STATEMENT OF THE

BIOTECHNOLOGY INDUSTRY ORGANIZATION

BEFORE THE

NIH BLUE RIBBON PANEL ON

CONFLICT OF INTEREST POLICIES

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The Biotechnology Industry Organization (BIO) is pleased to submit to the Blue Ribbon Panel its views on NIH Conflict of Interest Policies.

Summary

In brief, BIO believes that the biotechnology industry, and the patients whose diseases have been treated or cured through our members' biomedical innovations, have benefited enormously from the public-private partnerships envisioned by the Federal government's technology transfer programs. These relationships, particularly those involving members of the biotechnology community and the National Institutes of Health (NIH), provide our companies with the opportunity to fill those gaps in funding necessary to develop novel products and enable technologies, and often provide the NIH with access to resources not available through the federal funding process. Successful relationships between biotechnology companies and the NIH have led to the development of many FDA-approved therapeutics and vaccines. In addition, companies also rely on the general scientific expertise of individual NIH scientists through consulting agreements that must be reviewed and approved under NIH rules and regulations governing outside work and conflicts of interest. Consulting agreements also serve the important purpose of supplementing the income of NIH scientists and physicians; this can make compensation competitive with university salaries, and helps avoid a "brain drain" from the NIH.

Our members fully embrace the belief that in order for this public-private partnership to successfully continue, there must be clear and meaningful standards aimed at assuring that consulting agreements between our companies and NIH employees avoid

even the appearance of a conflict of interest. BIO supports the development of such standards with full public participation, and the disclosure to the public of the existence and financial terms of all consulting agreements between NIH employees and our companies.[1]

BIO and the Biotechnology Industry

BIO is a trade association of more than 1,000 companies, universities, worldwide research institutions and state affiliated organizations engaged in biotechnology research on medicines, diagnostics, agriculture, pollution control and industrial applications. BIO represents an industry that has already provided more than 325 million people with benefits from more than 155 commercially approved drugs, biologics and vaccines. More than 70 percent of these medicines have been approved in the past six years. There are over 370 biotechnology drug products and vaccines in late-stage clinical trials to treat more than 200 diseases, including various cancers, AIDS, Alzheimer's disease, heart disease, diabetes, multiple sclerosis and arthritis. In addition, biotechnology companies and researchers have developed hundreds of medical diagnostic tests, many biotechnology-derived foods, and environmental and industrial products.

The biotechnology industry is the most R&D-intensive and capital-focused industry in the world. Research and development in the industry is robust, focusing on

[1] Several years ago BIO adopted principles on Protecting Research and Research Participants in order "to protect the strong public interest in the results of research and public confidence in the research process." These principles emphasize responsiveness to institutions' efforts to identify conflicts of interests and full disclosure of compensation arrangements involving clinical investigators and sponsors. We reaffirm these principles in the context of compensation arrangements with NIH employees. See http://www.bio.org/bioethics/protect010303.asp.

new targets and highly innovative therapies. No industry spends more on research and development per employee, and no industry faces a lengthier or more complex regulatory process to bring products to market than the biotechnology industry. Biotechnology companies spent $20.5 billion on R&D in 2002, [2] with the top five companies spending an average of $133,000 per employee on R&D. Much of the success of the industry has been made possible by the close interaction between the National Institutes of Health and the biotechnology industry.

BIO commends this panel for undertaking a review of the NIH's conflict of interest policies and appreciates the opportunity to provide the panel with its position on appropriate relationships between the NIH and its collaborators. As the panel examines this very important issue and formulates its recommendations for improving rules and procedures, it should take into consideration the immense value and effectiveness of the public-private interaction in transferring biotechnology from the "bench to the bedside."

Background to Federal Technology Transfer

BIO believes that collaborations between NIH and industrial laboratories, and consulting agreements between NIH scientists and the biotechnology industry, are equally important components of the nation's scientific enterprise.

In the 1980s, Congress enacted legislation aimed at assuring that the wealth of biomedical advances being developed in federal and university laboratories would be commercialized as rapidly as possible for the benefit of diagnosis and treatment of human disease. Congress determined that the best vehicle was to rely on the resources and

[2] Source: Ernst & Young, "Resilience: America's Biotechnology Report 2003."

experience of the private sector to commercialize inventions developed in whole or in part with federal funds. The NIH has always been at the forefront of this movement, encouraging its scientists to collaborate with private industry to more quickly and effectively develop and commercialize biomedical products and services. Several studies have demonstrated that this movement has largely been a successful one, and it is clear that the federal policy in support of technology transfer should continue to be nurtured. [3]

Part of this collaborative process has been an expansion of the role that NIH scientists play as advisors to private industry, both under cooperative research and development agreements (CRADAs) under which NIH scientists will share in federal royalties on their inventions, and with consulting agreements approved and monitored by the NIH in which NIH scientists serve in the capacity of paid consultants.

