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CONFLICT OF INTEREST

WORKSHOP SUMMARY

Lister Hill Auditorium
National Institutes of Health
Bethesda, Maryland

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PREPARED BY:
Analytical Sciences, Inc.

Conflict of Interest Workshop

National Institutes of Health, Bethesda, MD
September 30, 2002

Executive Summary

Objectivity of researchers is an essential value in scientific research and the basis for public trust. Any research links with industry, while not intrinsically unacceptable raise the prospect that scientific advances will bring financial gain for the research scientist and his or her institution. Concerns arise when financial considerations may compromise—or have the appearance of compromising—the professional judgment of the investigator or the institutional official, independence in the design, conduct, publication of research, and/or the welfare of human subjects. As the major sponsor of biomedical research, the National Institutes of Health (NIH) seeks to work in partnership with research institutions and university groups to harmonize approaches to conflict of interest (COI) issues and to address these issues in a reasonable way without hindering scientific innovation and discovery. Although a specific outcome was not the goal of this workshop, the meeting elicited wide-ranging discussion from diverse viewpoints to inform officials involved in developing, implementing, and monitoring policies to disclose, assess, and manage conflicts of interest. Meeting attendees included research scientists; university administrators; representatives from professional organizations that have taken leadership roles in drafting guidelines for their members, such as the Association of American Medical Colleges (AAMC) and the Association of American Universities (AAU); and senior staff from the individual Institutes and Offices of the NIH. Although raising the bar on oversight in managing financial interests helps to underscore principled relationships that withstand public scrutiny, it is important not to over-react and over-regulate, which can limit patient opportunities and exact unintended and significant transaction costs in the conduct of research.

The issues associated with *individual* COI have already received a great deal of deliberation, with current attention now focused largely on developing and improving existing systems for managing such conflicts, as well as on sharing best practices and lessons learned. The understanding of Public Health Service (PHS) reporting requirements and individual COI policies and procedures varies widely at institutions across the country. These variations include management and monitoring practices, how and when the Institutional Review Board (IRB) is involved, and limits on equity holdings and company participation [1, 2]. Meeting participants generally agreed with the core principles the AAMC and the AAU have articulated to guide policy development in this area. These core principles include disallowing individuals who hold significant financial interest in research involving human subjects from conducting the research except under compelling circumstances; coordinating COI and IRB processes with adherence to a more stringent determination; and promoting disclosure and transparency of financial interests. The American Society for Gene Therapy (ASGT) has put forth a simple but rigorous policy disallowing investigators who have stock in a company that sponsors a trial to have any patient contact during that trial. Some participants emphasized that COI are highly situational and should be evaluated on a case-by-case basis, while others argued vehemently for standard rules,

particularly in non-clinical research to keep at a minimum the number of exceptions that will become precedents.

Guidelines associated with managing *institutional* COI are less developed but of increasing concern. This concern arises from the increase in equity holdings and royalties by universities in non-public companies that have spun off from university-based research findings, particularly in the decade following the Bayh-Dole legislation. Current efforts focus on developing *new* policies and principles since no regulations govern this area. In addition, workshop participants' reactions to the suggested guidelines and procedures often varied. The AAU issued general recommendations on managing institutional conflicts of interest in October 2001 [3] and the AAMC issued complementary recommendations in October 2002 [4] that apply specifically to institutional financial interests in human subjects research. The AAU concluded that a university's institutional financial COI process should follow a 3-fold approach: 1) *Disclose* always, 2) *manage* the conflict in most cases, and 3) *prohibit* the activity when necessary to protect the public interest or the interest of the university.

The recommendation to segregate research endeavors from financial and technology transfer activities generated lively discussion. Most participants, including those from the Department of Health and Human Services (HHS), were highly supportive. Others expressed skepticism that separating out technology transfer will foster clearer focus on COI issues. Even though the appearance of a conflict might exist, some institutions view technology transfer as an integral part of the academic function with reporting properly handled through academic research channels. Some expressed particular concern about talk of a "firewall" between research and technology transfer offices because they place enormous value on the technology transfer office as a frontline player in ensuring compliance and in promoting institutional values of scientific integrity. Participants acknowledged that the role of university officials is increasingly complex, particularly if they oversee IRBs and grants administration. They also underscored the importance of rigorous, effective, and disinterested monitoring of research protections for human subjects. In some cases, reciprocal IRBs may be a good approach for managing institutional COI. Participants articulated a key principle of separating lines of management and governance of protection for human subjects, technology transfer, and research management. They also acknowledged that oversight for all such issues must ultimately converge at a higher and appropriate level. There is need to further elaborate how institutions might generate firewalls between financial interests and oversight of research.

The role of the IRB in COI issues also generated significant discussion. Some expressed strong sentiments that potential conflicts of interest should be a material consideration in IRB deliberations. The overriding opinion, however, was that IRBs would adopt an increasingly adversarial tone, that IRBs are already burdened by a heavy workload and not competent to address COI issues, and that review of financial conflicts of interest should more properly be the purview of a separate committee dedicated to this purpose, as some universities have already done. On a related issue, participants noted that IRB members should report certain financial interests annually and should adhere to federal policies governing recusal from protocol review when necessary.

A proper balance between federal regulation and self-regulation is needed, with the primary onus on research institutions to develop guidelines and mechanisms to ensure and enhance research integrity. The research community understands that serious action on their part in demonstrating compliance can help to mitigate increasing public pressure for government regulation. As institutions strive to balance risks, public perception, and patient safety, their development of COI policies and procedures, including clear assignment of institutional responsibility, must occur in tandem with the education of researchers and the public about proper disclosure and management of potential and real conflicts of interest, both individual and institutional. Next steps for the NIH will likely include further discussion about involving students in COI issues to foster an understanding of the issues underlying these topics, linking human subject protections with COI guidelines, creating a shared knowledge base with data on the volume and type of COI issues, and developing best practices on how conflicts are resolved, including effective auditing and sanctions once an infraction has occurred.

Conflict of Interest Workshop

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Meeting Summary

Opening Remarks

Dr. Elias Zerhouni, M.D., Director of the NIH, opened the workshop by thanking the participants and organizers, Dr. Wendy Baldwin, Dr. Tony Demsey, and Dr. Steven Hausman. Dr. Zerhouni recognized the research community for working hard to address COI issues and noted that the NIH was pivotal in establishing regulations by the Department of Health and Human Services (HHS) in 1995 regarding this topic. He viewed this workshop as fundamental to NIH efforts at maintaining public trust and confidence in biomedical enterprises.

Having addressed conflict of interest issues both personally and at the institutional level as an extramural scientist, Dr. Zerhouni acknowledged how difficult it can be to implement policies and procedures. Government institutions and universities must be partners and deal with this issue in a realistic way. However, he cautioned against too much diversity in regulations and expressed his expectation that the workshop would help identify a proper balance by providing views on how regulations have been lived "on the ground." Ultimately, the workshop sponsors hoped to discern best practices and to harmonize the way academic institutions approach conflict of interest issues.

Dr. Zerhouni then focused on the subject of institutional conflicts of interest, noting the increased attention to this topic and how it has evolved since the enactment of the Bayh-Dole Act in 1980. Beyond science and translation, he emphasized that the American public has gained from this investment in science through the development of new products, drugs, and research tools. He shared his personal concerns that if further regulation were ever to become necessary, it should not impose unduly high "transaction costs" on the enterprise of science such that innovation and discovery are hindered. Dr. Zerhouni added that while NIH makes awards to institutions, it entrusts most of the oversight of research to partner institutions. Therefore, he was pleased to see strong representation from universities and from organizations, such as the AAMC and AAU, which have taken a leadership role on this topic. Dr. Zerhouni concluded by emphasizing the need to understand the differences between government regulations and underscored the important responsibility of universities to maintain their image as fair and objective arbiters of scientific knowledge.

