Advisory Committee on Conflict of Interest in Human Subjects Research and the AAMC task force on financial conflicts of interest in clinical care. He is currently the chair of FOCIA and serves on

conflict of interest–related task forces of the Institute of Medicine and the Pew Charitable Trusts.

Neal H. Cohen, M.D., M.P.H., M.S., F.C.C.M., is a professor of anesthesia and medicine and vice dean for the University of California, San Francisco (UCSF) School of Medicine. He also serves as the medical director of the international service. Dr. Cohen received a B.A. degree from the University of Wisconsin, an M.D. from the UCSF School of Medicine, an M.P.H. from the University of California, Berkeley, and an M.S. in management from the Stanford University Graduate School of Business.

Dr. Cohen is responsible for oversight and approval of all academic and clinical affiliations between the School of Medicine and other academic and clinical institutions as well as industry, both nationally and internationally. He recently chaired the committee that developed the policy on industry relations and serves on the task force that oversees the policy. He has extensive experience in addressing ways to manage conflicts of interest while fostering collaboration between the academic community and industry.

Dr. Cohen is the recipient of the Lifetime Achievement Award from the Society of Critical Care Anesthesiologists. Dr. Cohen has authored numerous articles and given lectures on a wide array of topics related to the care of the critically ill patients, practice management, industry relations and its impact on innovations in health care, and compliance and regulatory affairs.

Mary R. Grealy, J.D., is president of the Healthcare Leadership Council (HLC), a coalition of chief executives of the nation's leading health care companies and organizations. The HLC advocates consumer-centered health care reform, emphasizing the value of private-sector innovation. It is the only health policy advocacy group that represents all sectors of the health care industry. She was appointed to the position in August 1999.

Ms. Grealy has an extensive background in health care policy. She has led important initiatives on the uninsured, improving patient safety and quality, protecting the privacy of patient medical information, and reforming the medical liability laws. She testifies frequently before Congress and federal regulatory agencies.

She is a frequent public speaker on health issues and has been ranked many times by *Modern Healthcare* as 1 of the 100 Most Powerful People

in Healthcare and was named to *Modern Healthcare*'s list of the Top 25 Women in Healthcare for 2009.

Gabriela Lavezzari, Ph.D., M.B.A., joined P*h*RMA in July 2012 as assistant vice president, scientific affairs. In this role, Dr. Lavezzari is the primary staff lead for a variety of strategic initiatives aimed at establishing P*h*RMA as a valuable source of scientific expertise in innovative biopharmaceutical research and development within the scientific and regulatory affairs division of P*h*RMA. Dr. Lavezzari brings to P*h*RMA more than 10 years of combined research experience in the government and industry, with multi-disciplinary expertise in personalized medicine.

Prior to joining P*h*RMA, Dr. Lavezzari served as director of extramural development at the Medco Research Institute, a subsidiary of Medco Health Solutions, where she led clinical utility and cost-effectiveness research to create value-based reimbursement decisions in a variety of different therapeutic areas. Prior to working at Medco, Dr. Lavezzari spent a few years at Theranostics Health, a proteomics-based diagnostics company where she led the laboratory operations and the oncology product development. Prior to Theranostics, Dr. Lavezzari worked at Social Scientific Systems where she provided scientific support to and managed multiple AIDS clinical trials groups as well as laboratory science, laboratory technical, and specialty laboratory committees, subcommittees and working groups.

In addition to her experience in industry, Dr. Lavezzari spent almost 6 years in research at the National Institutes of Health and at Georgetown University, where she completed her postdoctoral training.

Dr. Lavezzari received her Ph.D. in biological sciences from the University of Milano (Italy) and received her M.B.A. from the New York Institute of Technology.

