Panel Report of the Forum on Sponsored Research Agreements: Perspectives, Outlook, and Policy Development

Ad Hoc Group of Consultants to the Advisory Committee to the Director, NIH

National Institutes of Health
Bethesda, Maryland

May 1994

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MAY 16 1994

Harold Varmus, M.D.
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National Institutes of Health
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Dear Dr. Varmus:

We are pleased to transmit to you the final report of the ad hoc consultant panel to the Advisory Committee to the Director, NIH, on "Sponsored Research Agreements: Perspectives, Outlook and Policy Development."

The Panel's mission was to discuss issues arising from sponsored research agreements between NIH grantees and industry and to provide specific recommendations on NIH's oversight role with respect to the following provisions of the Bayh-Dole Act--the scope and size of sponsored research agreements; the U.S. manufacturing requirement, preference for U.S. industry and foreign access; the utilization and licensing requirements for inventions made with Federal funding; the preference for small business (fair access); and, research freedom. The recommendations of the Panel are based upon presentations from invited speakers, testimony from public witnesses, the presentation and discussion of four case studies, and the deliberations of the Panel over the course of its two-day meeting in January 1994.

On behalf of the entire Panel, we were pleased to have had the opportunity to assist in this important initiative and trust that our report and recommendations will prove useful to the NIH in guiding policy decisions in this area.

Sincerely,

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Acknowledgments

National Institutes of Health staff members Dacia Clayton, Esq., Office of General Counsel, and Peggy Schnoor, Division of Science Policy Analysis and Development, are recognized for their important contributions in the conduct of the meeting of the Panel and in the development of the report.

For additional copies of the report, please call the Division of Science Policy Analysis and Development, 301-496-1454.

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Executive Summary

On January 25 and 26, 1994, the National Institutes of Health (NIH) convened an outside panel of experts in a public forum to discuss issues arising from sponsored research agreements between NIH grantee research institutions and industry. The Panel was asked to provide recommendations on NIH's oversight role with respect to certain provisions of the Bayh-Dole Act. The Panel specifically addressed the following issues:

> What factors should NIH consider with regard to the size of a sponsored research agreement and the scope of the intellectual property rights of an industrial partner to federally funded research when evaluating compliance with the Act's licensing preference for small businesses?
>
> How should NIH implement and monitor the Act's U.S. manufacturing requirement and preference for U.S. industry, given the increasing globalization of markets and the emergence of multinational corporations?
>
> How should NIH monitor and ensure that the Act's objective of promoting the utilization of inventions from federally funded research is being met?
>
> What is the most effective way for NIH and grantee institutions to ensure that small businesses are given adequate access to federally funded research?
>
> What should NIH's role be in safeguarding core principles of research freedom and scientific integrity in interactions between its grantees and industry?

The 12-member Panel was co-chaired by David M. Livingston, M.D., of the Dana Farber Cancer Institute in Boston, MA, and Edward Penhoet, Ph.D., of Chiron Corporation in Emeryville, CA. Other members of the Panel included research scientists; a Nobel laureate; patent attorneys; and executives and administrators from large pharmaceutical companies, State and private universities, research institutions and hospitals, and small biotechnology companies. The Forum consisted of introductory/background presentations, including the Government's perspective on technology transfer since Bayh-Dole, as presented by the Deputy Secretary for the U.S. Department of Commerce; fictional case study presentations and issue discussion; and Panel deliberations.

The members of the Panel agree that the Bayh-Dole Act has been effective in promoting technology transfer. As the Act has been implemented, it provides benefits for those conducting federally funded research. It also serves the public interest by stimulating local economies and providing an efficient mechanism for developing federally funded research into useful commercial products. The Panel therefore advises against the implementation of stringent rules or further regulations. However, the Panel also recognizes the usefulness of some guidance from NIH to its grantees so that they may better comply with certain requirements of the Act.

In response to NIH's request for guidance on the issues noted above, the Panel offers the following specific recommendations about agreements involving research sponsored in whole or in part by NIH:

Heightened scrutiny is advised for all exceptionally large, or "mega-scale," agreements and may also be advised for those that meet one of several threshold criteria, such as being in excess of $5 million per year or $50 million overall; involving several principal investigators or whole departments, labs, or major components of an institution; or specifying rights for technology for an undue length of time. The Panel advises against mandatory NIH review of these agreements, noting that the undue administrative burden on grantees and the adverse impact on technology transfer could far outweigh any benefit of the review.

The Act permits agencies to grant waivers to its explicit U.S. manufacturing requirement. The Panel recognizes that grantees are obligated to require their exclusive licensees to agree that any products embodying licensed inventions that will be used or sold in the United States must be substantially manufactured in the United States. However, other economic benefits should be regarded when considering waivers of the U.S. manufacturing requirement. The Panel urges NIH officials to continue to implement a flexible policy for fulfilling this part of the law, since in the biomedical area it is not always commercially feasible to manufacture substantially in the United States. Moreover, important public health and other economic benefits could be lost if product development is delayed because of rigid enforcement of this provision. The Panel adds that because national boundaries are increasingly ignored as science and science-based industries become more global in focus, it is becoming increasingly difficult to distinguish foreign and domestic entities. Moreover, these distinctions can be muddled further when a so-called U.S. corporation chooses to manufacture certain products in offshore facilities or when a foreign corporation manufactures its products at a U.S. subsidiary.

Because grantees are more familiar with the licensed technology, capabilities of the licensee, and the market for a particular product, they are far better

suited than NIH to undertake the primary responsibility of overseeing the utilization requirement of the Act or ensuring that federally supported research is being licensed and made available and useful to the public. The Panel indicates that the use and active enforcement of performance benchmarks and diligence requirements would greatly enhance grantees' capabilities to meet this oversight responsibility.

Although the Panel found minimal evidence that small businesses were not being given fair access to federally funded technology, it notes that grantees could employ certain safeguards to further ensure fair access. For example, option periods for granting licenses should be time limited so that other companies may have timely opportunities to license technology, and once a company decides not to exercise its option rights, it should not be given a second opportunity to obtain such rights by matching another party's offer for the rights. In addition, the Panel notes the importance of looking at fair access in terms of the entire research program at an institution as opposed to access to a particular project or invention.

The Panel recommends that NIH take the lead in upholding the basic principles of research freedom and scientific integrity by providing guidance through policy statements or other educational materials.

Other significant issues raised by the Panel at the Forum included the influence of the Bayh-Dole Act and technology transfer in general in shifting attention away from basic research toward applied research, and the sometimes adverse impact that biotechnology patents have had on the availability of research tools.

The Panel understands that NIH will consider its recommendations in developing public policy in this area and that NIH will present draft guidelines to the Advisory Committee to the Director, NIH, in June 1994 for review and comment.

Introduction

In response to concerns raised by the National Institutes of Health (NIH) and Congress regarding a proposed large-scale sponsored research agreement between the Scripps Research Institute and Sandoz Pharmaceuticals Corporation, NIH, at the request of its Director, formed an internal Task Force on the Commercialization of Intellectual Property Rights from NIH-Funded Extramural Research. To assess whether the proposed Scripps-Sandoz agreement represented an emerging trend in academic-industry interactions, the Task Force analyzed 375 sponsored research agreements and held numerous informal meetings with academic, industrial, and other Federal agency representatives. On January 25-26, 1994, NIH convened an outside panel of 12 experts in a public forum to discuss issues arising from sponsored research agreements between NIH grantees and industry.

The 12-member Panel was co-chaired by David M. Livingston, M.D., of the Dana Farber Cancer Institute in Boston, MA, and Edward Penhoet, Ph.D., of Chiron Corporation in Emeryville, CA. Other members of the Panel included research scientists; a Nobel laureate; patent attorneys; and executives and administrators from large pharmaceutical companies, State and private universities, research institutions and hospitals, and small biotechnology companies.

NIH Director Harold Varmus charged the Panel with providing recommendations on NIH's oversight responsibilities with respect to the following five key issues:

What factors should NIH consider with regard to the size of a sponsored research agreement and the scope of the intellectual property rights of an industrial partner to federally funded research when evaluating compliance with the Act's licensing preference for small businesses?

How should NIH implement and monitor the Act's U.S. manufacturing requirement and preference for U.S. industry, given the increasing globalization of markets and the emergence of multinational corporations?

How should NIH monitor and ensure that the Act's objective of promoting the utilization of inventions from federally funded research is being met?

What is the most effective way for NIH and grantee institutions to ensure that small businesses are given adequate access to federally funded research?

What should NIH's role be in safeguarding core principles of research freedom and scientific integrity in interactions between its grantees and industry?

The Panel understands that as part of its continuing efforts to respond to concerns raised by Congress and NIH with regard to university-industry interactions in general and the proposed Scripps-Sandoz agreements in particular, the Task Force will use the information derived from the Forum, the recommendations of the Panel, and the information from its internal review and analysis to develop a policy approach that it plans to present to the Advisory Committee to the Director, NIH, in June 1994 for review and comment.

Framework of Panel Discussions

During the course of the 2-day meeting, invited speakers and other participants discussed with Panel members both benefits and concerns that arise because of sponsored research agreements at universities and similar institutions. The Bayh-Dole Act is seen as benefiting both the public (through a more efficient development of basic research findings into useful products and an expansion of the economic base) and the research community (by providing another source of support for its activities and an additional source of jobs for the researchers it trains).

Some of the discussion also focused on how agreements with industry that are loosely structured or not carefully monitored by institutions may adversely influence the direction and shape of biomedical research and threaten academic freedom. The Panel generally agreed that grantee research institutions were doing a good job in controlling the extent of industrial influence on the direction of research and in safeguarding principles of academic freedom. However, guidance from NIH could be useful for grantee institutions that have not had extensive experience with industry or that need external support for their own internal policies. Some participants also noted concerns about the difficulty of implementing the Bayh-Dole Act and how increased pressure to patent might reduce the availability of new technologies.