Before introducing the first panel, Dr. Wendy Baldwin, Deputy Director for Extramural Research, NIH, described the goals for the workshop as 2-fold. The first half of the workshop addressed problems and solutions concerning *individual* conflicts of interest. The second part of the workshop focused on *institutional* conflicts of interest. No specific outcome was expected on these topics, other than a synthesis of the discussion. Dr. Baldwin acknowledged that these are

very complicated issues and will require considerable discussion if the academic community is to move toward a consolidated view. The workshop was intended to be an interactive process that would allow participants to share experiences and to inform officials involved in writing, implementing, and monitoring regulations.

Current Climate and Visions for the Future

Nils Hasselmo, Ph.D., Association of American Universities

After thanking senior NIH officials and the meeting organizers, Dr. Hasselmo spoke briefly about the perspective of the AAU on COI. He gave an overview of the AAU October 2001 report [3], noting that a task force addressed both individual and institutional COI in an effort to sustain public confidence and to assist members in reviewing and strengthening their policies. As a result of these activities, the AAU found that developing reliable systems to manage COI was a major challenge. Therefore, in regard to individual COI, they looked at improving existing systems. Dr. Hasselmo considered institutional COI to be more like an "unplowed field," and the AAU is focused on developing *new* policies and principles, since no regulations govern this area.

Dr. Hasselmo discussed AAU's approach to this topic in a broad way, noting the formation of a task force, workshops, and coordination with the AAMC. In terms of individual COI, the task force identified extraordinary complexities so case-by-case review is often necessary for specific situations. However, because universities still need guidance, the AAU developed 10 operating guidelines. One major recommendation is that related financial interests in human subjects research should generally not be allowable, absent compelling circumstances. Their guidelines also address the need to coordinate IRB and COI processes, since both are required by different government regulations, but need to be connected by campuses so that neither system operates in isolation from the other.

Turning to institutional COI, Dr. Hasselmo said it is important to focus on this topic because there has been a dramatic increase in start-up firms coming out of universities. Universities are receiving equity in non-public companies, as well as royalties. This means control of equity is sometimes managed by those who have research responsibility, thereby increasing the potential for conflict. The AAU task force came up with a "mantra" that illustrates a strategy for addressing potential institutional COI. First, institutions should always disclose potential conflicts. Second, if a conflict is identified, there should be a strategy for managing the conflict, and if necessary, the activity that caused the conflict should be prohibited. Most importantly, however, decision-making about financial activities and research activities should be segregated, so they are independently managed.

The AAU report has been distributed widely to its members and the science policy community. Although no comprehensive evaluation of the report has been done, the AAU has convened campus experts, consulted with government colleagues, and contacted some of their member organizations to discuss the implications of the report. The association has also helped to establish a new accrediting body, the Association for the Accreditation of Human Research

Protections Programs, and has encouraged member universities to undergo such evaluation. Dr. Hasselmo expressed the AAU's hope that these activities have helped universities tighten their COI policies and have demonstrated that the research community is serious about these issues. Dr. Hasselmo also discussed some future challenges for the academic community, which include monitoring research collaborations, educating researchers and administrative officials about COI issues, and fostering an ethic of accountability and responsibility. He concluded by emphasizing that the research community *must* act with integrity in addressing these important matters.

Janet Heinrich, Dr.P.H., R.N., U.S. General Accounting Office

Dr. Heinrich gave an overview of the November 2001 General Accounting Office (GAO) report, *Biomedical Research: HHS Directions Needed to Address Financial Conflicts of Interest* [1], which was prepared at the request of Senator Bill Frist (R-TN). As discussed in the report, she noted that there has been an increase in research collaborations since the 1980 Bayh-Dole legislation, which has led to new products and innovations. However, recent allegations of investigators with improper financial interests threaten to compromise research integrity and to jeopardize the safety of human subjects in research.

Turning to the methodology of the study, Dr. Heinrich reported that the GAO conducted interviews with many HHS officials, including those from the NIH, the Food and Drug Administration (FDA), and the Office for Human Research Protections, as well as case studies from five universities: UCLA; University of North Carolina (UNC), Chapel Hill; University of Washington, Seattle; Washington University, St. Louis; and Yale University. These five universities are among the top 20 institutions receiving NIH support and conducting major technology transfer activity.

As a result of the investigation, GAO evaluators found that universities had in place individual COI policies that covered both private and publicly funded research, but that these policies and procedures varied greatly. For instance, there were differences in how and when the IRB was involved in COI matters. GAO also noted that all of the universities allowed self-certification of compliance. However, research and COI information were kept in multiple locations and formats, making it a challenge to ensure that COI issues were managed properly.

Institutional COI is a more recent focus of attention, and Dr. Heinrich reported that the five universities GAO visited tended to manage institutional investments separately from academic affairs. In some cases, technology transfer activities were separated from academic affairs, but this practice varied. The five universities had, or were developing, policies on accepting equity in start-up companies, but they placed varying limits on equity holdings and their role in start-ups. For example, equity limits ranged from 2 to 49 percent, and roles in the company ranged from "no involvement" to having a seat at the table.

Overall, the GAO found no direct link in the federal regulations between oversight of financial interests and protection of human subjects. In addition, they noted that PHS and FDA financial

interest regulations are not uniform in timing or disclosure thresholds. They also noted that the universities in the GAO study were confused about PHS reporting requirements.

As a result of its investigation, the GAO identified a number of future challenges. First, they found that institutions need and want information on best practices. The GAO considered the draft interim guidance on financial relationships in clinical research by HHS to be promising but in need of revision, especially in addressing institutional COI. In addition, HHS needs to link the protection of human subjects and the financial interest regulations. Finally, the GAO stated that as more biomedical research becomes privately funded, it will be important to address potential financial conflicts of interest in settings that may not be operating under broad financial COI policies and procedures. The GAO recommended that HHS develop and communicate information on best practices for managing both individual and institutional COI. In addition, HHS should develop specific guidance or regulations concerning institutional financial COI.

David Korn, M.D., Association of American Medical Colleges

Dr. Korn gave a history of the AAMC's interest in this topic, noting that they were aware of AAU's efforts, and, as a result, decided to focus on financial COI and human subjects research. The AAMC undertook this effort in the context of a confluence of issues, including growing public concerns about potential conflicts of interest in research, increasing laxness in federal legislation and regulations, and the dramatically changing "ecology of biomedical research." In general, this includes the astonishing progress of biomedical science itself and, specifically, the advent of recombinant DNA technology, the 1980 Supreme Court ruling that living organisms can be patented, and the 1980 Bayh-Dole Act. Dr. Korn observed that there is a public sense that the national biomedical research enterprise is beset by a "virtual pandemic" of financial conflicts of interest.

Dr. Korn then provided a brief overview of the efforts the AAMC task force has undertaken to address this topic, noting that the AAMC was pleased that this diverse group of scientists, patient advocates, and industry leaders reached consensus. The core principles the task force developed are outlined in the AAMC December 2001 publication, *Protecting Subjects, Preserving Trust, Promoting Progress: Policy and Guidelines or the Oversight of Individual Financial Interests in Human Subjects Research* [5]. The five principles establish: 1) The "rebuttable presumption" that research in which there are financial interests should not be conducted by the affected individual or institution; 2) that institutions should ensure that administrative practices related to research administration are separate from investment management and technology transfer activities; 3) that separate COI committees should be established to review individual and institutional COI, and that they, especially the latter, should have public representatives; 4) that institutional COI policies and procedures should be comprehensive, unambiguous, well-publicized, consistently applied, and effectively enforced; and 5) that in the presence of financial interests, approved research must be managed through rigorous, effective, and disinterested monitoring, and that mandatory disclosure should be provided to prospective subjects and in all communications.