Allen S. Lichter, M.D., FASCO, is the chief executive officer of the American Society of Clinical Oncology (ASCO), a professional organization representing almost 30,000 physicians and health professionals in oncology. Prior to joining ASCO in 2006, Dr. Lichter was at the University of Michigan in two significant leadership roles. He served as chair and professor of radiation oncology from 1984 to 1998 and as dean of the medical school from 1998 to 2006. Dr. Lichter was named the first Isadore Lampe Professor of Radiation Oncology, an endowed chair, and also was the Newman Family Professor of Radiation Oncology. Prior to his tenure at the University of Michigan, Dr. Lichter was the director of the Radiation Therapy Section of the Radiation Oncology Branch of the

National Cancer Institute. Dr. Lichter's research and development of three-dimensional treatment planning led to a gold medal from the American Society for Therapeutic Radiology and Oncology. In 2002 he was elected to membership in the Institute of Medicine of the National Academy of Sciences. As a member of ASCO since 1980, Dr. Lichter has assumed many prominent roles in the society, including president (1998–1999) and founding chairman of ASCO's Conquer Cancer Foundation Board. Dr. Lichter earned a bachelor's degree (1968) and medical degree (1972) from the University of Michigan. He trained in radiation oncology at the University of California, San Francisco, before joining the faculty at Johns Hopkins University and, later, the National Cancer Institute.

Bernard Lo, M.D., is president of the Greenwall Foundation, whose mission is supporting bioethics research and young researchers in bioethics. He has been director of the Greenwall Faculty Scholars Program since 2001. He is professor emeritus of medicine and director emeritus of the Program in Medical Ethics at the University of California, San Francisco (UCSF). Dr. Lo serves on the board of directors of the Association for the Accreditation of Human Research Protection Programs and on the medical advisory panel of Blue Cross/Blue Shield. From 1996 to 2001 he served as a member of the National Bioethics Advisory Committee. From 1997 to 2001 he chaired the expert panel convened by the American College of Physicians to develop clinical, ethical, and policy recommendations regarding care near the end of life. He is a member of the Institute of Medicine (IOM) and previously served as chair of the Health Sciences Policy Board and as a member of the IOM council. He chaired an IOM committee, Conflicts of Interest in Medical Research, Education, and Practice. Dr. Lo developed a course on responsible conduct of research that 120 UCSF postdoctoral fellows and junior faculty take each year, and he is author of *Resolving Ethical Dilemmas: A Guide for Clinicians* (4th ed., 2010) and of *Ethical Issues in Clinical Research* (2010). He is a graduate of Stanford University Medical School, did his residency at both the University of California, Los Angeles, and Stanford, and completed a fellowship at Stanford as a Robert Wood Johnson Clinical Scholar.

Michelle McMurry-Heath, M.D., Ph.D., is assistant director for science of the Center for Devices and Radiological Health at the U.S. Food and Drug Administration (FDA). Prior to joining FDA, she was the founding director of the Health, Biomedical Science, and Society Initia-

tive at the Aspen Institute and adjunct assistant professor of health policy at George Washington University. Her Aspen Institute team focused on creating new policy strategies for stimulating biomedical research, disseminating emerging health care technologies, and reducing health care disparities domestically and internationally. Her science diplomacy work has included projects from Rwanda to Cambodia. From 2001 to 2004, she oversaw health and social policy issues for Senator Joseph Lieberman and was the senior health policy advisor for the Lieberman for President Campaign. While on the Hill, she worked on homeland security, health disparities, health care quality, and translational research bills, including the American Center for Cures initiative and legislation (later enacted as the Cures Acceleration Network). After studying biochemistry at Harvard, Dr. McMurry-Heath went on to become the first African American to receive both M.D. and Ph.D. degrees from Duke University. She trained in pediatrics and molecular immunology.

Charles Ornstein is a senior reporter for ProPublica, an investigative news organization in New York. He is also an adjunct professor at the Columbia University Graduate School of Journalism and president of the board of the Association of Health Care Journalists. Mr. Ornstein is a graduate of the University of Pennsylvania, where he was editor of the college newspaper, the *Daily Pennsylvanian*. In 1999–2000, he was a media fellow with the Henry J. Kaiser Family Foundation. Prior to joining ProPublica he was a reporter for 5 years at the *Dallas Morning News* and for 7 years at the *Los Angeles Times*.

Mr. Ornstein, in collaboration with Tracy Weber, was a lead reporter on a series of articles in the *Los Angeles Times* titled The Troubles at King/Drew, which won the Pulitzer Prize for Public Service, the Robert F. Kennedy Journalism Award and the Sigma Delta Chi Award for public service in 2005. His ProPublica series, also with Ms. Weber, When Caregivers Harm: California's Unwatched Nurses, was a finalist for a 2010 Pulitzer Prize for Public Service.