Part of the Panel's deliberations focused on presentations of four hypothetical case studies of technology transfer agreements, all deliberately flawed. In discussing these cases as well as details of the Scripps-Sandoz arrangement and NIH's review of 375 other agreements, members of the Panel identified important benefits and concerns associated with the Bayh-Dole Act and developed general recommendations to assist NIH in formulating its public policy.

Proposed Scripps-Sandoz Agreement Put Into Context

According to Ms. Daryl Chamblee, NIH's Acting Deputy Director for Science Policy and Technology Transfer, most agreements that were reviewed by the NIH Task Force—331 (88 percent) of the 375 agreements—represented small, project-specific arrangements that typically involved the work of only one or two scientists. Moreover, 85 percent of the agreements were for periods of 5 years or less. Only 44 agreements in the overall group were considered large scale, meaning that they involved a major component or the entire output of a research institution.

In most cases, licensing rights were promised to industrial partners in advance, but the vast majority of the agreements restricted the industrial partner's intellectual property rights to particular projects or discrete fields of research. Slightly under half of the agreements (167 of 375) were with small business partners. Eighty-seven percent of the agreements involved U.S. corporations or domestic subsidiaries of non-U.S. companies.

The proposed Scripps-Sandoz agreement, at $300 million, exceeded any other by nearly $200 million. It also was the only agreement that gave the industrial partner seats on the institution's board of directors, the right to review the grantee institution's invention disclosure reports before their submission to NIH, and the right to move a research project before completion from a grantee's laboratory to the company's facilities anywhere in the world. The agreement also appeared to restrict research freedom at the grantee institution more extensively and provided more pervasive control to the industrial partner than did any other such agreement reviewed in the NIH survey.

Ms. Chamblee noted that, from this analysis, the size and scope of the proposed Scripps-Sandoz agreement appeared to set it apart from the rest of this diverse group of sponsored research agreements, even from those classified as large scale. Thus, the proposed Scripps-Sandoz agreement is considered an aberration.

During the course of the 2-day meeting, several representatives from Sandoz Pharmaceuticals Corporation and Scripps Research Institute participated in discussions and also presented formal statements about their large-scale technology transfer agreement. In brief, the representatives indicated that some elements of this

technology transfer agreement have been misconstrued in public reports and that other elements, which may have been problematic, are being corrected. Given the criticism that the proposed agreement has attracted and statements made by Scripps representatives during the meeting, it appears likely that the final Scripps-Sandoz agreement will be more in keeping with accepted norms.

Bayh-Dole Act Enhances Technology Transfer

The members of the Panel agree that, by and large, the Bayh-Dole Act is working well for those conducting biomedical research, is serving the public interest, and does not need to be amended. The Act is intended to promote the efficient development of research findings into useful products, to provide economic benefits, and to enhance U.S. competitiveness in the global marketplace. Panel members suggest that when considering specific problems that may arise as the Act is implemented, it may be helpful to bear in mind its emphasis on efficient technology transfer for the development of useful products.

In looking at the general technology transfer mandate of the Bayh-Dole Act, the Panel members note that it applies broadly to researchers and institutions that receive NIH or other Federal support. Thus, NIH is required to promote technology transfer and to encourage institutions receiving Federal support to meet this congressional mandate. Panel members conclude that this arrangement has thus far served the public interest through the development of useful commercial products, such as drugs and clinical diagnostic materials. Indeed, the Bayh-Dole Act not only is contributing know-how to established companies, but also has encouraged the creation of many jobs and research-oriented companies, particularly within the biotechnology industry.

Panel members note that the Bayh-Dole Act has added an important obligation to NIH and to the research institutions it supports. The support and conduct of research do not by themselves meet the Act's technology transfer requirements. Hence, institutions receiving NIH or other Federal support are obliged to make additional efforts, including the development of licensing agreements with companies, to ensure that discoveries and inventions are brought into use. Moreover, because companies face risks for their part in this process, it may be appropriate to grant them exclusive licenses or to find other incentives for them to play a part in technology transfer.

Important Developments Associated With Bayh-Dole

Although the Bayh-Dole Act has markedly intensified efforts to transfer federally sponsored research findings into the private sector for commercial purposes, the process of transferring findings from university-based research into commercial technology has been under way for many decades—well before this law was enacted and before Federal funds played such a dominant role in supporting academic researchers.

According to meeting participant Alan Goldhammer of the Biotechnology Industry Organization, during the 1920s, representatives of Du Pont worked out an agreement with chemists at Notre Dame University to study polymer chemistry and share such information with the chemical company. Although no Federal funding was involved, university officials at that time expressed concerns over accepting outside funds. However, these company-sponsored efforts eventually led to the development of neoprene, the first commercially produced synthetic rubber, and royalties from sales of that material brought several million dollars in revenues as a further benefit to the university.

During the period between the World Wars and earlier, Federal support for university-based research was scarce, and reliance on support from the private sector was not unusual. In part because of that history, the academic community was generally wary of turning to Federal sources for research support after World War II when Federal sponsorship rapidly expanded, as pointed out by Dr. Ronald Lamont-Havers of Massachusetts General Hospital, a speaker at the meeting.

Following World War II, Federal support for university-based research expanded enormously, but more recently it has been leveling off. In the area of biomedical research, NIH plays a central role in supporting basic research and training, both of which contribute to private sector development of products to diagnose and treat diseases—either directly through the availability of new technology and techniques, or indirectly, by supplying well-trained personnel who can help bring inventions to commercial fruition.

Moreover, basic research supported by NIH led during the past 10 to 15 years to an explosion of the commercial activity known as biotechnology, which has led to the

formation of hundreds of new companies. It appears that the Bayh-Dole Act has helped stimulate this industrial growth by facilitating the transfer of federally funded technology to new commercial ventures. According to Dr. Goldhammer, since the enactment of the Bayh-Dole Act, approximately 1,000 new companies and 100,000 new jobs have been created, and the biotechnology industry continues to expand.

According to David Barram, Deputy Secretary of the U.S. Department of Commerce, which holds the central responsibility for overseeing the implementation of the Act and related policies, the Bayh-Dole Act is now part of a broader policy within the Clinton administration to foster cooperation between Federal agencies and industry.

Before the Bayh-Dole Act in 1980, the commercialization of federally sponsored research was a passive process, largely because ownership of discovery rights resided with the Federal sponsor rather than with institutions where the research was done. In changing that ownership, the Bayh-Dole Act gave research institutions new incentives to patent more of their research. It also provided a more efficient system for industry to obtain licenses to commercialize those findings. Thus the Act is sparking creativity and speeding technology transfer. Ultimately, those forces enhanc the competitiveness of U.S. industry, Deputy Secretary Barram concluded.

Bayh-Dole and Concerns About Basic Research

Despite general satisfaction with technology transfer agreements under Bayh-Dole, a concern was raised that the Act may be helping to shift attention away from basic research and more toward applied research at universities. In addition, there was some uneasiness that in the rush to patent research results and develop new sources of revenues, some of the newest and most powerful research tools may become less accessible, or inaccessible, to the research community.

However, the Panel does not know precisely what measures to propose to counter these potential problems. Some Panel members noted that the lines between basic and applied research have blurred and that, in fact, much of the research conducted at small biotechnology companies could be considered basic research. NIH Director Harold Varmus pointed out to Panel members that specific issues concerning intellectual property rights to research tools as well as broader questions about the direction and emphasis of research sponsored by U.S. agencies, including NIH, are being addressed in other forums.

The Panel strongly affirms the important underlying role of NIH in supporting basic biomedical research. This traditional role includes a responsibility for NIH officials to ensure the integrity of the research enterprise. The diverse efforts within the broader biomedical research community to satisfy the Bayh-Dole mandate thus should not undermine the widely recognized principles of academic freedom and general standards of conduct that pertain to researchers at universities and similar institutions.

Some institutions that have negotiated large sponsored research agreements with companies have also developed explicit guidelines to protect the rights of each of the parties to those agreements. According to Dr. Lamont-Havers, Massachusetts General Hospital has carefully laid out the goals and principles that its researchers, the administrators at the institution, and the corporate partners must observe. Many of the precepts he described correspond closely to those outlined during subsequent discussions of the Panel.

Part of the remedy to the problems affecting the general direction of research may rest with senior investigators, several members of the Panel noted. Those investigators

need to actively foster attitudes favoring the integrity of research among postdoctoral researchers and younger trainees. As one panelist said, senior scientists need to "lead by example. . . . A lot is in the hands of senior scientists to maintain the culture; it's not up to NIH."

Bayh-Dole and Concerns About Equity and Conflicts of Interest

The Bayh-Dole Act indicates a preference for small companies in fashioning technology transfer agreements with research institutions. In this context, the members of the Panel considered the granting of equity rights by small businesses to universities and their researchers as one of the few ways that small companies have to gain access to university research. That is, because small companies are likely to be short of cash, they may instead offer equity positions to potential university partners—a practice that some observers consider as risking conflict of interest.

During these discussions, a meeting participant described John Hopkins University's policy on this issue. That policy sets out clear terms indicating when faculty members may hold equity positions in a company involved in sponsored research and when they may not. Although several members of the Panel regarded the Johns Hopkins policy as a good model, they made no further effort to incorporate its precepts into their recommendations to NIH, concluding that universities need to establish their own policies to protect against conflicts of interest.