Importantly, the AAMC report did not contain language banning any activity. Rather, it emphasized that conflicts of interest are highly situational, and evaluations of conflicts should be on a case-by-case basis, considering the nature of the financial interest, as well as a host of other factors. Universities and their medical centers will establish their own standards for how compelling the circumstances must be to support rebuttal, although the task force intended highly rigorous standards.

The AAMC plans to promote the adoption of their principles, evaluate the influence of the reports, and ensure that practices do not exact unreasonable transaction costs. It is expected that widespread adoption of the stringent principles in these reports would significantly raise the bar of oversight in management of financial interests, reduce the disturbing variability in institutional policies and procedures that has recently been documented, and help sustain principled relationships between academia and industry that withstand public scrutiny. Quoting from the first report from the AAMC task force, Dr. Korn concluded by emphasizing that the Task Force did not intend that its reports should interfere with healthy academic/industry relationships or with the continued development of products from academic biomedical inventions that will benefit the public.

Lawrence Rudolph, J.D., National Science Foundation (NSF)

Mr. Rudolph began his presentation by emphasizing that the research community should neither do nothing, nor over-react to the issue of conflict of interest. He commended NIH's work on financial disclosure policies in the 1990s and described how the NIH and the NSF worked collectively to enact a joint individual financial disclosure policy for investigators. The real question will be how well institutions can self-regulate. Referring to an OER survey of 300 institutions, he said he endorses federal institutions such as the NIH to gather information on best practices, but believes organizations like the AAMC and AAU should provide leadership and take ultimate responsibility for these issues, noting that perfect behavior cannot be regulated. However, he warned that if something is not done, the public and Congress will pressure federal agencies to act.

Mr. Rudolph said his work with the NSF has shown that the "one size fits all" approach is not necessarily optimal. For instance, there are important differences between the research that NIH supports and the research that NSF supports, so policies will not be the same. He questioned whether even a government-wide policy was possible given the complexities and difficulties inherent in auditing and ensuring compliance. Mr. Rudolph stressed that the most practical policy is one that works for most, addresses real issues rather than paper issues, and separates management of institutional conflicts from research activity.

In conclusion, Mr. Rudolph cautioned against over-regulating. It is easy to create elaborate mechanisms to give an appearance that issues are being addressed, he noted, but it is more important to clearly identify what needs to be addressed and make sure those concerns are met.

Eve Slater, M.D., Office of the Assistant Secretary for Health, HHS
Dr. Slater said that HHS recognizes the presence of conflicts related to the protection of human research subjects and emphasized that the research community and governing agencies must promote an "exquisite and implicit" trust in clinical studies through openness, honesty, integrity, and responsibility. She applauded the group's efforts in trying to strengthen the infrastructure for the protection of human subjects and increase participation in clinical trials.

Dr. Slater then briefly discussed the evolution of the HHS guidelines on this issue. In 2000, HHS requested that experts comment on their experiences, ideas, and suggestions regarding HHS guidelines for protecting human subjects when financial interests are involved. In January 2001, draft interim guidance on this topic was published. Since then, HHS has obtained input through conferences and from organizations such as the AAMC, American Medical Association (AMA), and AAU. The guidance will soon be finalized. Dr. Slater said that HHS strongly supports suggestions to separate responsibility for institutional development and licensing from the actual conduct of research. HHS also supports recommendations that an investigator be recused from research when conflicts are identified.

Participant Discussion

Dr. Baldwin reiterated the importance of having flexible policies and firm principles in place. She also noted that NIH's recent survey of institutions captured the diversity of practices and level of understanding in the research community. She called for participants to contribute their ideas about the best ways to share "best practices" and reach out for help.

Participants expressed concern about the concept of separating technology transfer activities from research endeavors because there is no evidence that separating out technology transfer will foster a better focus on COI issues. At MIT for instance, the technology transfer office reports through the academic function because they do not view this as purely a business activity—although some money is made—but as an integral part of the academic function. Some participants felt this decision should be made on a case-by-case basis. Respondents agreed that these matters are complex, but suggested the key factor is how to develop a functioning system that separates research from financial decision-making. Dr. Korn added that the AAMC task force did not feel separating out technology transfer was a controversial idea, since the "appearance" of a conflict is clearly evident.

Another participant asked whether it would be a conflict of interest for a pharmaceutical company to reimburse an investigator based on patient accrual levels. Dr. Korn responded that the AAMC task force came out strongly against bonus payments for patient accrual, but payment of costs, such as staffing for recruitment, is reasonable, even if broken out on a per patient basis. Others echoed this sentiment, saying that it is acceptable if it does not impede objectivity or the payments are not outlandish, and that it was similar to receiving money from a grant. Participants also emphasized that skepticism should not automatically be triggered simply because a pharmaceutical company is providing financial support. The focus should not be on the dollars themselves but on the conditions that accompany the funds. One participant said their

institution considered payments to enroll human subjects to be a clear financial conflict, although manageable, and disclosed this as part of the informed consent process. Participants also pointed out that as a result of university uneasiness about financial relationships, pharmaceutical companies are increasingly turning to the commercial sector to manage clinical trials.

Discussion also addressed the best administrative lines of management to avoid conflicts of interest. Participants acknowledged that the role of university officials is difficult, especially when they oversee IRBs and grant administration. Participants also asked AAMC and AAU representatives how they see the role of the university official. Dr. Kelch said that key principles from both documents, especially the newest document, have separate lines of management and governance for things as disparate as protection for human subjects, technology transfer and research management. While the report was not prescriptive, it indicated consensus on the belief that functions can be separated, but can also come together at the level of the Board of Trustees. Dr. Korn added that the AAMC recognizes the processes have to come together, but they should not be too far down in the hierarchy, such as at the laboratory chief level; the "rule of reasonableness" should apply. Others suggested that Offices of Research Integrity, under the auspices of the president, should govern IRBs. Another alternative is to have a compliance officer provide independent verification to the president. Every organization should be able to identify appropriate senior officials to govern, and it is impractical to eliminate their interaction with researchers.

Case Study Presentations

Lisa Bero, Ph.D., University of California, San Francisco (UCSF)

Representing the perspective of a medical school, Dr. Bero gave an overview of UCSF's financial disclosure policies. She noted there are different courses of action depending on whether the funding source is private or public. She then discussed the extensive information gathering process undertaken when investigating a financial disclosure that exceeds certain thresholds. Dr. Bero explained that, in reviewing financial disclosures related to federal grants, the COI committee's main concern is whether the financial relationship could have a direct and significant effect on the NIH-funded research, and if so, how the relationship should be managed. Dr. Bero then presented two conflict of interest scenarios and discussed UCSF's response. These hypothetical case studies arose from an ORI-funded study, conducted by Dr. Bero and colleague Elizabeth Boyd, of how decisions are made at the institutional level to manage COI.

> **Case 1:** Case 1 involved an investigator, Dr. Toe, who had a $1.2M NIH grant to conduct a comparative evaluation of toe cancer diagnostic techniques. At the same time, Dr. Toe had a relationship with a company that manufactured her toe cancer detection device. She was named on the company's patent application as inventor and served on the scientific advisory board. Dr. Toe also received consulting fees to help train people to use the diagnostic test and to review samples to assess the technique and had stock options, of unknown value, in this privately owned company.

