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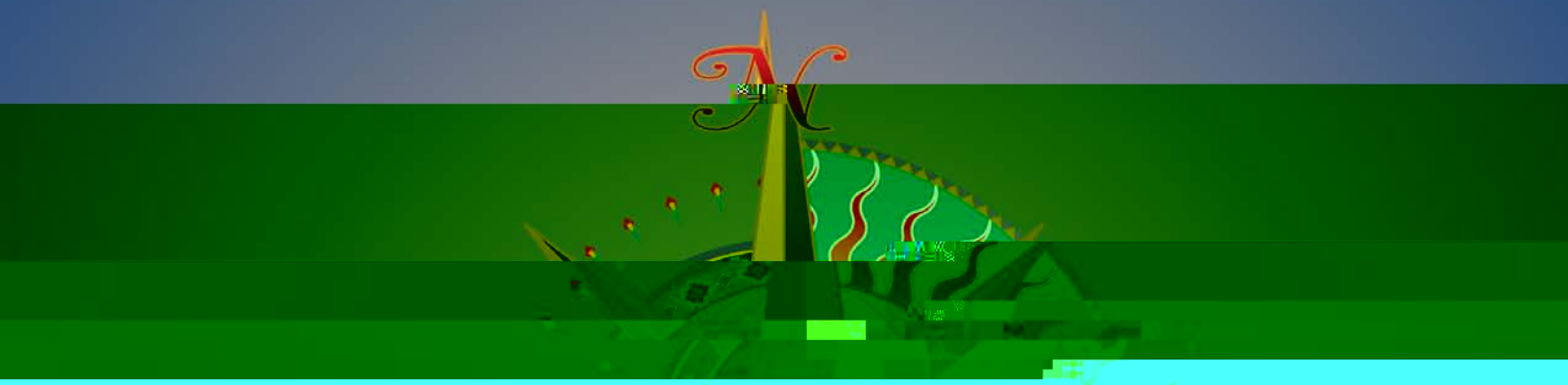

SHARED RESPONSIBILITY, INDIVIDUAL INTEGRITY: SCIENTISTS ADDRESSING CONFLICTS OF INTEREST IN BIOMEDICAL RESEARCH

March 13, 2006

The Federation of American Societies for Experimental Biology (FASEB)

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ACKNOWLEDGEMENTS

The committee greatly appreciates the participation of Richard Hodes, M.D., Director of the National Institute on Aging at the National Institutes of Health and Thomas Murray, Ph.D., President of The Hastings Center, in helping to develop the June 14-15, 2005 conference, "Shared responsibility, individual integrity: Scientists addressing conflicts of interest in biomedical research," in Washington, D.C.

In addition, the committee is grateful to the conference participants and speakers for providing perspectives that were important to ongoing discussions. Speakers were:

PREFACE

There are many benefits to joint and synergistic relationships involving academia and industry. However, research shows that these interactions have been accompanied by serious and sometimes unaddressed conflicts or potential conflicts of interest. Responses from the media and Congress in this regard have been rapid and notable, sparking discussions about expansion of regulatory requirements and other potential burdens to investigators.

As representatives and leaders within the biomedical research community, the Federation of American Societies for Experimental Biology (FASEB) believes that maintaining the public trust and assuring the integrity of basic and clinical research is of the highest importance. Given our representation of over 84,000 practicing scientists, FASEB is uniquely positioned to proactively address these issues. While other groups have addressed conflict of interest, we are particularly concerned with the perspectives of investigators who work in the public interest in all research-based institutions, particularly academic and not-for-profit institutions where the majority of FASEB society member scientists are represented.

In July 2004, FASEB announced the intent to address conflict of interest in biomedical research, and the FASEB Board of Directors approved this initiative in December. Shortly thereafter, a steering committee was formed that developed the conference agenda and the issues to be discussed, secured speakers, and outline plans for future work from FASEB.