Need for Guidelines and Other Educational Efforts

On the specific issue of the NIH role in ensuring that grantees comply with requirements of the Bayh-Dole Act, Panel members recommend that NIH develop general guidelines or other educational materials to be used by administrative officials and researchers at universities and other institutions as they implement the Act. Panel members believe that NIH should present these guidelines and other materials to grantees as informal examples and "points to consider," not as binding rules for universities and other institutions. The only exception to the Panel's recommendation for nonbinding guidelines is on matters related to traditional issues of academic freedom, which the Panel urges NIH to uphold forcefully and unequivocally.

Because many grantee programs that are intended to implement the Bayh-Dole Act are still new and relatively fragile, developing restrictive regulations to overcome perceived problems might seriously undermine the law's implementation. Panel members not only recommend against new restrictions, but also urge NIH not to increase reporting requirements, which absorb resources (such as time and personnel) and thus would tend to retard the overall process of technology transfer and conflict with a particular policy objective of the Bayh-Dole Act, which is to minimize the cost of administering patents.

After considering the views of other Forum participants drawn mainly from the academic and corporate research communities, the Panel members worked in an open session to develop recommendations addressing five specific areas relevant to NIH's oversight role in implementing the Bayh-Dole Act.

Panel Recommendations

I. Certain features of sponsored research agreements are useful alerts for extra scrutiny.

The Panel notes that guidelines and educational materials developed by NIH pertain only to those research projects that receive "co-mingled" support from NIH and a corporate sponsor. That is, if the sole support for a particular project is a corporate sponsor or some source other than NIH, then it lies outside NIH jurisdiction. However, because in practice many research projects may be jointly supported by NIH and a corporate partner, guidance to grantee institutions can be helpful. In identifying such projects, members of the Panel note, the goal is not to establish legal boundaries but to alert administrators to situations where scrutiny of the terms of an agreement would be prudent.

The Panel also believes that heightened scrutiny is advised for all exceptionally large, or "mega-scale," agreements and for agreements that are not restricted to a specific research area or field of use. However, the Panel advises against a mandatory NIH review of these agreements, noting that the administrative burden on grantees and the adverse impact on technology transfer would far outweigh any benefit derived from a mandatory review.

With that understanding of the general boundaries of NIH jurisdiction, the panelists assembled a series of additional conditions that could be used to trigger extra scrutiny when institutions are drafting technology transfer agreements with corporate sponsors. That scrutiny might entail notifying NIH officials of the impending agreement and considering whether modifications are advisable. Those conditions include the following examples:

The fraction of research being sponsored, as defined by the sponsored research agreement, exceeds 20 percent of the total effort supported by NIH.

The absolute amount of support from the corporate sponsor meets or exceeds $5 million per year or $50 million total.

The prospective rights to technology being developed cover an entire group within, or a major component of, the institution, or those rights represent a

substantial proportion of the anticipated intellectual output of the institution's research staff. However, the Panel believes that a precise percentage of the staff who are involved cannot be designated.

The period during which the sponsor has an exclusive option to specific patent rights without obligation for development is unduly prolonged.

The agreement involves any other unusual practice or stipulation that might trigger public concern, including stringent enforcement of claims to broadly useful research tools that would entail undermining rather than serving the public good.

II. NIH should consider other possible economic benefits when considering waivers of the U.S. manufacturing requirement.

As mandated in the Bayh-Dole Act, exclusive licenses to inventions made with Federal support must require that any products embodying such inventions that will be used or sold in the United States be manufactured substantially in the United State unless a waiver is obtained from the funding agency. To obtain a waiver, the institution must demonstrate that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that, given the circumstances, domestic manufacture is not commercially feasible.

Panel members agree that this preference is concrete and thus needs to be honored and that trying to change it through an amendment to the law is not warranted. However, the Panel urges NIH officials to continue to implement a flexibl policy for fulfilling this part of the law when considering proposed waivers of the domestic manufacturing requirement. Depending on the technology, it may be difficult for grantees to find companies capable of substantially manufacturing in the United States. Furthermore, important public health and economic benefits besides U.S. manufacturing could be lost because of rigid enforcement of this provision. The value of minimizing the time it takes to bring an important biomedical product to the American people must not be ignored or underestimated. Moreover, the increasing globalization of the economy often forces American firms to manufacture abroad to bring a new product to market. In this regard, the Panel members also recommend a broad interpretation of congressional intent on this issue wherever legally feasible.

The Panel also notes that because national boundaries are increasingly ignored as science and science-based industries become more global in focus, it is becoming increasingly difficult to distinguish between foreign and domestic entities. Moreover, these distinctions can be muddled further when a so-called U.S. corporation chooses

to manufacture certain products in offshore facilities or when a foreign corporation manufactures its products at a U.S. subsidiary.

III. Primary responsibility for meeting utilization and licensing requirements resides with grantee institutions.

The Bayh-Dole Act mandates the efficient transfer of federally supported research into technology that is available and useful to the public. Conceivably, this process could be deliberately disrupted or unnecessarily delayed. For instance, a company could license the rights to research at an institution but not develop that research, thereby thwarting the intent of the law. However, Panel members conclude that NIH is not in the best position to monitor the vast array of grantee institutions to enforce this part of the law. Although NIH and other Federal agencies are vested with "march-in rights" allowing them to take back a technology and find a more diligent corporate developer, Panel members consider this remedy too drastic and impractical except in extreme cases of abuse.

Hence, the main responsibility for ensuring that technology transfer agreements are carried out in accord with the Bayh-Dole Act remains with the NIH-supported institutions that are executing those agreements. In practice, the Panel members conclude that licensing agreements need to include clear and effective "due diligence" clauses or performance benchmarks, requiring corporate sponsors to develop in a timely manner the federally supported research they are licensing. Moreover, grantees should be prepared to aggressively enforce these requirements.

IV. Although fair access for small businesses is not a problem, certain safeguards would be useful.

Although the Bayh-Dole Act states a preference for small businesses, members of the Panel do not see strong reasons to change this preference into a priority so long as access to federally sponsored research at an institution, as opposed to access to a particular project or invention, remains fair. One circumstance was viewed as worth guarding against because it could lead to unfair or unlawful practices: A large corporation with a broad-termed first-right-of-refusal agreement might lock up a particular technology without developing it or might reclaim rights to a rejected technology when another corporate entity expressed interest in it.

The Panel members thus recommend that the terms of such broad-based agreements limit large sponsors to taking a single look at a research project before deciding whether to pursue it. That is, once a company decides not to exercise its option right, it should not be given a second opportunity to obtain such rights by

matching another party's offer for the rights. Moreover, large sponsors are to be restricted to no longer than 3 months of exclusive consideration before other corporate contenders may bid for the rights to further develop the research.

V. NIH should take a lead role in promoting basic principles of research freedom.

The members of the Panel urge NIH to make strong recommendations to research institutions that they continue to ensure broad academic freedom for researchers involved in sponsored research activities. For example, the freedom to choose research projects and to collaborate with other academic scientists should be maintained. In addition, individual investigators should be free to decide whether to participate in sponsored research programs, and they should be fully informed of the terms of such agreements. The freedom of students, postdoctoral fellows, and other researchers to seek employment also should not be infringed in any way.

Although proprietary information originating in the company is subject to nondisclosure agreements, researchers at academic institutions should in all other respects be free to communicate their research findings at meetings, by publication, and by other means. The Panel views publication as an obligation of researchers receiving NIH support. Moreover, making available research tools that are developed in the course of such work may also be viewed as an integral part of that obligation because their free and full use serves the public interest. The Panel recognizes the important advantages of delaying publication so that patent applications can be filed and corporate sponsors can consider the business applicability of specific research findings. However, the Panel prefers that such delay be minimal and that consideration be given to the importance of disseminating the research discovery rapidly and to the resources available to the company to quickly review disclosures and appropriately protect its rights.

Conclusion

The members of the Panel agree that by and large the Bayh-Dole Act is working well. Not only does it provide benefits for those conducting federally funded research, but it also serves the public interest by stimulating local economies and by providing an efficient mechanism for developing federally funded research into useful commercial products. The Panel also notes that small businesses seem to be obtaining adequate access to federally funded technology and that the U.S. economy has benefited substantially from the transfer of such technology from grantee institutions to industry. However, the Panel recognizes the benefit of some guidance from NIH to its grantees so that they may better comply with the Bayh-Dole Act. The Panel concludes that compliance problems with the Act appear to be minimal and therefore recommends that NIH provide its grantee research institutions with educational materials or points to consider, as opposed to stringent rules and regulations.

Appendix A

Forum Agenda

Agenda

FORUM ON SPONSORED RESEARCH AGREEMENTS: PERSPECTIVES, OUTLOOK, AND POLICY DEVELOPMENT

January 25–26, 1994
Marriott Hotel (Pooks Hill)
Bethesda, Maryland

January 25, 1994

8:30 - 8:45 a.m.	*Welcome and Opening Remarks*—Statement of Purpose and Role of the Panel; Focus of the Meeting; Introduction of Panel Co-Chairs. *Harold Varmus, M.D., NIH Director*
Session I:	**Historical and Legislative Perspectives—Background**
8:45 - 9:00 a.m.	*Government Perspective on Technology Transfer Since Bayh-Dole*—Original Expectations, Actual Performance, Future Challenges, Public Benefits, the Basic Principles and Key Provisions of the Bayh-Dole Act. *Presenter: The Honorable David J. Barram, Deputy Secretary, U.S. Department of Commerce*

9:00 - 9:20 a.m. *Industry Perspective*—What impact has the Act had on industry In particular, how has the Bayh-Dole Act influenced the establishment of the biotechnology industry, the birth of biotechnology, the availability of resources, public benefit, and the U.S. role as the world leader in biotechnology?