Resolution: UCSF determined that Dr. Toe's conflict was likely to have a direct and significant effect on her NIH research. The testing of the cancer devices overlapped with the NIH research. UCSF decided that Dr. Toe *should not participate* in the research portion of the grant, and she should disclose financial ties to the company in all publications and presentations. However, Dr. Toe participation in the training activities related to her consulting for the company did not pose a conflict with the NIH grant because they involved training and not research.

Case 2: Case 2 involved Dr. Fountain, the Principal Investigator (PI) of a large NIH grant in its 25th year of funding. Dr. Fountain is chairman of the board, founder, and owner of a biotechnology company, which he started in January 2000 to commercialize discoveries from his research. The company licensed the patent rights to Dr. Fountain's invention when a previous licensee failed to commercialize the invention. The company is not currently selling or manufacturing a product, but intends to do so someday.
Resolution: UCSF's COI committee found that the disclosed conflict could have a direct and significant effect on the NIH grant, but also that the NIH grant activities were adequately separate from the company's activities. The committee agreed the Dr. Fountain *should* continue to receive the funding, but must also disclose his financial ties to the company in all publications and presentations.

Participant Discussion

In elaboration of the first case, Dr. Bero clarified that the university had not patented Dr. Toe's work because she conducted the research before coming to the university. Dr. Bero said this highlights the differences between junior and senior faculty when conducting COI reviews. There was also discussion about how UCSF handles "conflicts of commitment" (e.g., the investigator's time is compromised due to multiple commitments). Dr. Bero noted that the COI committee does not address this issue, but they can refer it to the department chairperson who handles these matters.

In reference to Dr. Toe's case study, participants also discussed approaches to the valuation of privately held stock. One participant suggested that since Dr. Toe's stock had an unknown value on the disclosure form, the university could assign a value based on what the venture capitalist paid. Dr. Bero responded that the assigned value can be irrelevant if the investigator has a large management role in the company and suggested that the better alternative might be for the investigator/inventor, rather than the university, to declare a valuation range. Another participant suggested that having a stock that is not (yet) worth anything could create a further conflict and impair the investigator's judgment. For instance, the investigator may be motivated to do certain things because he or she wants to see the stock value increase.

Participants also inquired how UCSF handles research that involves testing an Investigational New Device (IND) for FDA approval. Dr. Bero responded that it depends on whether the investigator is an expert in working with the device or procedure. If the investigator is so expert that they must be involved in the research, the PI normally has to eliminate conflict, either by

divesting the financial interests or refusing the funding. A suggestion was made to remove chairpersons from COI decision-making because they are too close to the faculty.

Dr. Bero also explained that the UCSF campus' clinical trial policy does not allow an investigator to accept income from a company during the course of a trial if that company is funding the trial. Furthermore, state law governs conflict thresholds for private donations. She also noted that clinical trials are not treated as basic science when evaluating possible financial conflicts.

Mark Brenner, Ph.D., Indiana University-Purdue University, Indianapolis

Dr. Brenner represented the perspective of an institution that has parallel systems of COI review. He first gave an overview of the structure of the university system, noting that a large portion of its sponsored research goes toward the medical school. Dr. Brenner noted that Indiana University's COI committees are moving from a diversified, decentralized system toward a single, more functional COI committee. Existing policies address individual COI, conflict of commitment, and state laws regarding receiving contracts. A separate requirement addresses disclosure of financial interests for senior administrators, but this does not apply to deans or department heads. The university is also working to implement new policies on administrative conflict of interest, institutional conflict of interest, and potentially, ownership rights for textbooks.

Dr. Brenner said that at his institution, low-risk issues are managed locally, but higher-risk cases are referred to the COI committee. The university's COI committee categorizes the range of severity of financial relationships from normally acceptable to not allowable unless there is a compelling case. The severity of the financial relationships determines the level and extent of review the situation receives and the disclosure required. Dr. Brenner noted, however, the university's COI committee does not develop a plan for managing COI, it only validates the plan.

Dr. Brenner then presented examples of several draft case studies developed by the Council on Governmental Relations (COGR). The COGR series of case studies address consulting, licensing, clinical studies involving human subjects, procurement, mentoring relationships, and institutional conflicts. These case studies and resolutions are described in more detail on the COGR Web site, http://www.cogr.edu/.

> **Case 1:** Case 1 is an example of a low-level scenario. It involves Dr. Maple, a highly regarded oncologist at university medical college (UMC). A major pharmaceutical company, Blue Drug, wants to sponsor a clinical study testing whether its existing soft-tumor drug is effective in treating certain atypical forms of solid tumors. Dr. Maple has an existing relationship with Blue Drug that involves travel to company-sponsored conferences at no charge and receipt of honorariums that totaled $5000 the previous year. COGR suggested a number of questions to assess the scenario and then suggested an appropriate response.

Resolution: The recommended strategy for this particular scenario was to disclose all financial ties in publications and presentations and in informed consent for clinical trials.

Case 2: Case 2 is an example of a more complex scenario. It involves Dr. Teak, who is the inventor of a new drug that has been patented and licensed to a pharmaceutical company, Gray Pharmaceuticals. However, Gray misses some key development milestones that are part of the licensing agreement. Meanwhile, Dr. Spruce, the department chair, devotes resources to conduct phase II testing of the drug. The university's technology transfer office helps Dr. Spruce create a start-up company (Pink Drugs) to sublicense the drug from Gray Pharmaceuticals. Dr. Spruce solicits start-up funds from a friend who is the wife of Dr. Hickory, the IRB chairman. Dr. Hickory's research is unrelated to this study. His wife invests the money in exchange for company equity and stock. Dr. Spruce persuades the university president to approve this with the promise that the department can recoup sunk costs from future revenues. Dr. Teak serves as consultant to Pink Drugs and is asked to help with phase III trials. He receives generous compensation and insists the phase III studies be conducted at the university because of his unique expertise.

Resolution: In this example, COGR suggests a number of management strategies. First, many universities might conclude that a UMC should not be involved as a performance site for clinical studies given the complexity of the relationship, while still allowing Dr. Teak to assist Pink Drugs in developing the drug through a consulting relationship. Alternatively, Dr. Teak, if he serves as the PI, should, with UMC approval, divest himself of his stock options and modify the scope of his consulting activities. COGR also recommends full disclosure to human volunteers and all involved in the study.

Dr. Brenner concluded his presentation by issuing a general caution and reminders for addressing conflict of interest issues, including the need for full disclosure and the use of a higher standard when human subjects are involved. The greater the risk or complexity of the activity, the more likely the university will limit activity. Furthermore, when institutional and individual COI occurs, it is prudent for the clinical research to be conducted at other sites.

Participant Discussion

One participant noted that with the complexity of cases, the COGR management strategies are not as broad as they should be. Dr. Brenner explained that these management strategies are not meant to be a complete compendium, and COGR will eventually enrich what is listed in these case studies. These case studies seek to highlight items that need attention but do not prescribe solutions. Others noted that recusal from IRB *should* be mandatory where a conflict is present. Another participant suggested that reciprocal IRBs for clinical research might be a good approach for managing institutional conflicts of interests.

There was also significant discussion about the role of the IRB in COI issues. One participant thought it would be inappropriate to have the IRB responsible for investigating scholarly misconduct, adding that researchers should be made to feel they are working with the IRB, not investigated by it. Another participant urged that the IRB focus solely on human subject issues, otherwise, it would require the creation of a whole new skill set. Instead, the institution should

have a separate entity focus on financial interests. Many other participants echoed this sentiment and said that IRBs have a heavy workload and are not competent to address COI issues. Others countered that IRBs *do* have a significant role in protecting the right of the patient to be free from coercion and undue influence, and to be recruited in a fair, objective manner. While the IRB may not have the expertise to conduct the financial review, coordination between the two committees needs to occur. Another participant said it would be helpful for the IRB to have a checklist of standard criteria and conditions to help facilitate the process.