In June 2005, FASEB hosted the conference, "Shared responsibility, individual integrity: Scientists addressing conflicts of interest in biomedical research." The purpose of the conference was to allow investigators to consider and respond to serious challenges involving conflict of interest in biomedical research. The conference was held as part of the FASEB Board of Directors Meeting on June 14-15, 2005 in Washington, D.C. Speakers from academia, industry, government, and nonprofit associations outlined the issues. In a break-out session, groups of FASEB Board Members, society staff, speakers, and invited guests discussed issues related to four types of academia-industry relationships: research contracts, consulting and board membership, entrepreneurial activities, and training or education. The conference prepared FASEB for a continuing discussion of these issues, and a steering committee continued to develop several key issues that were raised. The FASEB Board of Directors reviewed the report in December 2005, and approved it on December 9, 2005.

This report represents a consensus statement on overarching principles and voluntary standards for the conduct and management of academia-industry interactions from the *scientists' perspective*. It is intended to be used primarily by scientists, as well as institutional leaders, policymakers, professional societies, and others. The guiding framework for this report is based on the assumption that in academia-industry relationships, there are 1) individual decisions that are made by scientists, 2) institutional, professional, and government requirements, and 3) goals and objectives that are specific to each sector. This report focuses on identifying those challenges that scientists confront in academia-industry relationships, and recommends guiding principles for these scientists that will help them appropriately secure the benefits and guard against risks of such collaborations. Although the document is generally

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EXECUTIVE SUMMARY

Relationships between academia and industry are a fundamental part of the modern life science enterprise. It is only through such interactions that advancements in the life sciences can most rapidly achieve the maximum benefit to society. The rise in academia-industry relationships has been accompanied by increasing concerns about risks due to financial conflicts of interest. These risks include the potential to bias research, delay trainee progress, compromise efficient and wide dissemination of research results, harm human research participants, and decrease public trust in medical research.

There are several rules and policies of the federal government, institutions, professional societies, and scientific journals that guide the oversight of academia-industry relationships. To date, many of the policy recommendations addressing financial conflicts of interest have focused on the role of institutions in the review and oversight of investigators' relationships with industry,[1, 2] whereas the role of investigators has not been as well-identified. The actions of investigators as a group will determine the effectiveness of policies and practices. But in the current debate over the limits of intimacy between industry and academia, there is a clear need for voluntary standards for the conduct of academia-industry interactions from the scientists' perspective. With this goal in mind, we propose a set of guiding principles that can help investigators anticipate common challenges in industry relationships and guide their decision-making to overcome these challenges. While the document was generally designed to address financial conflicts of interest faced by individual academic scientists, some of the general principles apply to scientists broadly and address challenges that are not exclusively financial in nature.

Specific challenges for investigators discussed in this report include:

> How do investigators protect against research bias in industry relationships?
> How do investigators work with institutions to ensure requirements are fulfilled and relationships are fairly and effectively reviewed and overseen?
> How do investigators address issues of access, analysis, and dissemination of research information, data, and materials in industry relationships?
> How do investigators operate with transparency and accountability in industry consulting relationships (consulting, advisory board membership, speaker bureaus)?
> How do investigators address conflict of interest issues in their entrepreneurial activities (involvement in start-up companies and technology licensing)?
> How do investigators with industry relationships minimize the negative impacts of those relationships on training and education?
> How do investigators with industry relationships protect against risks to human research participants?

Guiding principle 12: Investigators shall not use federal funds to the benefit of a company, unless this is the explicit purpose of the mechanism used to fund the research (e.g., Small Business Innovation Research and similar grants).

Guiding principle 13: When investigators own significant equity in a company with which research is conducted, all parties shall be aware of the special circumstances involved.

Guiding principle 14: When holding a significant role in a start-up company, investigators shall be guided by agreed-upon limits to the scope of the relationship.

Guiding principle 15: Investigators shall be aware of and adhere to requirements of federal funding related to disclosure of inventions. Investigators shall adhere to patent law and institutional requirements.

Guiding principle 16: Investigators shall not seek to influence their institution's technology transfer decisions for personal gain.

Guiding principle 17: A mentor's outside commercial interests shall avoid impeding a trainee's timely progress toward his/her degree, restricting a trainee's right to publish his/her dissertation research in a timely manner, compromising a trainee's career progress, or restricting a trainee's freedom of inquiry.