Presenter: Alan Goldhammer, Ph.D., Chief Scientist, Director of Regulatory Affairs, Biotechnology Industry Organization

9:20 - 9:40 a.m. *Nonprofit Perspective*—How is the Act working from the perspective of universities and nonprofit institutions? How do funded institutions balance core academic and research freedom principles and commercialization?

Presenter: Ronald Lamont-Havers, M.D., Deputy Director for General Affairs, Cutaneous Biology Research Center, Massachusetts General Hospital

9:40 - 10:00 a.m. *The NIH Experience*—Purpose of and Highlights From NIH Survey; Overview of Key Issues; Other Federal Agencies' Perspectives.

Presenter: Daryl A. (Sandy) Chamblee, J.D., Acting Deputy Director for Science Policy and Technology Transfer, NIH

10:00 - 10:15 a.m. **BREAK**

10:15 - 10:30 a.m. Comments by Panel Co-Chairs explaining the format of the remainder of the meeting and introducing the five critical issues to be addressed.

Session II: **Case Studies—Short, fictional case studies based on existing cases to illustrate important issues of concern under the Bayh-Dole Act**

Case studies will be presented to the Panel by a discussant group consisting of four experts (representatives from a large company and a small business and two technology transfer experts from nonprofit institutions).

Each member of the discussant group will present a case study. After each presentation, the other members of the discussant group will comment and offer perspectives or approaches. Following this, each case will be open for broader discussion by the Panel members. After each case study, the Co-Chairs will summarize the key points of the discussion.

10:30 - 10:45 a.m. *Case Study 1*—**The Case of the Clumping Platelets**
Who benefits from sponsored research agreements, and what are the benefits? What are the risks? What are the benefits and risks to the taxpayer, business, and funded institutions, and what are the multiple facets of public and private interests? What utilization and licensing issues are involved?

Presenter: Susan E. Cullen, Ph.D., Associate Vice Chancellor for Research and Professor of Molecular Microbiology, Washington University in St. Louis

10:45 - 11:20 a.m. Discussant Group Discussion and Questions from the Panel

11:20 - 11:30 a.m. Co-Chair Summary

11:30 - 11:45 a.m. *Case Study 2*—**The Case of the Sniffily Nose**
Should a distinction be made between U.S. and foreign companies? How do funded institutions find commercialization partners? What is the present nature of the biotechnology and pharmaceutical markets?

Presenter: Joshua A. Kalkstein, J.D., Senior Corporate Counsel-Research, Pfizer, Inc.

11:45 a.m. - 12:20 p.m. Discussant Group Discussion and Questions from the Panel

12:20 - 12:30 p.m. Co-Chair Summary

12:30 - 1:30 p.m. **LUNCH BREAK**

Session II:	**Case Studies—Continued**
1:30 - 1:45 p.m.	*Case Study 3*—**The Case of the Enzymatic Dilemma** What problems are associated with providing fair access, monitoring utilization, and promoting collaborations? *Presenter: Sandra Shotwell, Ph.D., Director of Technology Management, Oregon Health Sciences University*
1:45 - 2:20 p.m.	Discussant Group Discussion and Questions from the Panel
2:20 - 2:30 p.m.	Co-Chair Summary
2:30 - 2:45 p.m.	*Case Study 4*—**The Case of the Sleeping Giant** What issues arise in complying with the preference for small business? What is the impact of resource limitations of small business? What issues emerge related to free competition and free enterprise? *Presenter: Donald Drakeman, Ph.D., President and CEO, Medarex*
2:45 - 3:20 p.m.	Discussant Group Discussion and Questions from the Panel
3:20 - 3:30 p.m.	Co-Chair Summary
3:30 - 3:45 p.m.	**BREAK**
Session III:	**Discussion of Issues (Co-Chairs)—Objectives of the Bayh-Dole Act and historical perspectives; further analysis and discussion of the issues raised by the case studies. Are there additional considerations that must be taken into account?**
3:45 - 4:30 p.m.	*Issue 1*—**The Scope and Size of Sponsored Research Agreements (Balancing of Interests, Benefits, and Risks)** What factors must be considered when entering into sponsored research agreements with regard to the scope of rights that industrial partners acquire to federally funded research? What are the risks and benefits associated with project-specific agreements and larger scale or more loosely defined agreements?

4:30 - 4:40 p.m.	Public comments in response to Issue 1 (individual comments not to exceed 3 minutes)
4:40 - 5:25 p.m.	*Issue 2*—**The U.S. Manufacturing Requirement, Preference for U.S. Industry, and Foreign Access** What does the U.S. manufacturing requirement really mean? How should the Government ensure compliance? How has the formation of multinational corporations and the growth of global economies influenced U.S. pharmaceutical and biotechnology markets? What role should foreign and multinational firms play? Should participation by foreign firms be restricted or encouraged?
5:25 - 5:35 p.m.	Public comments in response to Issue 2 (individual comments not to exceed 3 minutes)
5:35 - 6:40 p.m.	**DINNER BREAK**
6:40 - 7:25 p.m.	*Issue 3*—**The Utilization and Licensing Requirements for Inventions Made With Federal Funding** How can the government best ensure that its inventions are being developed and used? What should grantee institutions require or expect from licensees? Should precise licensing terms be incorporated into the sponsored research agreement when an up-front license is granted, including benchmarks? Should there be limitations on the time an option is open?
7:25 - 7:35 p.m.	Public comments in response to Issue 3 (individual comments not to exceed 3 minutes)
7:35 - 8:20 p.m.	*Issue 4*—**The Preference for Small Business (Fair Access)** What is the most effective way for the Government and grantee institutions to ensure that small businesses are given adequate access and preference to research funded with Federal money? Is the preference for small business efficient?
8:20 - 8:30 p.m.	Public comments in response to Issue 4 (individual comments not to exceed 3 minutes)

ADJOURN

January 26

8:30 - 8:35 p.m.	Opening Remarks
Session III:	**Discussion of Issues—Continued**
8:35 - 9:25 a.m.	*Issue 5*—**Research Freedom** What should NIH's role be in ensuring that the core principles of research freedom are preserved? How much and what kind of control by the industrial partner is problematic? What consulting or publication restrictions are reasonable? How have grantee institutions addressed this issue?
9:25 - 9:35 a.m.	Public comments in response to Issue 5 (individual comments not to exceed 3 minutes)
9:35 - 9:45 a.m.	Summary of issues by Co-Chair
9:45 - 10:00 a.m.	**BREAK**
Session IV:	**Public Comment on Forum** (flexible time)
10:00 a.m. - 12:00 p.m.	
12:00 - 1:00 p.m.	**LUNCH BREAK**
Session V:	**Summary and Drafting of Recommendations**
1:00 - 4:00 p.m.	Panel Discussion

ADJOURN

Appendix B

Invited Speakers

Perspectives on Technology Transfer Since the Bayh-Dole Act

Invited Speakers

The following individuals presented the historical and legislative perspectives of technology transfer since the Bayh-Dole Act:

The Honorable David J. Barram
Deputy Secretary
U.S. Department of Commerce
Washington, DC

Daryl A. (Sandy) Chamblee, J.D.
Acting Deputy Director for Science Policy
and Technology Transfer
National Institutes of Health
Bethesda, MD

Alan Goldhammer, Ph.D.
Director of Technology Affairs
Biotechnology Industry Organization
Washington, DC

Ronald Lamont-Havers, M.D.
Deputy Director for General Affairs
Cutaneous Biology Research Center
Massachusetts General Hospital, East
Charlestown, MA

FORUM ON SPONSORED RESEARCH AGREEMENTS: PERSPECTIVES, OUTLOOK, AND POLICY DEVELOPMENT—THE GOVERNMENT PERSPECTIVE

Presentation by The Honorable David J. Barram
Deputy Secretary, U.S. Department of Commerce

Good morning, and thank you for having me here today.

You have a great topic for your conference—one I think is critical—and one I have my own perspective on. In my former life, I became glad that Bayh-Dole was on the books. But, frankly, I did not even realize it because we didn't want the Government to get near us.

Now, I go around telling my former colleagues that I am from the Government and I am here to help.

I really do believe that we are carrying through on candidate Bill Clinton's promise to make technology a centerpiece of his Administration. I had no idea how unbelievably backward—technologically—this town was. I actually thought I'd see much more smart use of productivity technology like e-mail; graphical, easy to use interfaces; even some CD-based data bases.

It isn't the case. The good news is that we can improve our own productivity. The bad news is that so few people even know what they are missing.

But, back to the policy issues.

Technology has always been with us and has always shaped our lives. When Fred Flintstone discovered fire and invented the wheel he changed the Bedrock neighborhood forever. He changed his relationship with Wilma and even had his kids thinking about new career directions because of the way technology impacted their lives.

Later on, Robert Fulton invented the steam engine and Eli Whitney gave us the cotton gin; Olds and Ford, the car. These and a number of other technology-created changes gave us a whole new way of thinking and ushered in and powered the industrial revolution.

Now, the chip and fiber optics have revolutionized how we process information, use it, and move it around.

Such technological advancement is nothing new. What has changed, and changed dramatically, is the rate at which technology evolves. Previously, such advances occurred in epochs, such as the Iron Age, and the Industrial Revolution. Those epochs occurred thousands or hundreds of years apart. The human species had time to assimilate and even make friends with change. Today,

new technologies' life spans are no longer measured in centuries or decades, but rather in years or even months.

The rate of change has increased beyond the point of psychological comprehension. While it has always been important to our lives, it now dominates our existence. The pace of technological advancement never stops for us to catch up. That's tough enough to deal with on an individual basis, but imagine what it means for such bureaucratic institutions as the Department of Commerce or the House Committee on Science and Technology where change is not always welcomed with open arms. And the technological juggernaut just keeps hurtling on ahead, building up speed all the time.