Dr. Faye Austin also cautioned that in our zeal to protect subjects and the study's integrity, we must take care in determining which site should be part of a multicenter trial. Multisite studies are beneficial to patients, and we should lean more toward management strategies rather than prohibitions. In protecting patients, it is important not to be paternalistic and take away their opportunities.

Gerald Gotterer, M.D., Ph.D., Vanderbilt University School of Medicine
Dr. Gotterer spoke from the perspective of an institution with a single, unified process for addressing COI issues. He noted that the publication of guidelines in 1989/90 by the NIH, the AMA, and the AAMC stimulated review of COI policies at Vanderbilt University. A Vanderbilt dean's committee recommended in the early 1990s that the Medical School develop a system for annual disclosure by all faculty, operational standards for faculty addressing COI issues, and a COI committee. The committee assigned categories of risk to faculty activities, ranging from routinely allowable to not allowable, and also now has a process for annual disclosure and review. Dr. Gotterer then presented Vanderbilt University itself as a case study.

> **Lessons Learned (Disclosure Forms):** A simple one-page screening document with checklist for initial screening yields good compliance. A supplemental form can obtain the needed information from those with something significant to disclose. The use of "nested" questions minimizes the need for follow-up inquiries. The disclosure forms should also contain brief statements that serve to educate faculty.
>
> **Lessons Learned (Process of Review):** Centralized review assures uniformity in application of criteria, while the use of subcommittees supports efficient gathering of needed information and developing management plans without overburdening committee members. Since the issues are complex and there will be a learning curve for committee members, it is important to include members who have a history of working with industry and to maintain a stable membership. A number of factors, most especially patient risk, should be considered when assessing COI in human investigations. Additional factors that committees must examine include the implications of a phase I versus phase II trial, a single versus multicenter trial, a double-blind versus open-label study, and independent data analysis compared to analysis by the investigator.
>
> **Lessons Learned (Oversight Committees):** Oversight provides the opportunity to have continuing review of a conflict situation. Three individual oversight committees took time to

understand and reach comfort with their roles. The faculty members found it difficult to monitor their peers' data. Individual committees were combined into a single committee. This approach takes advantage of the members' cumulative experience and facilitates efforts to ensure a firewall between financial conflicts and research efforts.

Additional Lessons. Furthermore, if conflicts are managed appropriately, oversight may not be necessary. IRBs are responsible for ensuring patients' awareness of financial conflicts of interests, whereas the COI committee assures that COI situations are managed in a manner that avoids inappropriate influence of conflicts on research design and outcome. IRB approval is contingent upon satisfactory clearance from the COI committee.

In conclusion, Dr. Gotterer noted that the faculty truly wants to do the right thing. Therefore, assessment of COI and education of scientists by COI committees need to occur simultaneously.

Responder Panel

Michael Corn, J.D., University of Washington School of Medicine

Mr. Corn, who has experience in industry as well as in higher education, emphasized that policy should not be based on random, rarely occurring events. He too receives a range of responses from others about the impact of potential conflicts of interest in research, ranging from "what's the problem" to "the sky is falling." He emphasized that Bayh-Dole is still the prevailing public policy and expressed concern that over-reaction could lead to future policies that create significant and excessive transaction costs while at the same time denying patient opportunities and delaying important research advances.

He also noted that earlier presentations had featured a number of comments about COI becoming pandemic, some of which were accompanied by complex charts depicting multiple organizational and review schemes. He cautioned that the research community needs balance in this area and must remain rational. He also said that we needed to be sensitive about protecting the morale of researchers. He expressed the view that COI must be taken in context, that not all research difficulties are caused by COI, and that every problem does not require an ethics/COI analysis.

Timely reviews as well as standards to guide investigators' behavior are needed if a policy is to be effective and useful. Some degree of predictability and certainty are necessary in order that investigators can know what is and what is not allowable. Mr. Corn said "appearance of a conflict" is being applied in a very unclear manner. While taxpayer support and public confidence for the research enterprise is important, appearance of conflict should not be equated with bad publicity and unfavorable media coverage. He said that the legal test should not be "the front of the newspaper test" but instead should be whether the purported "appearance" interferes with the discharge of a professional duty by a researcher or the institution.

Mr. Corn also called for an improved theoretical framework in which to analyze research-related COI issues and suggested that policy development would benefit from more legal expertise. He

agreed that committees have a role in COI reviews but suggested that overuse of committees be guarded against because of time constraints, expenses, need for uniformity of decision, and other issues.

Mr. Corn commented that the "compelling circumstances" test in the AAMC and AAU reports might be interpreted by some in an excessively high manner and suggested that there could have been a better choice of words to indicate when research could proceed. Although portions of the actual text from the AAMC and AAU reports suggest that "compelling circumstances" means something less stringent, a court or others may interpret it to mean "rare or never." In addition, the "compelling circumstances" test may fail to adequately consider those types of human subjects research that present little or no risk to human subjects, such as minimal risk or exempt human subjects research.

Finally, Mr. Corn expressed concern that increased attention to institutional COI may jeopardize contributions of gifts and endowments. He also noted that, due to recent news articles, attention to non-financial conflicts might spiral out of control.

Susan Ehringhaus, J.D., University of North Carolina (UNC) at Chapel Hill

Ms. Ehringhaus spoke about conflict of interest from the perspective of a university general counsel and as one of five institutions reviewed by the GAO audit team on conflicts of interest. She commended both the GAO audit team, as well as the workshop organizers, for their efforts. Ms. Ehringhaus first outlined a number of issues that are currently at stake, including integrity of research and the university, fiscal responsibility, independence of IRB and Institutional Animal Care and Use Committee (IACUC) review, research compliance, primacy of interests of human subjects, and external credibility.

She then discussed the current status of universities' activities, describing first what they have done well. Universities have developed comprehensive policy statements; clear definitions of what triggers a review. Universities have work to do in terms of explicit delineation (e.g., clear scripts) of review criteria for researchers and reviewers, such as documenting institutional management of COI, education to correct errors, and disciplinary action to correct wrongs. Critical areas that need more work also include establishing external credibility by involving those outside the institution and maintaining transparency.

Ms. Ehringhaus continued by outlining some of the key processes universities need to implement. These processes include a clear assignment of institutional responsibility, interactive searchable databases to help research COI issues, separation of responsibility for research from entities such as finance and technology transfer, workable review mechanisms, training programs for researchers and reviewers, and public education efforts. In particular, universities should consider implementing review mechanisms that are risk-based and that minimize unnecessary burdens.

Ms. Ehringhaus also addressed the question of whether the work of the AAMC, the AAU, and from various professional associations constituted "standards of care" for research on human subjects. Whatever characterization is used, the standards articulated by the national organizations will help to reduce problematic variability of operating principles across institutions and organize processes along common themes yet preserve necessary self-determination for individual institutional responses to instances of financial conflict of interest.

Christina Hansen, University of California, Irvine

Ms. Hansen spoke from the perspective of a senior official in research administration. As Assistant Vice Chancellor for Research, she oversees staff responsible for sponsored projects and the regulatory committees such as the IRB and IACUC, and she serves as staff to the COI and research conduct policy committees.