Guiding principle 18: Mentors and institutions should make trainees aware of their rights and responsibilities in industry relationships.

Guiding principle 19: Investigators shall regard all significant financial interests in research involving human subjects as potentially problematic and thus requiring close scrutiny.

Both individuals and institutions must work together to address the conflict of interest challenges academia-industry relationships can pose. Industry and academic institutions should work together to steer investigators away from key challenges and roadblocks. But individual researchers still must diligently strive to maintain the objectivity and integrity of their investigations.[3] Integrity embodies a commitment to intellectual honesty in proposing, performing, reporting and reviewing research, and fairness in interactions with colleagues and for those an investigator has a responsibility.[4] Investigators must continue to show individual accountability in deciding to enter into relationships with industry, complying with institutional, government and journal policies, and proactively addressing conflict-of-interest challenges using these guiding principles. With careful disclosure and oversight, investigators can minimize or eliminate the risks of industry-academia collaborations and maximize the benefits to the scientific community and public. Failure to do so could have

INTRODUCTION

Frequently academic scientists, administrators, and institutions carry out research for, or provide intellectual property to, industry in return for research support, honoraria, consulting fees, royalties, and equity, and other forms of compensation.[5] But the scope and nature of academia-industry collaborations have recently increased in size and complexity. This creates changes in the research environment that present both opportunities and challenges for scientists and their institutions.

BENEFITS OF ACADEMIA-INDUSTRY RELATIONSHIPS

Many important societal benefits stem from scientific collaborations between academia and industry, including translating basic scientific findings into clinical applications, and fueling local economies. Collaboration between industry and academia has led to many important therapies and research tools, such as the gene splicing technology that initiated the biotechnology industry, diagnostic tests for breast cancer and osteoporosis, and vaccines. Institutional licensing activities from FY 1998-2003 made 2,230 products commercially available, one report found.[6] Studies also reveal how academia-industry relationships make significant contributions to local economies.[11] Evidence shows academia-industry relationships are a key component of economic competitiveness and increase the future research and development spending by industry.[12]

Academic investigators also benefit by their collaborations with industry through increased access to resources to support their on-going projects. These collaborations enable academic investigators to participate in the application of their research, and it allows students and academic investigators to work on applied research projects. Studies show that industry funding correlates with increased faculty academic productivity (published articles) and commercial productivity (patents and licenses, products under review and on the market, and start-up companies).[8] Academic investigators, government researchers, and industry scientists also benefit professionally by interacting with colleagues. Such interactions facilitate the bidirectional flow of knowledge and materials. Interaction with industry provides academic investigators opportunities to participate in the application of their research, and it allows students and academic investigators to work on applied research projects. Finally, industry support may help offset wage differential between industrial and non-industrial sectors that may assist in recruitment and retention of scientists and administrators to academia.

CHALLENGES OF ACADEMIA-INDUSTRY RELATIONSHIPS AND CONFLICTS OF INTEREST

The rise in academia-industry relationships has been accompanied by increased concerns regarding conflicts of interest that are largely, but not exclusively, financial. A commonly used definition of financial conflict of interest is: a condition in which a primary interest (institutional responsibilities for research and education) is in conflict (whether real or perceived) with a secondary interest (such as financial gain).[13] A conflict of interest is a situation, and not a behavior. The presence of a conflict of interest is not necessarily an indictment of an individual, but rather an acknowledgement of a potentially challenging situation. By focusing on relationships and not conflicts of interest in this report, we hope to direct the guidance towards smart practices and other useful tools for scientists.

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

Correlations between industry funding and published scientific conclusions that could be viewed as favorable to industry

compensation in excess of $25,000 from a corporate sponsor for a trial in which the investigator is engaged must disclose to the FDA at the time of filing for a new drug application.