In the past 15 years we have been living through that transition, where technological advancement began to outpace our ability, or even our willingness, to deal with it. In 1994, we have arrived at a place in history where we have to reevaluate our whole attitude toward change.

I used to tell my two children that those who do not learn from history are doomed to repeat it. They would look at me, as children do, rolling their eyes, thinking, "There you go again, Dad." I have thought about that a lot, and they may have been more right than I wanted to admit. While I still value the lessons history has taught me, we must not let it dictate and dominate how we think about the present.

I watch MTV periodically. I don't love it, but I think we need to understand what it is doing and the impact it is having. I am appalled by the way it celebrates short attention spans. And I despise the fact that we get so much of our information from a medium as passive as television. But maybe there is something there that I don't really understand.

There is a lot of power in learning from images, the quickness and juxtaposition we see. I don't know, but I think we have to accept the pervasiveness of technology and how it changes the way we think about life.

Out natural instinct is to resist change and embrace the status quo, but progress, like time, stops for no one. Instead of trying to stifle it or slow it down, our task must be to master the skill of adapting quickly to our constantly changing world. That skill will never become obsolete.

One of the things we need to adapt to is a whole new way of thinking about industrial policy.

Many people in leadership roles over the past 12 years didn't want to hear about, let alone talk about, industrial policy. They have argued that the best thing government can do to help is stay out of the way. In some instances, and maybe in many instances,

that may well be true. But as I think back on those years—the strange battle we fought, it was an example of a square ideology trying to encase a round and slippery reality. Partly because of the time we are in, 1994, and partly because this Administration has a different attitude, we think we are taking a more realistic approach.

One of the Clinton Administration's top priorities is to strengthen the ability of U.S. companies to compete around the world. You know that, and I hope we've made that clear to everyone. A key part of that strategy is to foster cooperation between federally funded research institutions—for example, universities, contractor-operated labs—and U.S. industry to deploy and commercialize technology. Why? Because they do it best.

After WWII, the Federal Government operated from a de facto policy that said technology was important, but we'd do it and then maybe let industry have it.

The idea was that government technology would make its way to industry through trickle-down, spin-offs, and technology transfer after the fact.

Prior to the Bayh-Dole Act the Government made Federal technology available to anyone on a non-exclusive basis. While this may sound reasonable, it left little incentive for the private sector to invest in a technology for commercial application. Firms were unwilling to invest in technologies they didn't own. By the late 1970s the Federal Government had an inventory of 28,000 Government-owned patents, of which only three percent were licensed to private companies. Bayh-Dole gave us the chance to change all that.

The Bayh-Dole Act was a response to a new reality, that two relationships were merging. One is the relationship between developing technology and producing the products that technology lets you make. No longer can the lab engineer and the marketing manager act like they're from different worlds. Second, the relationship between private technology development and government technology development is getting stronger.

Beginning with the Bayh-Dole Act of 1980 and continuing throughout the decade, the Government enacted several pieces of legislation drastically revising its approach to the management of technologies created by its R&D investments. As a result, companies were allowed to secure the rights to technology they invented in the course of performing federally funded R&D. Perhaps as important, it authorized Federal labs to enter into cooperative research and development agreements with the private sector.

These policies encourage industry involvement in Federal research programs from the inception of the program. The result is a clearer picture of the commercial potential of any research program. Early industry involvement will help reduce the costly and time-consuming transfer gap when technology moves from the Federal lab to industry. It will also help to exert some "market-pull" on the system. A good, common sense idea.

The Bayh-Dole Act and related legislation are lessons in good government. Legislation in the field of technology should serve to spark creativity, not smother it. They are also good lessons in free market forces, where the unintended consequences of our work often overshadow that which we intended. We must be able to recognize those new opportunities and exploit their potential.

These new policies have begun to dissolve old antagonisms between industry and government. We have seen remarkable growth in the number of cooperative and development agreements between Federal labs and industry—from 34 in 1987 to approximately 1,600 in 1993.

We've made a lot of progress. We have more to do. We need to help industry become more aware of the benefits of working with government labs.

Let me conclude by saying that Bayh-Dole was a very important piece of legislation. Could they have foreseen all of its benefits? Probably not. But they did show some vision and the good sense to employ it.

The vision thing has always been important. You can't lead without it—else where would we think we were being led? Vision today is more important than ever before. Because the world around us changes so fast, we have to have a vision and keep updating that vision. Then we have to adapt to the changes in our vision and how we implement it. It requires us to dream and to believe that dreaming is important.

One of my favorite quotes is from Henry David Thoreau. He said: "If you have built castles in the air, your work need not be lost; that is where they should be. Now, put foundations under them."

Many of you have spent years building these castles. Now, we have the chance to put foundations under them. We have a great journey ahead of us, and I am looking forward to traveling this road with you.

TECHNOLOGY TRANSFER AND BIOTECHNOLOGY: THE IMPORTANCE OF THE PUBLIC/PRIVATE PARTNERSHIP

PRESENTATION BY ALAN GOLDHAMMER, Ph.D.
DIRECTOR OF TECHNICAL AFFAIRS,
BIOTECHNOLOGY INDUSTRY ORGANIZATION

TO THE NIH FORUM ON SPONSORED RESEARCH AGREEMENTS:
PERSPECTIVES, OUTLOOK AND POLICY DEVELOPMENT

JANUARY 25-26, 1994
BETHESDA, MARYLAND

In the early 1920s, the Du Pont Chemical Company was beginning to explore the emerging field of polymer chemistry. The company augmented its own internal research efforts by signing a consulting and research agreement with Julius Nieuwland, a chemistry professor at Notre Dame. In 1931, following a decade of research, neoprene the first commercially produced synthetic rubber was introduced into commerce.

This research partnership is important from two perspectives: the agreement between the company and the researcher and between the company and the university. The consultation agreement between Du Pont and Nieuwland was unusual because of his status as a Holy Cross father. Because of his vow of poverty, it was agreed that Du Pont would make a grant to the university library. As the research program continued, it became apparent that an arrangement had to be structured with the university to address any patents arising from Nieuwland's work. This was done and Notre Dame realized $2 million in royalties.

It is clear that both parties as well as our society benefitted from the transfer of technology. Notre Dame was compensated for important research conducted by a faculty member. Du Pont continued to increase its internal research efforts in polymer chemistry. Five years after the initial contact with Nieuwland, Wallace Carothers moved from Harvard to direct this emerging research program. The Du Pont developments spawned a multi-billion dollar polymer industry whose products have affected us all.

This early example of industry-sponsored research took place during an era markedly different from today. Government support for basic research was minimal. The infusion of large sums of money from the National Institutes of Health and the National Science Foundation did not come about until the post-World War II years. Industry and foundations provided the major source of funding for research. Despite these funding limitations, a remarkable research infrastructure was built up in the chemistry and engineering disciplines.

The increase in federal involvement during the past forty

years has created research universities of a magnitude that could not be imagined in the 1920s. The biomedical research enterprise, minuscule during that earlier time period, has become a major economic force. It is an understatement to say that the societal benefits of new developments in health care technology have been significant.

Even with this government largess, sponsored research continues. Companies will undertake to sponsor research under two conditions. The first is to get a window on an emerging technology that they may seek to utilize but have not had an ample time period to evaluate. Secondly, a company may sponsor research that is closely related to its own internal R&D efforts. Such sponsored research spans the range from an agreement with a single investigator or the form of an endowment to an entire department.

Before turning to the issues that are the subject of this forum, I would like to take a brief look at the transfer of technology its cyclical relationship to product development. Former Genentech Vice President Thomas Kiley presented this diagram at a meeting on this same topic ten years ago.

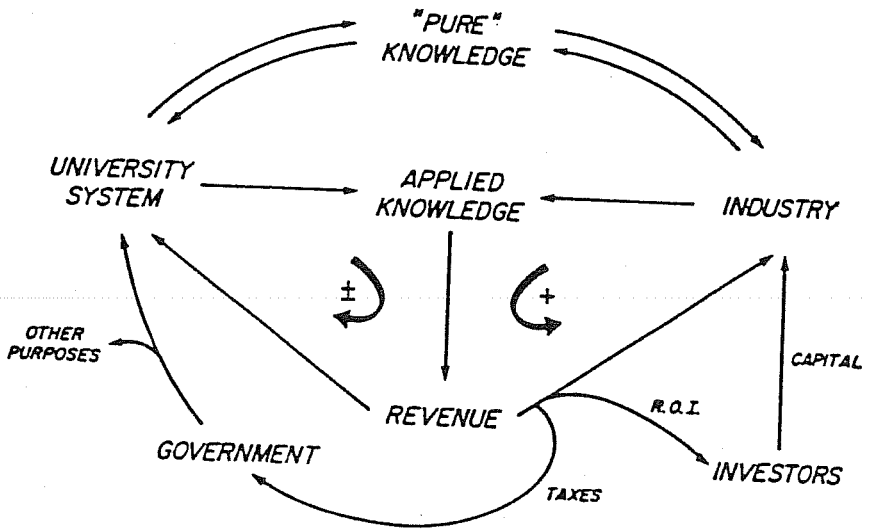


Figure 1

The key to economic development is the ability to convert "pure" knowledge to "applied" knowledge which can be translated into product development. "Pure" knowledge can be generated by both the public and private sectors.

Private sector research is first and foremost product driven. This is not to say that basic findings will not come out of such research; certainly the development of polymerase chain reaction technology that took place in the private sector is

having profound impacts in many areas of biological research. However, the absence of marketable products in the long run forces restructuring in large corporations and smaller companies out of business altogether.