Heather H. Pierce, J.D., M.P.H., is senior director for science policy and regulatory counsel at the Association of American Medical Colleges (AAMC). She serves as AAMC's staff leader for scientific issues, including clinical research, regulatory compliance, conflicts of interest, evidence-based regulation, and interactions between industry, government, and academia in biomedical research. She is also the program leader for the AAMC's Forum on Conflict of Interest in Academe.

Ms. Pierce regularly speaks at national forums on issues related to the protection of human subjects, conflicts of interest, scientific misconduct, and the regulation of research. She has served on ad hoc committees and task forces convened by organizations, including the Institute of Medicine, the Pew Charitable Trusts, the National Dialogue on Healthcare Innovation, and Public Responsibility in Medicine and Research.

Prior to joining AAMC, Ms. Pierce was an attorney in the health care group of the law firm of Ropes & Gray LLP in New York. Her regulatory practice focused on medical research and clinical care. She received her law degree from New York University and her M.P.H. in health law from Boston University.

Sally J. Rockey, Ph.D., is the National Institutes of Health (NIH) deputy director for extramural research, leading the extramural research activities of the agency. Her role is to oversee the development and implementation of the critical policies and guidelines central to the successful conduct of NIH-supported biomedical research. Dr. Rockey works in close partnership with the biomedical research community around the world.

Dr. Rockey received her Ph.D. in entomology from Ohio State University and has spent the majority of her career in the area of research administration and information technology. In 1986 she joined the U.S. Department of Agriculture, soon becoming the deputy administrator of the cooperative state research, education, and extension service, overseeing the extramural grants program and portfolio. In 2002 she became the agency's chief information officer, applying her breadth of government knowledge to information technology. In 2005 Dr. Rockey was appointed to the position of NIH deputy director of the Office of Extramural Research and brought her extensive experience in research administration to biomedical research. She assumed her current position as NIH deputy director for extramural research in 2008.

Dr. Rockey leads or is active on a number of federal committees related to science and research, federal assistance, and electronic government. She works most closely with other federal science and university administrators, small businesses, professional societies, and the scientific communities. In 2012 Dr. Rockey co-led a groundbreaking effort on the biomedical workforce. Dr. Rockey is a skilled public speaker, giving countless presentations on extramural research priorities and policies, grantsmanship, the competitive peer review process, workforce, scien-

tific integrity, and information technology. She is the author of the widely read "Rock Talk" blog.

Todd Sherer, Ph.D., is associate vice president for research administration and executive director of technology transfer at Emory University. He has worked in technology transfer for 22 years on both coasts at public and private universities. Before coming to Emory, he was the director of the Office of Technology and Research Collaborations at Oregon Health and Science University in Portland. He earned his doctorate in toxicology at Washington State University in Pullman, where he studied gene expression in the developing brain. Dr. Sherer became a registered patent agent with the U.S. Patent and Trademark Office in 1995. He continues to be an active speaker at technology transfer, economic development, and commercialization conferences across the globe. Dr. Sherer is immediate past president for the Association of University Technology Managers, where he has been an active board member and volunteer for several decades. His current efforts have been focused on encouraging and adopting positive changes in technology transfer, nationally, through creative new initiatives that reduce barriers and improve impact.

Sharon Terry, M.A., is president and chief executive officer of the Genetic Alliance, a network of more than 10,000 organizations, 1,200 of which are disease advocacy organizations. Genetic Alliance improves health through the authentic engagement of communities and individuals. It develops innovative solutions through novel partnerships, connecting consumers to smart services.

She is the founding chief executive officer of PXE International, a research advocacy organization for the genetic condition pseudoxanthoma elasticum (PXE). As co-discoverer of the gene associated with PXE, she holds the patent for ABCC6 and has assigned her rights to the foundation. She developed a diagnostic test and is conducting clinical trials.

Ms. Terry is also a co-founder of the Genetic Alliance Registry and Biobank. She is the author of more than 90 peer-reviewed articles. In her focus at the forefront of consumer participation in genetics research, services, and policy, she serves in a leadership role on many of the major international and national organizations, including the Institute of Medicine (IOM) Health Sciences Policy Board, the National Coalition for Health Professional Education in Genetics board, and the International Rare Disease Research Consortium Interim Executive Committee, and she is a member of the IOM Roundtable on Translating Genomic-Based Research for Health. She is on the editorial boards of several journals.