Academic institutional policies are designed to protect the integrity of research, the missions of the institutions, stakeholders (including investigators, trainees and research participants), and public confidence.[22] Medical school conflict-of-interest policies vary widely, but policies governing research involving human participants are generally more stringent than for other types of research.[23]

Scientific journals, the major gatekeepers of research results, began adding disclosure requirements in their instructions to authors in the 1980s. The International Committee of Medical Journal Editors Uniform Requirements, adopted by 150 journals, includes guidelines for addressing conflicts of interest. A 1997 survey of 1396 highly ranked scientific and biomedical journals found that 16 percent had published conflict-of-interest policies.[24] Of those, 87 percent were medical journals. Nearly three-fourths of editors of those journals with policies publish author disclosure statements. A more recent survey (albeit with a smaller sample of forty-one biomedical journals) showed 59 percent of journals surveyed contained financial disclosure requirements in their published instructions to authors.[25] In addition, many scientific conferences require disclosures of financial interests in presentations.

ONGOING CHALLENGES FOR ACADEMIC INVESTIGATORS

Of course, one way to eliminate unintended negative consequences of academia-industry relationships is to eliminate the relationships themselves. But ending all academia-industry relationships is not a viable alternative. Such drastic measures are neither feasible nor beneficial to society. In fact, calls for *increased* collaborations between academia and industry are being heard.[26] By virtue of its increased participation in academia-industry relationships, the scientific community has indicated that the benefits outweigh the risks. The many medical advances academia-industry relationships have brought to society cannot be overstated. However, increased concerns about the integrity of medical research are evident. Although concerns about *potential* risks may not be well-aligned with *real* misbehavior, these issues must continue to be addressed by the scientific community to assure the credibility of medical research. The challenge for the scientific community is to disclose and manage these relationships.

The vast majority of biomedical researchers are guided by the highest ethical and professional standards. The focus of the report is to discuss and provide guidance to academic investigators to address challenges that may occur due to financial relationships between academia and industry, not to judge whether a real or perceived conflict of interest exists. Although the document is generally designed to address financial conflict of interest issues faced by individual academic scientists, some of the general principles apply to scientists broadly and address challenges that are not exclusively financial in nature.

CHALLENGES AND GUIDING PRINCIPLES

HOW DO INVESTIGATORS PROTECT AGAINST RESEARCH BIAS IN INDUSTRY RELATIONSHIPS?

Public support for research is built on a foundation of trust that reported research results are credible. Therefore, the potential for academia-industry relationships to bias research and investigators is a concern shared by the scientific community and the public. A challenge for investigators is how to address the perceived or real loss of objectivity when forging a relationship with industry.

Researchers diligently strive to maintain the objectivity and integrity of their investigations[3] by their:

Intellectual honesty in proposing, performing, and reporting research;
Accuracy in representing contributions to research proposals and reports;
Fairness in peer review and collegiality of scientific interactions (including communications and sharing of resources);
Transparency in industry relationships;
Protection of human subjects and humane care of animals in research; and
Adherence to mutual responsibilities between investigators and their research teams.[4]

Unfortunately, the perception of bias that results from having a financial interest can be damaging to the credibility of biomedical research. People understand money and its potential for influence. This potential for influence may cause public anxiety about financial interests in biomedical research. But the public may not understand the inherent checks and balances of scientific research designed to weed out research bias. Peer review and institutional review boards prevent investigators from obtaining or publishing any information that is not accurate or appropriately obtained. While recognizing the peer review system has limitations, ongoing review and revision is critical in minimizing individual subjectivity.

Guiding principle 1: Investigators have a responsibility and commitment to conduct scientific activities objectively and with the highest professional standards. These commitments and review processes must encompass all aspects of the research process (including research design, data collection, analyses, and communication of research results to the scientific community and the public) and professional responsibilities. This is a first and important step in addressing any challenges that may occur in financial relationships between academic investigators and industry.

HOW DO INVESTIGATORS WORK WITH INSTITUTIONS TO ENSURE REQUIREMENTS ARE FULFILLED AND RELATIONSHIPS ARE FAIRLY AND EFFECTIVELY REVIEWED AND OVERSEEN?