The public sector's responsibilities are education, training, and the conduct of basic research. It is clear that many of the underpinnings of modern biotechnology came directly from basic research programs funded by the NIH. The directions that basic research will take science in the long run are unpredictable. Who could have understood the value of restriction enzymes, plasmids, or thermostable DNA polymerases when they were first discovered. Each man-hour of research conducted builds upon another in a cumulative fashion. Let me cite but one example. The chemical synthesis of useful genetic material is now automated and can be conducted in hours. Would we have this technology available today without the hundreds of man-years of research into nucleic acid chemistry that took place during the 1960s and early 1970s. Obviously, numerous other examples could be pointed to that are equally important.

Product development generates revenue that flows back to the parties in different ways. The private sector is absolutely dependent on revenue. If the investors do not get a return on investment the cycle will be broken as capital can no longer be raised. The government gets a return from the payment of individual and corporate income tax. This "return" is often neglected by those critical of technology transfer agreements.

Ultimately this cycle stimulates the economy if product development is successful. Jobs are created, increasing the revenue flows that fund research. Biomedical research leads to improved healthcare products. New tools to diagnose, treat, and prevent disease results in a healthier populace.

Commercial research and development is critical to the financial well being of the company. It is both inherently costly and risky. Regulatory compliance issues are markedly different across the industrial spectrum. A new microprocessor or memory chip can be brought to the market swiftly. The principal concern is meeting industry standards. Products coming from biomedical research routinely require regulatory approvals. These approvals vary with respect to cost and time needed to generate the supporting data.

A new antibody-based <u>in vitro</u> diagnostic test can be developed rather quickly. This is in contrast to the drug development process. It is lengthy with the costs for demonstrating safety and efficacy running into the hundreds of millions of dollars for each new successful product. We praise the development of new bio-pharmaceuticals such as TPA, erythropoietin, alpha-interferon, and the colony stimulating

factors G-CSF and GM-CSF. We cannot forget the projects that have not been successful such as tumor necrosis factor for cancer therapy and soluble CD-4 for AIDS. Unsuccessful products consume significant amounts of R&D monies.

The university need not be "directly" dependent on the revenue flow because it receives financial support from the government. Universities also receive support from the private sector in the form of unrestricted funds for graduate and post-doctoral fellowships. Surveying of our membership three years ago, we found the biotechnology industry spending over $12 million for unrestricted pre- and post-doctoral fellowships.

In recent years research consortia have been formed to bridge the public/private research interface and promote basic and applied research. Consortia may be composed of only industrial members or include a combination of university, industrial, and federal laboratories. The goal is to leverage financial and intellectual resources to further research goals. Research can be directed toward a particular end goal or to increase basic knowledge on a specific subject. One of the most successful has been the Semiconductor Research Cooperative (SRC). This group, made up of a large number of semiconductor manufacturers and end users, funds basic research at many universities. The Mid-West Plant Biotechnology Consortium is carrying out directed research in the plant biotechnology area. That consortium is made up of all three parties: industry, government, and university.

Key to any technological development is the ability to protect the intellectual property that comes from the research. The protestations of the past decade regarding the patentability of biological inventions has been puzzling. Patents do not guarantee an income, only the ownership of an invention. The worth of an invention is dependent on its marketability. Chakrabarty's oil eating microorganism, which triggered the court decision on the patentability of life forms, has generated more legal footnotes than revenue to the inventor.

Recent technology transfer legislation has encouraged agressive patenting of life science inventions by universities and the government. This is not particularly novel given past history in other sectors such as engineering and the physical sciences. It is our ultimate expectation that university research will be published and available to all. The patent system is the means by which intellectual property can be protected and its value enhanced. The private sector does have the option of protecting inventions as trade secrets, witness the formula for Coca-Cola. It is difficult if not impossible for public sector research to be protected in such a manner. Thus, whether the university sets up its own patent and licensing office or uses an already extant foundation for such purposes,

patenting of inventions should be something that society encourages.

The preceding discussion has established a framework for technology transfer and the importance of intellectual property protection. Both of these factors have heavily contributed to the establishment and growth of the biotechnology industry in the United States. Biotechnology is perhaps the best example of appropriate technology transfer from the public to private sector in the post World War II era. Even if one looks at the microelectronic revolution, many of the original developments took place in the private sector at places such as Bell Laboratories, Texas Instruments, and other semi-conductor companies. The astounding number of companies dedicated to commercializing federally funded biomedical research indicates that the federal research efforts have not been in vain.

It must be noted that the direct societal benefits tend to be slower in coming because of the regulatory requirements that new drugs and vaccines must meet. However, products are coming to the marketplace and it appears that during this decade that number will increase significantly.

It is not surprising that biotechnology companies located proximal to major research institutions. This is where the intellectual capital was located. Biomedical researchers were interested in seeing their expertise translated into practical results. Industrial research opportunities were suddenly increased for life scientists. With applications in pharmaceuticals, food, and agriculture, the new advances in molecular biology were quickly being commercialized.

The passage of the Bayh-Dole Act in 1980 gave research institutions title to the inventions developed from federal funding. This allows the institution to commercialize the research results through the granting of a license to a private company. The evolution of the biotechnology industry is shown in Figure 2. Prior to the enactment of this technology transfer law, 336 public and private biotechnology companies were founded. In the subsequent years, the number is 936; almost a three fold increase. This is not to say that Bayh-Dole is solely responsible for the large number of new companies established since 1980. Many business plans of emerging biotechnology companies point to technology that they have acquired from NIH-funded investigators.

NIH-funded researchers participated in the founding of biotechnology companies, served on scientific advisory boards, or were active consultants. Just as their predecessors in physical science and engineering departments, these biomedical researchers continued to run active research programs. Some have moved into management positions in the companies on a full time basis.

Figure 2 also shows some of the economic impacts of the emergence of the biotechnology industry. It is important to note that the sales are still modest relative to more mature industries such as pharmaceuticals and chemicals. Most analyses have pointed to continued dramatic product development and job growth in biotechnology through the remainder of this decade. Ashley Stevens of the Dana Farber Cancer Institute has also looked at the data from the perspective of one who is involved in technology transfer. His economic analysis attributes 53,000 of the jobs as directly related to academic technology transfer. Furthermore, these jobs have generated $1.8 billion in tax revenues to all levels of government. Certainly these data demonstrate that Bayh-Dole is having a positive effect on the establishment of a biotechnology industry.

Over the next two days the forum participants will discuss a number of issues, critical to the successful implementation of Bayh-Dole. There are likely to be no straight forward answers to the questions that have been posed in the distributed materials. NIH should be cautioned against the develop of overly stringent guidelines since they will ultimately work against the original Congressional intent of Bayh-Dole: "... to use the patent system to promote the utilization of inventions arising from federally supported research or development."

Overly stringent controls on agreements can adversely impact technology transfer agreements. Under the Federal Technology Transfer Act, commercialization of NIH intramural research can facilitated through Cooperative Research and Development Agreements (CRADAs). BIO has found that the CRADA process is undermined by the reluctance in some cases of NIH to grant exclusive patent rights and the inclusion of a "reasonable pricing" clause in the agreements. Earlier this year Congressman Wyden legislation that would extend reasonable pricing into Bayh-Dole agreements. Should this occur, technology transfer would be markedly inhibited.

Various commentators have criticized "foreign" access to U.S. technology. The issue must be examined in the context of global research into new technologies. We are operating in a global economy. Recent trade agreements are facilitating the sales of goods and services. Many U.S. based companies conduct research activities throughout the world. They have research agreements with universities in other countries as well as those in the United States. There have been numerous documented examples of emerging biotechnology companies entering into these types of agreements. Companies seek the best "intellectual" capital in accord with their business plans.

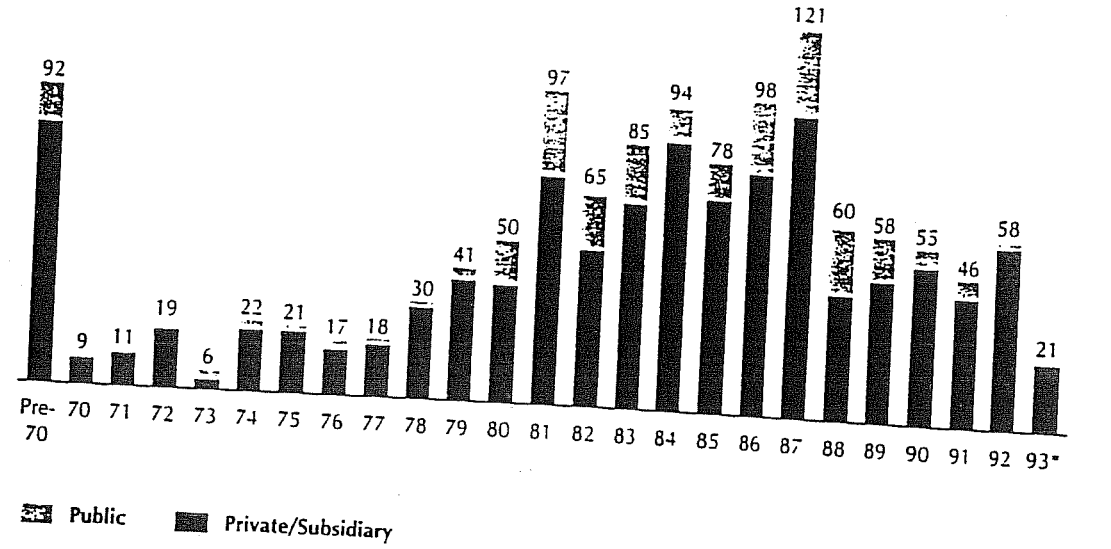
Many foreign-based companies have significant research and manufacturing operations in the U.S. These subsidiaries hire tens of thousands of U.S. citizens. They and their employees pay

U.S. taxes which ultimately go into the continued research and product development cycle shown earlier. It is clear that they have an important stake in the transfer of technology.