She was instrumental in the passage of the Genetic Information Nondiscrimination Act. In 2005 she received an honorary doctorate from Iona College for her work in community engagement; the first Patient Service Award from the University of North Carolina Institute for Pharmacogenomics and Individualized Therapy in 2007; the Research!America Distinguished Organization Advocacy Award in 2009; and the Clinical Research Forum and Foundation's Annual Award for Leadership in Public Advocacy in 2011. She is an Ashoka Fellow.

Jill Hartzler Warner, J.D., is acting associate commissioner for special medical programs at the U.S. Food and Drug Administration (FDA). She oversees FDA's Office of Pediatric Therapeutics, Office of Orphan Products Development, Office of Good Clinical Practice, and Office of Combination Products, as well as the advisory committee oversight and management staff. In this position Ms. Warner provides leadership and direction in the coordination of internal and external review of pediatric science, safety, ethics, and international issues. She oversees the implementation of the orphan products provisions of the Federal Food, Drug, and Cosmetic Act to encourage the development of drugs of limited commercial value for use in rare diseases and conditions to advance public health. She promotes and directs good clinical practice and human subject protection regulation, policy, harmonization, and outreach activities. Ms. Warner provides leadership and direction on issues involving the regulation of combination products, the classification of human medical products, and jurisdiction over human medical products. Further, she oversees management of FDA advisory committees to provide consistent application of laws and policies applicable to such committees, and directs development of policy, procedures, and processes to maintain and improve the agency's advisory committee program.

Prior to her current position, Ms. Warner served FDA's Office of the Commissioner and the Center for Biologics Evaluation and Research in a variety of roles, including acting assistant commissioner for accountability and integrity, senior policy advisor and counselor, and associate chief counsel for biologics. Ms. Warner received her B.A. in environmental sciences, with distinction, from the University of Virginia and her J.D. from the University of Virginia School of Law.

Dorit Zuk, Ph.D., is the science policy advisor to the deputy director for extramural research at the National Institutes of Health (NIH). She is responsible for coordinating and disseminating policies and procedures

on a variety of research-related issues, such as financial conflicts of interest and the biomedical research workforce. Dr. Zuk came to NIH in 2009 after a year as a Hellman Fellow for Science Policy at the American Academy of Arts and Sciences. Before that she was an American Association for the Advancement of Science (AAAS) Science and Technology Policy Fellow in the Office of Extramural Research at NIH. From 2000 to 2007 Dr. Zuk worked as a scientific editor at Cell Press, where she was deputy editor of the journal *Cell* (2000–2002) and editor of *Molecular Cell* (2003–2007). Dr. Zuk also serves on the education and professional development committee of the American Society of Biochemists and Molecular Biologists and chairs the AAAS Fellowships Advisory Committee.

C

Statement of Task

An ad hoc planning committee will plan and conduct a public workshop to examine and discuss transparency in medical research. The goal of the workshop will be to examine the effect of current conflict of interest regulations on medical innovation. The workshop will advance discussions among a broad array of stakeholders, which may include government officials, pharmaceutical company representatives, academic researchers, regulators, funders, providers, and patients. The planning committee will develop the workshop agenda, select and invite speakers and discussants, and moderate the discussions. An individually authored summary of the workshop will be prepared by a designated rapporteur in accordance with institutional policy and procedures.

D

Registered Attendees

Nicholas Allen
PXE International

Margaret Anderson
FasterCures

Ronald Anson
American College of Cardiology

Daniel Arias
Enetic Alliance

Krishna Balakrishnan
National Center for Advancing Translational Sciences

Jeannie Baumann
Bloomberg BNA

Paul Billings
Life Technologies Corporation

Julie Bolliner
Johns Hopkins University

Khaled Bouri
U.S. Food and Drug Administration

Henry Brem
Johns Hopkins University School of Medicine

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Joel Brill
Predictive Health, LLC

Eric Caplan
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Ann Cashion
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Alyna Dada
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Rebecca English
Institute of Medicine

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Complete Genomics

Stephanie Fischer
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Rachel Hickey
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Jennifer Hobin
American Association for Cancer Research

Kathi Huddleston
Inova Translational Medicine Institute

David Innes
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Fair Chance, Inc.

David Wierz
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Erin Wilhelm
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