The Importance of Cooperative Research and Development Agreements (CRADAs)

Under a CRADA, the government shares resources such as personnel, facilities and equipment with private entities, but does not make cash outlays to the private sector participant. The private sector entity funds its own activities under the CRADA, thus sharing the total cost of the collaboration. CRADAs can be an important opportunity to use the private sector resources of biotechnology companies to bring intellectual property developed in federal laboratories to useful application in the treatment of patients. This is the essence of the federal policy in support of technology transfer: moving intellectual property rights on biomedical inventions to the private sector where they can be most

[3] General Accounting Office, Report to the Vice Chairman, Joint Economic Committee, U.S. Congress, Technology Transfers: Benefits of Cooperative R&D Agreements (1994); Blumenthal et al, Relationships Between academic institutions and industry in the life sciences – an industry survey. N. Engl. J. of Medicine (1996) 334.

effectively commercialized. CRADAs can also allow private companies to use specialized equipment or tools that are sometimes available only in federal laboratories to test the validity of innovative concepts and new ideas. CRADAs are thus important mechanisms to enable start-up biotechnology companies to bridge the gap between a useful idea or theory and a successful and profitable product.

NIH has entered into over 400 CRADAs since 1985. At least 16 therapeutic drugs and vaccines approved by the FDA have been developed through NIH-industry relationships.[4]

The Importance of Consulting Agreements

The role that NIH scientists play as advisers to private industry has expanded beyond the CRADA mechanism to consulting agreements approved and monitored by the NIH. Typically, BIO members seek the expertise of outstanding members of the research community to augment their scientific endeavors. Some biotechnology companies gain valuable insight from independent Scientific Advisory Boards whose members may include NIH scientists. Many of our companies also rely on the advice of scientific experts from academic medicine, research centers and government. Many larger companies involve outside scientific experts to assist in clinical investigations, and otherwise to augment their scientific missions. The use of experts from the National Institutes of Health - bench scientists, clinicians, and statistical experts – is of significant benefit to biotechnology companies in focusing their research and development activities. NIH rules specifically prohibit consultants from disclosing non-public information from

[4] See http://ott.od.nih.gov/NewPages/therapeutics.pdf

the NIH and the company's proprietary data and from consulting on matters in which they are involved as government employees.

The Importance of Conflict of Interest Protections

All of the participants in the technology transfer process, including BIO members, recognize the importance of assuring that these financial relationships do not taint the integrity of the research being performed. To these ends, federal law and regulation guard against conflict of interest in technology transfer.[5]

The primary conflict of interest provision relevant to technology transfer derives from Section 208 of Title 18 of the U.S. Code. NIH employees are prohibited by this felony statute and implementing regulations from participating *personally and substantially* in a contract, or other particular matter in which the employee, or a family member or outside employer, has a *financial interest.*[6] The term *financial interest* means anything of monetary value "that may be directly and predictably affected by the employee's official action".[7] *Personal and substantial participation* means through "decision, approval, disapproval, recommendation, investigation, giving advice, or other significant effort".[8] Waivers may be granted only where the interest is "not so substantial

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[5] Thomas N. Bulleit, Jr.,"Public-Private Partnerships in Biomedical Research: Resolving Conflicts of Interest Arising Under the Federal Technology Transfer Act of 1986." Journal of Law and Health. Vol. l4 Issue 1 (1989-90).

[6] 18 USC § 208; 45 CFR 73.735-801.

[7] 45 CFR 73.735-801(b)(1).

[8] 45 CFR 73.735-801(b)(2).

as to affect the integrity of the employee's official duties".[9] Government employees also must meet an "appearance" standard: they are prohibited from having any direct or indirect financial interest that conflicts substantially or *appears to conflict substantially with performance of duties as a federal employee.* [10]

BIO Position

The Need for CRADAs and Consulting Relationships

BIO supports the continuing efforts of federal agencies to use the vehicles that Congress has authorized for transferring valuable technology from the public to the private sector where it can be most effectively utilized to diagnose and treat disease. As noted, partnering under CRADAs is a critical vehicle for private sector companies to gain access to technology developed with federal support. Indeed, NIH's technology transfer programs have resulted in collaborative relationships between NIH laboratories and the biotechnology community that produce lifesaving diagnostics, vaccines and therapeutics in the fields of oncology, AIDS and other diseases. Consulting agreements between NIH scientists and members of our industry are an equally important part of the nation's technology transfer program, providing expertise and judgment to the private sector in a host of circumstances other than those appropriate for CRADAs. [11]

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[9] 45 CFR 73.735-801(c) This standard is also described in slightly different ways elsewhere in the regulation: the interest is "so remote and inconsequential that it would not affect the integrity of his or her official duties", 45 CFR 73.804(a), or the interest is "not so substantial as to give the appearance of affecting the integrity of the services that the Government may expect". 45 CFR 73.735-904(a).).

[10] 45 CFR 73.735-802(a).