Federal law gives academic institutions the authority to develop and enforce policies governing relationships with industry. Concerns have been raised about the varying scope of

academic policies, why some policies are more stringent than others, and what the effects of this variation may have.[27, 28] The alternative is a uniform policy for all academic institutions mandated by the government or developed voluntarily by the institutional community. We do not intend to make recommendations on institutional policies. Rather, our focus is on describing the response of investigators to current institutional policies. This report considers whether or not it would make a difference in the lives of investigators if standard institutional policies, or some aspects of them, were implemented.

Most institutions use peer review to monitor industry relationships. These can take the form of institutional conflict of interest committees, for example. Challenges in using peer review committees include a "culture of collegiality," such that colleagues are not inclined to "police" their peers from their institution or outside their institution; a "culture of envy," such that peers are too strict when reviewing conflict-of-interest disclosures; and institutional conflict-of-interest issues. Investigators need to be aware of these dangers and guide their actions accordingly.

Guiding principle 2: The primary responsibility of full-time investigators is to the institutions. Outside activities shall complement, not compromise, institutional responsibilities. Technology transfer is one of the missions of academic institutions that serve the public interest. Investigators play an integral role in fulfilling this mission through their collaborations with industry. The challenge for institutions is promoting awareness and understanding of established requirements regarding such collaborations. To fulfill the perceived need of increased awareness of institutional requirements and potential challenges, a list of common institutional requirements appears in the Appendix. In addition, investigators must:

> Be aware of, and adhere to, their institutional policies on investigator conflict of interest and academia-industry relationships.
>
> Call for improvements within their institutions when the institutional conflict-of-interest policies are not clear or not sufficiently well disseminated.
>
> Consider specific aspects of institutional requirements *before* entering into and *throughout* their relationships with industry.

Guiding principle 3: It is appropriate and beneficial for academic institutions to develop and enforce their own mechanisms of review and oversight of investigator relationships with industry. In general, the non-uniformity of institutional policies of review and oversight does not appear to be a major challenge for many investigators; however, it is a problem for many institutional leaders**.** A major benefit of the discretion given to institutions by federal regulation allo6os0Mchalleng1.14999 Tdminstitut l8dsnve35 0 yJ-0cs

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Work towards common standards, while preserving case-by-case analysis and situational-driven decision making. Institutions should study the effectiveness of their policies and improve them based on input from investigators. This will help protect the investigator, the institution, the industry partner, and the public.

Strive to develop uniform policies of disclosure of academic-industry relationships. Investigators would benefit from more uniform *disclosure* requirements.[29] The benefits of variable disclosure requirements are not clear and such non-uniformity may result in confusion and non-compliance by investigators. Although a specific model of institutional review and oversight is not endorsed, it would be beneficial to investigators if institutions used similar disclosure policies. These policies should be consistent in describing when disclosure occurs (annually, upon initiation of a relationship, or upon application for funding), and to whom (institutional committee, Dean, department Chair). Specifically, it is recommended that institutions ask all research investigators to *annually* disclose whether or not they have relationships with industry and to update this information upon starting or ending such relationships.

Guiding principle 4: The academic community can and shall monitor itself through *peer review* of industry relationships. Institutional committees that include peer members from the same institution are appropriate and effective in reviewing investigators' industry relationships. Peer review provides fair and effective review of industry relationships. Despite its challenges, peer review is the established, fundamental, and trusted adjudication mechanism of the scientific community. If the institution has rigorous standards and thorough training programs, this method of review and oversight should be effective and is in the interest of investigators and the public.

If committees are not used for disclosure review, more than one individual should review relationship disclosures. This should occur regardless of whether the relationship was approved by the first person who reviewed it. For example, some institutions or departments review relationship disclosures "up the ladder" (first by a department chair then by a dean, or simultaneously).

Committee composition, including the use of public representatives, is an important consideration. Several groups have endorsed having public members of the community in conflict-of-interest committees.[1, 2, 29] There are concerns, however, about confidentiality and proprietary information that may occur if committee members are not bound by confidentiality agreements. Institutions should carefully choose their public representatives and may have public representatives sign confidentiality agreements. Community members should be knowledgeable about ethical issues. They could include, for example, retired judges or lawyers not associated with the institution).

Training for conflict of interest committees is crucial, especially the training of committee members not affiliated with the institution. Regular training and review of members should occur.