Researchers should have the ability to publish their research results. We are aware that agreements often have clauses allowing for review of results for the purposes of patent filing. These review times are of brief duration and do not inhibit the advancement of scientific knowledge.

NIH's own survey of sponsored research agreements showed that 375 conformed with all aspects of Bayh-Dole. The act was designed to make technology transfer more efficient. This end has been achieved. Today the United States enjoys the most vibrant and innovative biotechnology industry in the world.

Figure 2



SALES: $7 BILLION

R&D EXPENDITURES: $5.7 BILLION

NET INCOME: -$3.6

EMPLOYEES: 97,000

MARKET CAPITALIZATION: $45 BILLION

Data from Ernst & Young

Presented January 25, 1994

NIH FORUM ON SPONSORED RESEARCH AGREEMENTS
How Do Funded Institutions Balance
Core and Research Freedom Principles and Commercialization?

Ronald W. Lamont-Havers, M.D.

Many academic institutions and their research scientists become actively involved in conducting research sponsored and paid for by industry. Since this involvement in industry-sponsored research occurs frequently, and in order to reduce the opportunity for misunderstandings that may give rise to disputes, it is imperative that there must be a clear understanding of the involved academic issues and principles which are fundamental to the conduct of the institution's research programs regardless of the funding agency. This can only be achieved if these issues and principles have been considered and recognized by all levels of the institution's governance and faculty. One advantage of a change in the relationships of academia to its outside supporters of research is that it forces a reconsideration and rededication to the fundamental goals and principles governing the research community. This same introspection, by the way, occurred in the 50s when, in many quarters, the great influx of NIH funding engendered similar perceived threats to academic values that industry tends to do today. To those of us who remember the past, it is of great interest that the NIH support which had been accepted with so much suspicion has now become the standard of virtue.

My remarks today with regard to academic freedoms are based in large part on the introspection and concerns of my own institution over the past decade and a half in which we have learned from our unexpected mistakes and problems. As in the past the general cultural issues which govern those offering support and those receiving must be recognized. While there are clear differences between the goals and objectives of industrial sponsors and the research institution, these differences must be appreciated to avoid misunderstandings and unrealistic expectations.

These cultural issues can be synoptically summarized on the following slides:

Industry—Cultural Issues (slide)

- **Not philanthropic**
- **Specific expectations—even though seemingly vague**
- **Responsive to Stockholders/Board of Directors**
- **Concerned with protection of rights**
- **Accountability**

First, industry does not sponsor research in order to meet its philanthropic objectives which it achieves by other means. It provides institutions with funds solely for the purpose of meeting specific corporate needs, which the sponsor expects and the academic institution through its scientists agrees to fulfill.

Second, the agreement that describes the relationship between the parties frequently fails to fully describe the research expectations. Other items are carefully negotiated, but when the research objectives are discussed, they often are left vague and uncertain. This is particularly true in large, broad agreements. The sponsor usually has a clear understanding of its expectations—the academic institution and its scientists often either do not fully appreciate the sponsor's goals and expectations, or choose a variant interpretation.

Third, the corporate sponsor has different pressures than the research institution. The sponsor needs to provide its investors with a return on their investment; it also has a fiduciary duty to those investors to refrain from wasting corporate assets. The sponsor is not engaging in research to benefit the academic institution. It is in its best interest, though, to enter into and maintain a fair arrangement.

Fourth, corporate sponsors are very concerned with the ownership of any intellectual property resulting from the research. This is of paramount importance to the sponsor, so much so that it will not proceed without a clear statement as to the ownership of any intellectual property and its access to it.

Most research sponsors, including government, industry, or foundations, also require the institution and its scientists to account for and defend the methods and approach used in carrying out the sponsored project. Sponsors may have different ideas of what constitutes accountability—they all are interested, though, in the methods utilized and the progress and results of the sponsored research.

Academia—Cultural Issues (slide)

- **Self-interest in preserving academic norms**
- **Expectations may be specific though vague but tend to wander**
- **Concerned more with the excitement of science than the protection of rights**
- **Oversight is general**
- **Chatty**

The academic institution and its investigators are foremost concerned in preserving academic norms. More so than before, most investigators are also concerned with being allowed to continue to pursue their research and professional objectives. With the considerable pressures at present being brought to bear on the

academic research scientist, it is not surprising that their interest is heightened in protecting themselves.

The expectations of academic scientists, though, are typically vague, tend to wander, and their research efforts are not easily directed. Academic professionals are often more concerned with the excitement of science, for example, rather than carrying through research to the prototype stage, or in assisting patent counsel in pursuing patent protection for an invention. As a result, research administrators are often required to make up for these defects, expending considerable effort in trying to protect the institution's intellectual property rights, while the scientist is busily working on the next project.

This attempt to protect inventions also runs afoul of the scientist's willingness to share information, and to teach about their discoveries. Most industrial scientists do not have this problem, and usually are well schooled in avoiding the sharing of secrets that impact the company's well being. With time and a realization of self-interest, however, academic scientists are willing to comply with restraints related to submission of patent applications.

Academic Goals and Principles (slide)

The fundamental institutional goals and principles as they apply to research must be clearly articulated in documents available to overseers, faculty, administrators, and sponsors. These should include:

1. The Purpose of Research

One result of the reexamination of the goals is to rearticulate the institutional research objectives although these objectives may be broad and flexible. It may be as simplistic as "the institution will conduct and support meritorious research on life processes and function." Nonetheless, such definitions are useful in defining the role, nature, and scope of projects which will be pursued.

2. Academic Freedom

A. to choose the field of research;
B. to collaborate;
C. to communicate; and
D. to determine governance and academic structure.

Academic freedom is essential to a vibrant academic research environment. These freedoms have limits, comprised mostly of practical exigencies. A cornerstone of the philosophy of academic freedom is a commitment to the preservation of its concept. The essential elements of academic freedom which should be preserved include:

A. Freedom to choose the field of research

The investigator should have the freedom of choice in the areas of study and should be free to seek appropriate sources of funding.

B. Freedom to communicate

Exchange of information between scientists either verbally or written is essential for the learning process, for critical evaluation, and for accelerated scientific progress. Freedom of access to laboratories and research personnel is closely related to the need for free communication and should be maintained. Confidentiality restrictions which have been entered into by the investigator must take this freedom into account. This is usually not a substantive problem so long as the intellectual property rights of discoveries have been first protected through a patent application.

C. Freedom to collaborate

Full opportunity to collaborate is a necessary component of academic freedom and the basis of collegial groupings of scholars in a university, hospital, or other nonprofit institution.

D. Freedom to determine governance and academic structure

The administrative organization of an academic institution should be geared principally to academic goals, the search for new knowledge, and the training of students and younger scholars. Academic officers and faculty have, as a prime mission, responsibility for teaching, scholarly activities, guidance, and inspiration. These features usually do not impact the industrial relationship.

3. Disposition of the Results of Research

Because the institution is accountable for the documentation and products of research conducted using its resources, the disposition of the documentation and products is its responsibility.

Institutional Research Policies and Responsibility for Research

There should also be clear generally accepted guidelines governing the institution's research programs.

1. The scientific documentation of all research is the property of the institution.

Laboratory manuals and supporting data are the property of the research institution, and the investigator does not have the

right to determine their disposition. While this restriction may seem to interfere with the scientist's professional freedoms, it is, in fact, essential to maintain the integrity of the research center. The research institution bears ultimate responsibility for meeting the requirements of the research agreement regardless of the sponsor.

2. The laboratory chief, immediate supervisor, and all collaborators must have free access to review all data and products of an investigator's research.
In order to maintain scientific integrity, an investigator has an obligation to provide free access to all data and products of the research to the laboratory director, the immediate supervisor, and all collaborators.

3. All primary data should be promptly recorded in clear, adequate, original, and permanent form which should not leave the laboratory or clinical unit at any time. These records must be kept for at least a period to be determined by the institution.
It is important for the data describing a discovery to be properly prepared, to allow the research results to be repeated, and to leave clear records that indicate that a discovery was made at a given time in the laboratory. This is important among other things, if later the data is needed to support patent prosecution, or to defend against an infringement or other suit. This requirement may not be enthusiastically received by investigators until they recognize the need for the data in the patent prosecution process, which later may give rise to some monetary benefit to them.

4. Material products—cell lines, bacterial clones, other specific organisms and substances, or software developed and prepared during the course of research, are the property of the institution. The individual investigator does not have the right to make any disposition without institutional authorization.
As with research documentation the individual investigator does not have the right to make any disposition of material products contrary to institutional policy. This is generally recognized at the present time and will be commented upon later.

5. The laboratory chief has primary responsibility for decisions regarding publications, authorship, and the substance of grant or contract applications. All authors of any publication are expected to share in the responsibility for its scientific content, including its reliability.
There is considerable discussion, and a number of well-publicized examples, where scientists are unwilling to take responsibility for improperly conducted research that is published with their names on the article. In many institutions, the lab chief has primary responsibility for decisions regarding publication of research results. Also, all authors on publications are expected to share in the responsibilities for scientific accuracy, and will bear the burden of any associated misconduct.

6. Free and open discussion of all research activities within the laboratory should be encouraged. Frequent critical review of ongoing projects by all participants as well as informal review by uninvolved colleagues of active work, manuscripts, and projected studies are important in setting the tone for critical self evaluation. Restrictions on free and open dissemination of the results of research activities by outside sponsors of research cannot be accepted without the approval of the institution.