[11] If consulting agreements are to be permitted because they contribute to the development of useful biomedical products, the NIH should be loathe to proscribe compensation in the form

The Need for Full Public Disclosure

The Blue Ribbon Panel is performing a critical and important service by analyzing whether current conflict of interest guidelines meet statutory requirements, including the requirement that financial arrangements avoid even the appearance of a conflict of interest. BIO supports public disclosure of the financial terms of *all* consulting agreements with NIH employees (with appropriate protections for the confidentiality of research plans and data that may contain a company's intellectual property and other proprietary information).[12]

Likewise, the process of policy development should be conducted in the open. It appears that the changes made in 1995 to the NIH's conflict of interest policies that have been the subject of so much recent controversy were made without notice and apparently were not even made publicly available until their publication in the NIH manual. This unfortunately denied members of the public – including our companies – the opportunity to comment on revisions (or even know of them). BIO members rely on government agencies to make their policies and procedures publicly available so that the companies may comply with them. When biotechnology companies enter into consulting

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of stock or stock options, because to do so would be likely to disadvantage small and startup companies. Unlike larger biomedical enterprises, biotech companies are often small, cash-poor operations whose limited resources would be severely strapped if they were required to compensate consultants only in cash. If the conflict of interest rules at NIH are working – precluding NIH employees from consulting on any matters that constitute part of what they are doing as government employees – the fact that the scientists have an equity interest in the company for which they consult should not present any potential for conflict.

[12] This may require amendments to the Ethics In Government Act in order to assure public disclosure of consulting relationships by many NIH senior scientists who are not compensated at a high enough level to reach the current public disclosure threshold. See 5 U.S.C. App. 4 § 101 et seq. In general, government employees whose pay is greater than 120% of the minimum rate of basic pay for GS-15 are required to file annual public financial disclosure reports, while the financial reports filed by employees compensated at a lower level are confidential. 5 C.F.R. § § 2634,202(c), 2634.604, 2634.904. See also OGE Forms 278 and 450.

agreements with NIH employees, the companies have every reason to believe that such agreements are consistent with the law and its implementing guidelines. It would be virtually impossible for companies to police compliance with these agreements, nor is it appropriate to expect them to do so. Nonetheless, transparency in the creation and dissemination of the rules governing consulting relationships, as in information on the relationships themselves, will aid the process of public trust and acceptance as well as compliance.

BIO urges the NIH to adopt procedures under which it will announce consideration of conflict of interest policies applicable to technology transfer and consulting agreements, receive public comment on those policies, and finalize them only after receiving such comments. Such a system should seek to strike a balance between the rigors of formal notice and comment rulemaking under the APA and complete secrecy.

Indeed, the entire research community would benefit were NIH to notify the public that such policies are under consideration and receive comments about the policies' potential scope and effect. Rules do not exist in a vacuum and, therefore, should not be developed in secret. The insights and wisdom offered by consumers, industry, and other governmental agencies will lead to more effective approaches to the conflict of interest policy, among others. Moreover, publicly-aired policies possess greater legitimacy. Public participation results in greater "buy-in" by industry and patients, and the public process serves to publicize the policies at issue resulting in higher compliance by all interested parties.

A good model for public participation is the Food and Drug Administration's "good guidance practice" policy, through which FDA publishes and receives public

comment on a host of procedural and regulatory policies.[13] Under FDA's approach, the agency issues draft guidance documents explaining how the agency believes the law applies to particular regulated activities.[14] FDA has also publicly committed that it will receive comment about and formally finalize the majority of draft guidances before implementing the policies that they describe.

After receiving comments on guidances that propose new or changed policies or interpretations of law, the agency will often revise (and sometimes withdraw) its approach or procedure based on industry and consumer participation in the process. FDA also publishes all draft and final guidance documents on its website and publishes annually in the Federal Register a list of guidance documents that are under development. This system keeps industry and the public informed about FDA's position on important issues. [15]

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[13] 21 CFR 10.115.

[14] S*ee* 65 FR 7322 (Feb. 14, 2000).

[15] FDA also publishes internal organizational and procedural policies on its website so that industry is informed about procedural issues that might affect regulatory submissions.

Conclusion

BIO strongly believes that cooperative efforts between biotechnology companies and the nation's preeminent scientists must continue. Therefore, we urge the Blue Ribbon Panel to quickly and comprehensively address the policy issues that it is charged to consider. To that end, BIO strongly supports your efforts to review and, as appropriate, recommend revisions in conflict of interest policy governing the participation of NIH scientists and employees in private research and other activities. In order to ensure the integrity of these policies, the Blue Ribbon Panel's recommendations should be drafted as revisions to current requirements, broadly disseminated, subject to public comment and finalized only after broad public participation. In addition, the financial terms of all consulting agreements between NIH employees and our industry should be disclosed to the public (with appropriate confidentiality protection for intellectual property and other proprietary data and information). In our view, these actions are in the best interests of NIH scientists, BIO companies and the NIH itself.

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