Guiding principle 5: Investigators want and need clear guidance, efficient processes, and adequate support mechanisms from their institutions during the disclosure and review process, and throughout their participation in industry relationships. Disclosure of relationships is the first step, but what is done once disclosure has taken place is critical part. Investigators need efficient, streamlined review of relationship disclosures. Investigators should be able to seek guidance from their institutions in this regard. The need for clarity is also true for policies from funding sources, professional associations, and journals. More specifically, institutions should:

Act quickly in reviewing a new industry relationship for approval.

Have a process for investigators to appeal decisions made by individuals or committees reviewing disclosures. The appeals process is an important safeguard for investigators.

Consider using electronic databases for internal management of disclosure submission and review. Using electronic records would ease the burden on investigators, facilitate and expedite the administrative process, and provide better methods of communication and review between the necessary parties, including institutional review boards, technology transfer offices, and research offices. Electronic disclosure and review records should be "living" documents, not simply forms that are stored and not regularly updated. Extreme caution should be taken that personal and proprietary information is kept confidential.

Make investigators aware of potential challenges that might be encountered during the relationship review process, and provide sources of information helpful in addressing these potential situations. Such institutional guidance and expertise would be particularly helpful to investigators if it was in the form of Frequently Asked Questions, case studies, or provides other tools and examples that highlight common challenges and provide guidance in resolving them.

Clarify to investigators the consequences of non-compliance with their conflict-of-interest policies.

Have statements that specify the basis for their approving or rejecting investigators relationships with industry.

HOW DO INVESTIGATORS ADDRESS ISSUES OF ACCESS, ANALYSIS, AND DISSEMINATION OF RESEARCH INFORMATION, DATA, AND MATERIALS IN INDUSTRY RELATIONSHIPS?

It is crucial that academic investigators be able to access, analyze, and disseminate research information, data and materials. Research success, promotion, and tenure depend heavily on information generation (through research that relies on access to data and materials) and dissemination (through publications, presentations, mentoring and teaching). Sometimes these academic principles conflict with industry's need to protect proprietary information and materials. When considering a relationship with industry, what principles and practices might help investigators address access, analysis, and dissemination of research information, data and materials?

Guiding principle 6: Investigators shall have access to, and be involved in the analysis and/or interpretation of all data generated in the research. All academic investigators participating in research (industry-funded or not) have a professional obligation to the integrity of the study.

> Logistical challenges in following this general principle may occur, especially in the case of multi-institution studies. A research committee or a principal investigator (PI) should be designated for the purpose of coordinating data access and analysis. This often works best when the PI and other key academics in a study with industry actually come to the company, work with the statisticians and others to access the database, ask questions, and challenge conclusions before finalizing the study results.
>
> Even in cases where a PI or research committee is used for data access and analyses, each participating investigator must be assured of the study's integrity in other ways. One way is to insist that research methods, including data selection and statistical analyses, are discussed and agreed upon by participating investigators *prior* to data collection.[30] This is standard operating procedure to help prevent bias from entering into data analyses.

Guiding principle 7: Mutual understanding of constraints, principles, and policies regarding access, analysis, and dissemination of research information, data, and materials among investigators and their students and trainees, institutions, and sponsors is beneficial. Mutual understanding of each parties' goals and constraints before and during the relationship will go far to ensure the success of the relationship.

> Once a study is published, academic investigators expect that effort will be made to provide data and materials to other investigators. This is often a condition of journal publication. Access to data and materials for use by other investigators in the field helps to validate research results, an important aspect of the peer review system. Every effort should be made to appropriately share data and materials for replication purposes.

"ghost written" manuscripts describing results of industry-funded studies. All authors must be prepared to accept accountability if the content of the article is questioned.[33]

Transparency entails disclosure of relationships as required by institutions and journals, but also voluntary disclosure. Investigators should disclose all relevant industry relationships (including consulting) in publications and presentations.

Investigators should keep their non-industry funded research and consulting activities as separate as possible and in accordance with each contract.[34] Companies choose experts in a particular field. Thus, keeping institutional duties and consulting activities separate is challenging for investigators. It is important that investigators demarcate institutional duties and any activities covered in a consulting contract.