Ms. Hansen first discussed the organizational issues related to conflict of interest. Earlier in the conference, support was registered for new protections for the IRB from institutional pressures related to conflicts of interest in clinical situations. Ms. Hansen noted that the IRB is established under federal regulations as an independent body. Thus, her experience at two campuses of the University of California is that the IRB would not be swayed by these external forces. With respect to other organizational issues, she then pointed out that other university offices are involved in COI issues and these were not mentioned at this workshop, such as personnel and academic affairs, purchasing, and the graduate schools. These offices deal with conflicts of commitment, procurement for research activities, and protection of students from coercion, respectively, and should be considered in discussions of COI.

In terms of policy, Ms. Hansen stressed the importance of conveying the institutional message and fostering a culture of compliance. It is also important to define terminology since many terms are used interchangeably. For instance, words such as technology transfer, equity, consulting, patents, and licensing have very different meanings and should be recognized for varying levels of concerns related to potential risks in conflict of interest situations. .

In developing policies and procedures, it is important to address the real question: What is the value added? That is, are policies and procedures being developed to manage serious conflicts, and then pulling in situations that are only minimal risk? And, do these policies ultimately protect subjects or hinder important research? AAMC and AAU guidance can help us refine the task but, ultimately, policies should be tailored to the type of research that is occurring on the campus.

Lastly, Ms. Hansen emphasized that communication is the key in developing processes, whether it be through electronic media, shared databases, or handwritten methods. This information can and should be shared among IRBs, COI committees, and grant and contract staff. IRBs, in particular, need feedback from the COI committee, and the COI committee can obtain valuable information from the protocol review.

Debra Lappin, J.D., NIH Council of Public Representatives
As a member of the NIH Council of Public Representatives, Ms. Lappin said it was a tough challenge to represent the public. She said she was here because of her concerns about maintaining public trust and partnering with the American public and suggested that these goals were often easier to espouse than to implement. COI issues and human research protections *do* intersect—it is not just about objectivity in science.

She described the public's relationship with science as having evolved from a relationship comfortable with paternalism to one respecting of autonomy and to one demanding equality and partnership. This transformation has occurred in part because of media headlines announcing clinical trial deaths (e.g., research subjects Jesse Gelsinger and Ellen Roche) and depicting humans as guinea pigs (e.g., *Time Magazine's* cover story "Human Guinea Pigs," which depicted a woman trapped in a cage). Given the events of the past few years, it is little wonder that the public trust in institutions of science is at risk. Much is at stake if public trust is diminished: this is the same public that funds endowments, gives their tax dollars to support federal appropriations, heroically offers to participate in clinical trials, and ultimately "owns" the magnificent enterprise of the NIH.

In sharing her perspective on both individual and institutional COI, Ms. Lappin said institutions must develop a new "culture of conscience" created through examples set by the most senior leaders at the institution. Institutions should expect intense scrutiny as trust is no longer free and is increasingly viewed as a business commodity. In terms of individual COI, the patient weighs the risks and benefits of participating in clinical trials. Patients should also be allowed to consider the impact of an investigator's financial interests when deciding to participate. Not revealing this information to the patient is paternalistic, reinforces the disparity between individuals and institutions, and contributes to a further misunderstanding of research.
Ms. Lappin added that IRBs *must know* about conflict of interest issues. Keeping this information from IRBs takes away critical pieces of knowledge about safety, welfare, and objectivity in research on human subjects.

Christine Maziar, Ph.D., University of Minnesota
Although she recently became Provost, Dr. Maziar also comes to this workshop with the perspective of a Vice President of Research who had oversight responsibility for technology transfer, sponsored projects administration, and supporting IRB and biosafety committees. She also spoke from the perspective of a land-grant institution, which has Board of Regent meetings that are open to the public.

Dr. Maziar stressed the importance of being clear that punishing investigators for their commercial success is *not* the goal of COI policies. She also emphasized the importance of considering the language that is used when talking about COI issues. She expressed particular concern about talk of a "firewall" between research and the technology transfer office. The technology transfer office can promote institutional values in this regard and can be enormously valuable as a front-line player in ensuring and promoting compliance.

In discussing institutional COI, Dr. Maziar noted that many university vice presidents feel "on the edge" of these conflicts because many institutions have been promoted as the "economic engines" of their state. However, many state legislators do not fully comprehend the intricacies of the research enterprise. She concluded by emphasizing her pleasure that associations are dealing with this and that guidance from the federal government is needed to help universities proceed.

Lita Nelsen, M.S., M.B.A., Massachusetts Institute of Technology (MIT)

Ms. Nelsen commented from the perspective of an institution that conducts no clinical research, but is active in technology transfer activities. With this in mind, Ms. Nelsen asserted that clinical research versus other types of research should have different rules. Since many institutions such as MIT handle a massive caseload, it is important that oversight use simple, but strict, rules on COI. She denounced the idea of weighing conflict of interest issues on a case-by-case basis because exceptions set precedents, and because it is impossible to manage large numbers of cases by oversight committees and still have these committees do their oversight with any degree of thoroughness.

Ms. Nelsen also strongly advocated that technology transfer offices should remain part of the academic process. She said that technology transfer is a byproduct of the academic mission and that it should be integrated within the academic process so that conflict of interest decisions are made primarily with the academic mission in mind. There are very positive benefits in addition to technology development from technology transfer; it allows investigators to see their research used for practical purposes, and teaches students to foresee practical applications. Ms. Nelsen concluded by emphasizing that the implications of separating technology transfer from the academic environment could cause more problems than it solves by making the technology transfer function an "outside, money-making function" that is adversarial to COI rules rather than proponents and enforcers. (She noted that her staff is not on any sort of bonus or commission system and sees itself as part of the university research process rather than a separate business.) She concluded by thanking the AAMC for their clear firm guidelines, even if she disagreed with some of them.

Savio Woo, Ph.D., Mount Sinai School of Medicine

Dr. Woo opened his presentation with an anecdote of a tragic gene transfer clinical trial in 1999 that led to much negative publicity, while he was serving as president of the ASGT. He said this traumatic experience has given him strong opinions on financial conflict of interest issues. Three years ago, the ASGT adopted a "just say no" policy—that is, society members who own stock in a company that sponsors a trial should not have any patient contact during that trial. This simple but rigorous policy demonstrates the intent that most investigators try to do the right thing. But is it sufficient to simply try to do things right from the investigator's and institution's perspectives, or should the focus also be on earning and winning back the public trust? Dr. Woo urged the participants to keep the public and academic community in mind when developing policy.

The topic of equity is a serious issue, and Dr. Woo reiterated the ASGT policy on equity. Royalties have a different connotation, however, since the product must have undergone numerous clinical trials, been subjected to rigorous FDA reviews, and licensed for sale. The influence that a single investigator or institution can exert on a product's ultimate success is rather limited. Dr. Woo described the most potentially corruptive situation as occurring when an investigator conducting clinical trials also has equity in non-publicly traded biotechnology companies that sponsor the trial. When an investigator announces the successful completion of an early phase single-site clinical trial, equity prices can escalate significantly without a product.

Dr. Woo then addressed some of the case studies that were presented earlier. In the case of Dr. Toe, he said the situation is fine if nothing adverse happens to a patient. However, a misdiagnosis can lead to widespread publicity. Moreover, the press may present the facts in a way that implicates conflict of interest when an investigator has a financial stake in the product. This will be viewed negatively by the public and can lead to escalating negative publicity. In the case of Dr. Oak, the situation as presented is full of conflicts and that any adverse event will lead to not one, but a series of news articles that question the roles of the investigators and the academic institution. Therefore, if the goal is to win back the public trust, academic medical institutions must not consider the investigator's and institution's conflicts of interest in isolation, but also view the impact of public perception.