Guiding Principle 11: When investigators have consulting relationships with investment firms related to their area of expertise, all parties shall be aware of the specific circumstances involved. Relationships between investigators and the investment industry are becoming more frequent. Almost one of ten U.S. physicians has such a relationship[35] and it is likely that some of these physicians are involved in research. Although many of the same benefits and risks exist for these relationships as with traditional consulting, there are unique characteristics worthy of attention. For example, there are many potential legal entanglements involving securities law and confidentiality agreements.[35]

Investigators should be especially careful when a consulting relationship with the investment firm might overlap with relationships the investigator has with other companies (such as those potentially affected by the investment firm or those with which research is conducted).

Investigators should not engage in premature communication of unpublished or non-publicly discussed information regarding ongoing research studies, particularly clinical trials, to individuals or organizations in the investment industry other than to a company sponsoring those studies.

HOW DO INVESTIGATORS ADDRESS ISSUES IN ENTREPRENEURIAL ACTIVITIES?

Academic institutions are more frequently licensing inventions to companies. The growth of licensing activities has given rise to questions about whether and under what circumstances institutions should license technology to a company in which investigators or other members of the institution have financial interest. There are many benefits in investigator participation in entrepreneurial activities (start-up companies and technology licensing). Challenges for investigators include the potential to bias research to encourage company growth, the potential harm to individual and institutional reputations, and conflict of commitment with other institutional responsibilities. Often, a condition of consulting contracts is that discoveries are owned by the sponsor if relevant to the consulting area. Conflicts between industry sponsors and institutions can occur when intellectual property issues arise. For the individual scientist, the challenge is how to participate in these activities in a transparent and accountable manner and address any challenges that may arise with their institutions (ideally, before they develop into serious disagreements).

Guiding principle 12: Investigators shall not use federal funds to the benefit of a company, unless this is the explicit purpose of the mechanism used to fund the research. These mechanisms include projects funded by

Guiding principle 15: Investigators shall be aware of and adhere to requirements of federal funding related to disclosure of inventions. Investigators shall adhere to patent law and institutional requirements. An obligation of the Bayh-Dole Act is that federal grantees must disclose inventions resulting from federally-funded research to their institutions. Investigators may lack awareness of this requirement**.** Proper disclosure policies and procedures should be followed, and investigators should not condone moving technologies and discoveries "out the back door" to companies with which they have a relationship.

Guiding principle 16: Investigators shall not seek to influence their institution's technology transfer decisions for personal gain. It is recognized that investigators often have a financial interest in companies and that the resulting potential for conflicts of interest requires oversight and resolution. In some cases, the expectations of the investigator may not be in line with the interests of the institution. Institutions own intellectual property resulting from an investigator's federally-funded research. Whether or not the individual is involved in licensing arrangements is up to the institution. Government guidelines might be helpful, but investigators should always go to their institution first.

> Investigators should understand their institution's royalty distribution policies and standards for licensing. Investigators expect that the institution will provide ways for inventors to participate in, and benefit from, the commercialization of their discoveries. Institutions should consider practices that will continue to provide incentives to investigators.
>
> Situations may occur when royalty income causes difficulties between investigators (e.g., an investigator that provided assistance may find fault in not being listed as an inventor of the patent and thus entitled to royalty shares). Patent law requires including collaborating inventors 999 Td(in 4999 Td(in 4999 TdJ012 126or)Tj0.0004 Tc -0.00369 0

in this relationship is an unequal distribution of power and influence between the individuals in the relationship. As a result, the person being mentored may not feel he/she has the freedom to refuse the mentor's request. In addition, whenever the possibility exists that a mentor's advice or counsel might be influenced by personal financial interests, then there also exists the potential for significant negative impacts to the training or career development of the person being mentored. Potential financial conflicts of interest may occur in any relationship when there is a real or perceived imbalance in power or influence between a mentor, advisor, or supervisor and a student, trainee, or junior co

HOW DO INVESTIGATORS WITH INDUSTRY RELATIONSHIPS PROTECT AGAINST RISKS TO HUMAN RESEARCH PARTICIPANTS?