Participant Discussion

Several questions were directed to Dr. Woo. One participant asked whether a clinical trial should be conducted at an institution if the institution has equity in that trial. Dr. Woo responded that the institution has to make that decision, considering a number of factors, including the impact of potential adverse effects on the institution and the academic medical community. Another participant asked Dr. Woo his opinion on the case study where a PI could not participate in the NIH research. Dr. Woo explained that the investigator actually has two options, either to divest or not participate. He added that, in general, the investigator should not put his/her personal interests ahead of the institution's and more importantly, the patients who volunteer to participate in the trial. Another participant said this response would be appropriate for clinical research, but not basic research, since many inventions stem from an investigator's long history with a research study. Therefore, telling an investigator he cannot accept NIH funding or work in his given field is a strong message that could potentially hinder technology transfer activities. Dr. Woo indicated that the ASGT policy is indeed applicable in clinical trials only.

Dr. Koski of the Office for Human Research Protections (OHRP) stimulated significant discussion on the "rebuttable presumption" provision. Dr. Koski expressed concern that some provisions in Dr. Gotterer's case studies seemed to be inconsistent with the "rebuttable presumption" against doing research when conflicts are identified. Dr. Koski posited that if compelling circumstances allow the vast majority of human research to go forward in the presence of conflicts, it will undermine the credibility of the public in these efforts, will be of little value, and will be destructive. He asserted that the "rebuttable presumption" should mean that the vast majority of cases would not go forward. Dr. Koski also commended the AAMC for

its stated intention to begin auditing Academic Medical Centers to determine the level of self-imposed compliance with the AAMC guidelines. He suggested that without a demonstration of compliance, in the near rather than extended term, government regulation might ensue.

Several participants responded to Dr. Koski's discussion. Dr. Gotterer stated that the case studies simply provide an overview of the situation, not a precise response. In addition, many projects that are approved with disclosure are actually low-risk situations. Dr. Maziar noted that it is important to communicate clearly that a situation was "managed" and not just tolerated. Another participant claimed there are legitimate and compelling cases, especially in the early stages of clinical testing when only one researcher can do the work safely and effectively because the technology is too new. One participant suggested that the group should marshal its efforts to inform the public that while a high standard relates to conflicts of interest, the problem is not insurmountable.

Participants turned next to strategies for assessing risk. Institutions need to look at risks when setting the bar for what is an acceptable compelling situation. If risk is considered minimal, a committee might accept a compelling argument; if the risk is large, the committee might not, but it must have criteria on which to base that judgment. Other participants sought to broaden the discussion of risk, suggesting that health policy studies, for instance, may have minimal individual risk but major implications for public policy.

The issue of intellectual property rights for graduate and postdoctoral students was also raised. For example, in some cases, a company may want to support a student's work and retain the intellectual property rights. Institutions must consider issues such as "intellectual capital" and work to preserve this. Other institutions consider whether students are involved when weighing conflict of interest issues. However, students tend to take their concerns to the Academic Freedom Committee rather than other committees.

Participants also discussed the advantages and disadvantages of public involvement in the conflict of interest review process. The majority of respondents felt public representatives were extremely useful in these discussions, and their institutions either currently involve the public or plan to integrate them in the future. Many provided anecdotal evidence and emphasized that institutions need the public perspective, especially in developing language for informed consent documents. Others expressed reservations, however, about involving the public before the conflict of interest process was fully implemented and working well.

Finally, the ethics of weighing basic research differently from clinical research was discussed. One participant said the standard of trust should be uniform for all, and objectivity is important. Guidance specific to clinical research is needed but does not imply that basic research scientists do not have to be held to the same standard. Some emphasized that while such distinctions are important, clinical research generally attracts a great deal more public and congressional attention if a patient is harmed in the course of research.

Institutional Conflicts of Interest

Joseph Martin, M.D., Ph.D., Harvard Medical School

Dr. Martin provided an overview of the AAMC Task Force Report on Institutional Conflicts of Interest in Research. The three councils of the AAMC—which represent teaching hospitals, medical school deans, and professional societies—unanimously approved the guidelines this task force developed. Dr. Martin discussed the AAMC framework for assessing institutional conflicts, which essentially states that an institution may have a conflict of interest in research involving human subjects whenever the financial interests of the institution appear to affect institutional processes for conducting, reviewing, and overseeing such research.

Dr. Martin went on to discuss some of the key points of the framework. He noted that institutions should ensure that administrative responsibilities related to human subjects research are separated from investment management and technology licensing activities. The guidelines also state that an institutional official's financial interests may at times be in conflict with his or her position of authority. At these times, options include being recused from official responsibilities, managing the conflict, or not performing the research at all. Ultimately, there should be a "culture of conscience" at the institution whereby senior officials lead by example and rigorously enforce COI policies.

Dr. Martin also discussed a number of circumstances that may create or appear to create an institutional COI and thus require intense scrutiny. Generally, these situations may occur when the institution or a responsible official receives royalties or has a significant role or ownership interest in a company. Officials that engage in major purchases or managing and soliciting gifts may also have a financial relationship that warrants close scrutiny.

Dr. Martin outlined the AAMC guidelines for the specific organizational structure of institutional COI reporting and review processes. Specific recommendations for IRB members include reporting certain financial interests annually and adhering to federal policies governing recusal from protocol review, when necessary. Overall, the AAMC urged that disclosure to the IRB of record, to research subjects, and in publications, should be *required* whenever the institution holds a financial interest that could *reasonably* present a conflict to research involving human subjects.

Dr. Martin also reported on an AAMC-AAU survey, which sampled the opinions of seventy people over the past 9 months. He presented the following seven recommendations:

1. Use an open, informed, transparent, and timely process to prevent COI and other threats to academic independence.
2. Make flexible arrangements to accommodate certain research collaborations with industry; however, each approach should be considered experimental and subject to periodic scrutiny.
3. For faculty who wish to found or play an active role in a company, increased latitude might be best obtained through part-time appointments or leaves of absence.

4. Adopt very specific working definitions of allowable activity under basic research, clinical research, and research on devices.
5. Adopt the same standards for both devices and drugs by precluding the physician or inventor from evaluating the device or compound. However, in special cases, the inventor may be allowed, under objective supervision, to perform *initial* clinical use of a device.
6. Apply the same standard for commercially sponsored research and government-funded research.
7. Adopt the AAMC framework for *deciding* whether a conflict of interest exists; if one arises, manage the conflict by a separate, objective party.

Panel members echoed these sentiments, agreeing that one overarching theme is absolute transparency and allowing patients to make informed decisions. They also emphasized that maintaining public image is most important and that decisions to commercialize should be driven by public good, not institutional or individual good.

Faye Austin, Ph.D., Dana-Farber Cancer Institute

Dr. Austin noted that Dana-Farber Cancer Institute is a teaching hospital of Harvard Medical School, and as such, its investigators are Harvard faculty and must adhere to the COI rules of both Harvard Medical School and Dana-Farber. She described how the culture of her institution changed in the wake of a fatal overdose seven years ago and emphasized the importance of a "culture of conscience." Even though financial arrangements may not have been a factor in some of the more recent tragic episodes at other institutions, the press may still frame it that way. Therefore, her institution has tried very hard to learn from those unfortunate circumstances by continually assessing their systems when others' are criticized to determine if Dana-Farber has any systems or policy gaps, and if so, how to remedy them.

While COI policies for individual investigators are very clear at Dana-Farber, she acknowledged the complexities of trying to develop reasonable institutional COI policies. Dr. Austin explained that Dana-Farber conducts many early stage clinical trials. Technologies owned by Dana-Farber could be licensed to companies that, in some cases, would want to sponsor early phase clinical trials of these technologies at the place with the most experience with it. She said it would be difficult not to be the performance site for a clinical trial solely because of institutional financial interest. For instance, if their institution has the expertise for a technology, it is probably the safest environment for the patients to participate in the clinical trial. Thus, it will be very important for institutions to examine how they balance risks, public perception, and patient safety. Dr. Austin stressed that for science to move forward, complex technologies must be given a chance to be tested in the environment where they have been developed, when warranted, to allow for the best chance of success for the technology as well as the best and safest patient outcome. Financial conflicts must be disclosed to all involved parties and must be managed in a meaningful way.