Conflict of interest is not exclusively a clinical research challenge. However, the potential for risks to human research participants is a higher level of risk than with basic research. Investigators and institutions have a responsibility to maximize the benefits to research participants, while ensuring their protection against any negative consequences of competing interests. More stringent institutional review is appropriate, and many medical schools conducting research apply such stringency.[23] The Association of American Medical Colleges issued recommended guidelines for the oversight of individual financial interests in research involving human participants in 2001.[2] One of the core principles is that *institutions* should regard all significant financial interests in human subjects research as potentially problematic and, therefore, requiring close scrutiny. Central to the recommendations is a rebuttable presumption that in the presence of significant financial interests (defined as more than $10,000 or 5% equity ownership in any one relevant company), the research should not be conducted by the affected individual or in that institution, absent compelling circumstances. In a 2004 survey of member medical schools, sixty-one percent had adopted the rebuttable presumption or similar standard, [23] indicating a positive reaction to this recommendation.

There are many types of research involving human participants from basic research to clinical trials. Even within the realm of clinical trials, different benefits, risks, and protections occur. For example, .14999 Td 0 t4eiinTJ0A79 Tw 16.57E9n/2Dd(0 Tw T[*clin)6(ry from)8(l of

Investigators with significant financial interests should not play a role in the research, absent compelling circumstances.[2] If they are involved, they should not solely determine experimental design or data analyses. These aspects of the study should be decided upon by peer-review mechanisms using investigators without financial interests in the study outcome.

CONCLUSION

Academia-industry relationships ultimately have the ability to bring multiple resources to scientific advancement and the battle against disease. It is only through such relationships that advancements in the life sciences can most rapidly achieve the maximum benefit to society. Clinical and basic science investigators benefit from industry relationships through increased resources to support on-going projects, interactions with colleagues that facilitate the bidirectional flow of knowledge and materials, and participation in the application of research.

Investigators are individually responsible for maintaining accountability in their choices to enter into relationships with industry, complying with institutional, government and journal policies, and taking responsibility to guard against bias in research. The scientific process requires scientists to work within a culture of the highest standards for research and professional conduct, and to identify and manage conflicts of interest as an inherent responsibility of their job. They must continue to make efforts to provide access to research st ran.496(gmum)9ses through

including identifying and addressing conflicts of interest. There are legitimate benefits to

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[27]

APPENDIX

Academia-industry relationships: Arrangements in which academic scientists, administrators, and institutions carry out research or provide intellectual property to industry in return for considerations of various types such as research support, honoraria, consulting fees, royalties, and equity.

Are you considering, or do you currently have any of the above relationships? If so,

1. What are your institution's requirements for disclosure of industry relationships?

    a) What criteria are used for defining a conflict of interest? What are the thresholds for disclosure?
    b) Must you disclose to the department Chair, Dean or other supervisor; institutional committee or university official; legal counsel?
    c) When must you disclose (annually, ad hoc basis, upon application for funding, prior to signing an agreement)?
    d) Must you disclose this in publications, presentations or to research participants?
    e) What types of relationships must you disclose (funding, consulting arrangements, company boards, equity, etc.)?
    f) What are the penalties for non-disclosure?

2. What are your institution's policies on investigators having financial interests (equity, royalties, consulting fees, membership on a board of directors, etc.) in a company sponsoring your research?

3. What are your institution's policies on investigators having financial interests in a company sponsoring clinical research involving human participants?

4. What are your institution's policies on the use of institutional resources and personnel in outside activities (e.g. consulting)?

5. What are your institution's policies involving trainees in industry-funded research?

Are you considering entering into any of the above relationships with a company? If so, please consider the following *prior* to the start of the relationship:

1. What are the conditions of publication?
2. What are the conditions of ownership and access of research data and materials? What are these conditions in multi-institution research projects? Do any of these conditions conflict with any institution's policies?
3. How are experimental designs negotiated?
4. What types of compensation are paid, and for what work?
5. What are patient inclusion criteria for enrollment?