Robert P. Kelch, M.D., University of Iowa College of Medicine
Dr. Kelch commented that his work on the AAMC's conflict of interest task forces was educational and has made his job easier. He noted that the AAMC report contains wonderful guidelines for managing complex institutions but emphasized that these guidelines are not prescriptive. Dr. Kelch also underscored the difficulties medical schools face in achieving their missions while managing the additional challenge of developing ideas in an entrepreneurial manner. He suggested that the academic community balance the societal good of commercializing research discoveries with business aspects. This approach will help medical schools stay true to their "core missions" of creating and sharing knowledge.

Cornelius Sullivan, Ph.D., University of Southern California
Dr. Sullivan summarized some of the questions and major observations that arose from an AAU workshop on institutional COI in May 2002. Dr. Sullivan said that one of the overall themes was that participants did not want to build a system that is impossible to administer. They also recommended separate procedures for reviewing personal, financial, and institutional COI. It is also important to develop guiding principles and to establish a code of conduct that meshes with the campus conduct principles. Recognizing that one size does not fit all, the workgroup also recommended the use of risk-based response. The group also suggested local control of institutional COI management that does not preclude public comment, as well as reliable, cross-linked information technology systems.

Dr. Sullivan said the workshop participants responded to 13 key questions that dealt with how to grapple with this formidable task. To facilitate risk-based analysis, they also developed a graph depicting a non-linear relationship with potential for conflict correlated to the degree of scrutiny warranted. The risk factors are additive—the more factors, the more scrutiny. At low levels of risk, certain activities are acceptable; at higher levels of risk, more resources are devoted to reviewing the situation.

Dr. Sullivan concluded by complimenting the AAU, AAMC, and COGR for their work on this topic, and for not reinventing the wheel. He said it was gratifying to be part of an academic research enterprise and emphasized that when institutional leadership is on board, everything falls into place.

Carl Gulbrandsen, Ph.D., J.D., Wisconsin Alumni Research Foundation (WARF)
Mr. Gulbrandsen discussed WARF as an alternative method for managing institutional conflicts of interest. WARF is the university's patent management organization. He said that the University of Wisconsin-Madison does not require assignment of intellectual property as a condition of employment unless the federal government or private industry funded the invention. This increases the potential for personal COI but decreases the potential for institutional COI.

In a brief history on WARF, Mr. Gulbrandsen explained that it was established in 1925 by Professor Harry Steenbock to commercialize his discovery that UV radiation produces vitamin D in food and prevents rickets. WARF is a nonprofit foundation that supports research at the university, protects technology, and licenses it to industry. It has an 18-member Board of

Trustees, all alumni, which is self-perpetuating. The only university employee on the board is the Chancellor. The foundation has sole discretion regarding what will be patented and licensed. It also gives an annual grant to the university, but allows the university to determine how the funds will be used. WARF also consults daily with university personnel regarding grant-making and intellectual property policy.

Mr. Gulbrandsen then outlined the separation of functions between WARF and the university. He explained that the university focuses on its roles as educator, grant recipient, and recipient of research materials, but does not take title in intellectual property. By contrast, WARF can hold title to intellectual property, manage patent and license activities, provide research materials, and have stock in faculty start-up companies. Mr. Gulbrandsen said the advantage of this structure is that the university does not have a direct commercial interest in the research activities, and researchers at the university are not employed by WARF. However, the university still assesses and manages COI issues and benefits from WARF grants.

Participant Discussion

Participants talked briefly about Mr. Gulbrandsen's presentation on WARF, and whether or not it solves the problem of institutional conflict. The AAMC documents also were discussed. Many participants felt that they were excellent and a good tool for planning and assessment. Others questioned to what extent the AAMC was promoting or discouraging commercialization of technologies. Dr. Martin said that he is personally in favor of Bayh-Dole, but the universities vary greatly in the extent of their technology transfer activities. He emphasized that it is important to sustain interest in these activities while managing them in a realistic way.

Mr. Roumel from the NIH Office of Technology Transfer (OTT) informed the audience that NIH has a new, Web-based training module to educate scientists about technology transfer and related COI issues. It is located at: http://tttraining.od.nih.gov and can be viewed by the public. In addition, NIH has internal COI policies related to technology transfer that will be posted on the OTT public Web site (http://ott.od.nih.gov) under "Current Issues." While these policies deal with intramural research and federal regulations, they may still be helpful to the academic community. In response to an earlier suggestion that the AAMC and AAU educate the media about financial interest issues, Mr. Roumel said that, like the Centers for Disease Control and Prevention (CDC), the NIH has Knight-Ridder fellowships to educate members of the media about research. This may be a model for universities and associations that want to conduct similar outreach efforts.

A representative from the Center for Science in the Public Interest asked whether disclosure to research subjects and the public is simply a management strategy, or whether it is done in good faith. Dr. Austin responded that disclosure is a minimum requirement at her institution. However, IRBs have discretion about what kind of information to disclose to patients. Dr. Austin stressed the importance of providing information in the appropriate context and to not overwhelm patients with information. Dr. Kelch echoed these sentiments, saying there must be a balance. It may seem paternalistic, but too much information can be harmful as well.

Where Do We Go from Here?

Dr. Baldwin summarized the day's discussions by suggesting a slogan for the workshop: "Public Funds, Public Trust, and Public Benefit." She said the meeting was valuable, particularly the discussion on institutional COI. She then outlined issues that need to be addressed more fully. For instance, very little discussion focused on involving students in COI issues; we cannot wait until students are full-fledged investigators to educate them about these issues. We also need more data and cannot rely solely on anecdotal evidence. She called for more systematic data on the volume and type of COI issues and how they are being resolved. In addition, little discussion addressed auditing and sanctions once an infraction has occurred.

Next steps will involve institutionalizing how the research and academic community can tap into shared experiences. She asked participants to provide suggestions on how to do this in the best way possible. However, she expressed caution about using listservs for this purpose and suggested that more structure may be needed. Dr. Baldwin concluded by thanking the workshop participants and fellow sponsors for their participation.

Dr. Korn of the AAMC added that the meeting was wonderful and thanked Dr. Baldwin and colleagues. He reiterated that the treatment of conflicts of interest has a lot to do with institutional culture and requested that federal agencies limit their involvement to allow institutions time to work these issues out internally.

References

1. General Accounting Office (GAO), *Biomedical Research: HHS Directions Needed to Address Financial Conflict of Interest,* November 2001.

2. National Institutes of Health (NIH) Office of Extramural Research, *Financial Conflict of Interest: Objectivity in Research,* July 18, 2002. [http://grants.nih.gov/grants/policy/coi/nih_review.htm].

3. Association of American Universities, *Task Force on Research Accountability. Report on Individual and Institutional Financial Conflict of Interest*, October 2001.

4. Association of American Medical Colleges, *Task Force on Financial Conflicts of Interest in Clinical Research. Protecting Subjects, Preserving Trust, Promoting Progress II – Principles and Recommendations for Oversight of an Institution's Financial Interests in Human Subjects Research,* October 2002.

5. Association of American Medical Colleges, *Task Force on Financial Conflicts of Interest in Clinical Research. Protecting Subjects, Preserving Trust, Promoting Progress – Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research,* December 2001.