This research policy is designed to enhance the quality of the research conducted at the institution. With this in mind, though, the academic scientist can, without undue burden, delay disseminating the research data to allow the filing of a patent application or, more frequently, to protect his/her own inherent interests. This policy was, at one time, considered more onerous to industry than it is at present. I should quickly add that, as has been pointed out to me, the phrase "without approval of the institution" is capable of being misinterpreted. For all intents and purposes it is not applicable—unfortunately I did not have the opportunity to redo the slide.

Obligations of Investigators Under Sponsored Research (Slide)

When accepting industry sponsored research the investigator and the institution undertake obligations to the research sponsor. These obligations reflect the valid interest of the sponsors, foster academic freedom, and protect the rights of all parties, including the investigator's.

These obligations are in four areas:

A. Publications and Oral Presentations

1. Intent to publish or present;
2. Submission of manuscript or plan of presentation;
3. Submission of a draft of an abstract.

Notice of oral presentations and proposed publications that describe research results should be disclosed in advance and in a timely manner to the industrial sponsor, allowing for the sponsor to determine whether there is any material in the presentation or publication which could be patented prior to the disclosure, or where applicable privileged information has been disclosed. At present investigators usually see such review as being in their own best interest. The time limits during which such reviews must occur prevent abuse of this privilege. Prevention of submission of publication or presentation is not allowed except in exceptional circumstances.

B. Biological Materials

1. Agreement from other institutions;
2. Agreements when providing material to investigators outside the project; and
3. Agreements when obtaining material from or sending to the sponsor.

Biological materials, such as cell lines, bacterial clones, other specific organisms and substances that are prepared during the course of research, are the property of the institution, and cannot be sent to other parties without an agreement in place that governs disposition of ownership interests.

While material is freely provided for academic research purposes, restrictions are placed on the use which will involve rights for commercial use. While this indeed may be an annoying impediment to the free flow of research, resolution about ownership, prior to the creation of potential problems, is necessary. While this is not optimal, at least a degree of clarity is being brought to an otherwise unclear situation.

C. Outside Funding

Apart from Federal Agencies, all other sources must be cleared by the institution. In general, most noncorporate sources are acceptable.

Other funding to individuals who are also receiving industrial support for the same project can create serious problems. In general, apart from the Federal Agencies, all other funding sources must be cleared by the institution. Other noncorporate sources, such as foundations, may have restrictive policies with respect to patent rights. These policies must therefore be reviewed either at the time of the grant application or they need to be negotiated with the funding source at the time of a patent application.

D. Confidentiality

Agreement when sponsor's confidential information is transmitted to the investigator.

Institutional response to this issue varies. It is our experience that the institution cannot assume responsibility for any confidential material or information which the sponsor provides to an investigator. It may be essential that the investigator have such confidential information, but the institution cannot guarantee confidentiality. Therefore, any such agreement has to be between the investigator and the company or sponsor, not the institution.

Additional Considerations (slide)

Consulting Agreements

Consulting agreements are between the investigator and an industrial concern. The academic institution, however, must be assured that its own intellectual property and other resources

are not being exploited and that the obligations of the investigator under any institutional/industrial agreement is not being abrogated. To accomplish this, a clearly defined institutional consulting policy must have been promulgated.

Elements To Assure Protection of Academic Freedom

- Statement of Academic Goals and Principles
- Statement on Responsibility for Research
- Institutional Policy on Patents and Intellectual Property
- Institutional Policy on Consulting Agreements
- Policy on Potential Conflicts of Interest
- Material Transfer Guidelines and Policy
- Oversight Mechanism With Authority To Review Industrial Agreements, Intellectual Property Issues and Related Concerns of Conflict of Interest
- A well-staffed and knowledgeable Office for Technology Transfer Affairs, under whatever rubric.

By the adherence to these elements and the recognition that there is no such thing as a secret agreement, the academic community has found that the Bayh-Dole Act and its amendments have been an effective instrument to encourage academic/industrial relationships.

FORUM ON SPONSORED RESEARCH AGREEMENTS: PERSPECTIVES, OUTLOOK, AND POLICY DEVELOPMENT—THE NIH'S PERSPECTIVE

Presentation by Sandy Chamblee, J.D.
Acting Deputy Director for Science Policy
and Technology Transfer

Good morning. I am here today to present the NIH's perspective on academic or university/industry interactions—specifically, our perspectives on sponsored research agreements. As you know, this topic is of tremendous interest to the NIH, its grantee institutions, and Congress.

As Dr. Varmus has said, this meeting is part of NIH's efforts to develop some guiding principles to assist grantee institutions in their dealings with industry. This task is complicated by the enormous variety of academic/industry relationships; the multinational and multifaceted nature of the biotechnology and pharmaceutical industries; the shrinking availability of Federal research funding; and concerns about conflicts of interest.

Academic/industry interactions take many forms, including industrial liaison programs, spinoff companies, commercial licensing, and consulting. In the wake of the Scripps-Sandoz controversy, however, the NIH has focused its attention on what we refer to as sponsored research agreements, as distinguished from other types of interactions or methods of commercializing research.

In order to develop responsible public policy in this area, the NIH formed an internal Task Force on the Commercialization of Intellectual Property Rights from NIH-supported Extramural Research. This Task Force analyzed 375 sponsored research agreements within the legal framework of the Bayh-Dole Act and held a number of informal roundtable discussions with other government organizations, grantee institutions, and industry. The information derived from these informal meetings and from the analysis of the sponsored research agreements, together with the input and recommendations we receive over the next two days will form the basis for the policy guidelines that are tentatively scheduled to be completed by next summer.

Today, I will focus on questions arising from the Scripps/Sandoz agreement and the more striking results from our review of the 375 agreements, highlighting a few of the issues that we think are critical in providing guidance in this area.

Background

As many of you know, the Scripps Research Institute announced last winter a proposed $300 million sponsored research agreement with Sandoz Pharmaceutical Co., a U.S. subsidiary of Sandoz Ltd.

of Switzerland. The agreement purported to give Sandoz first rights to license virtually all inventions made at Scripps for up to 20 years. The overwhelming breadth of the proposed agreement raised concerns in Congress and at the NIH that this agreement and possibly others like it could violate the letter and spirit of the Bayh-Dole Act. Initial discussions were dominated by concerns about U.S. competitiveness, fair access to federally funded technology by small U.S. businesses, and potential conflicts of interest. A further concern was that such agreements might infringe on academic freedom or unduly restrict the dissemination of research results.

When the Scripps-Sandoz story broke, Congressman Wyden, Chair of the House Small Business Subcommittee on Regulation, Business Opportunities, and Technology asked the NIH why it did not know about this agreement and, now that it did know, what was the NIH going to do about the agreement?

At the time, the NIH had no knowledge about the agreement beyond what had been announced by Scripps. We certainly had no legal obligation to review such agreements and, absent any formal request by the NIH, Scripps had no legal obligation to submit their agreement for review.

Although the breadth and magnitude of the Scripps-Sandoz agreement seemed unusual, we really had no way of knowing just how unusual the proposed agreement was in relation to others. Therefore, we requested copies of sponsored research agreements like the one between Scripps and Sandoz from our top 100 grantee institutions. We ultimately collected and reviewed a total of 375 sponsored research agreements, only 44 of which we considered to be large-scale agreements. At the same time, we carefully reviewed the Scripps-Sandoz agreement for compliance with the Bayh-Dole Act.

To gain additional insight into the issues surrounding sponsored research agreements, we held two ad hoc meetings with representatives of industry and grantee institutions. From these meetings, we learned that the overall consensus in the research community is that the current statutory framework for technology transfer has been effective in encouraging academic-industry interaction, and that the Scripps-Sandoz arrangement is an aberration that is unlikely to be duplicated.

The participants at these meetings stressed that rigid or elaborate Federal regulation of sponsored research agreements could prove unwieldy and perhaps disastrous to often fragile academic/industry relationships. However, because varying levels of experience in university technology transfer offices and ambiguities in the Bayh-Dole Act have caused increasing anxiety about compliance in the university community, the participants agreed that guidance from the NIH would be helpful.

We also held a meeting with representatives from other Federal agencies, including the Departments of Commerce, Energy, Defense, and Agriculture, the National Science Foundation, the Advanced Research Projects Agency, and the Internal Revenue Service (IRS). Much of the discussion at this meeting involved the degree and kind of oversight that Federal agencies currently exercise or should exercise over interactions between grantee institutions and industry.

Perhaps most striking was the perspective of the IRS, which held that, in extreme cases, sponsored research agreements could lead to the loss of an organization's tax-exempt status. There is no "bright line" where that status can be said to change, and many factors would need to be analyzed before making such a decision, but agency officials noted that the focus would be on the degree of control that the tax-exempt organization cedes to its industrial partner.

In addition to the revocation of an organization's tax exempt status, other seldom-used sanctions such as march-in rights and exceptional circumstances determinations were discussed. March-in rights can be employed if grantee institutions fail to meet utilization requirements under the Bayh-Dole Act. March-in rights allow a funding agency to either force its grantee to license federally funded technology to another party, or in extreme cases, the agency may license the under-utilized technology itself. The current regulatory framework makes march-in rights extremely difficult to use however, and although threatened, they have rarely if ever been used.

Exceptional circumstances determinations allow a funding agency to restrict the rights that a grantee receives to inventions made under future funding agreements. Again, this is a cumbersome mechanism.

Most agencies have found the U.S. manufacturing requirement of Bayh-Dole to be ambiguous. However, the Department of Energy has implemented an innovative and arguably more flexible policy that considers other economic benefits, such as job creation, when determining compliance with the U.S. manufacturing requirement. As reflected in our meeting, agency representatives seemed to prefer improving the dissemination of information and educating the research community, rather than imposing stringent rules. Agency officials also agreed that the great diversity of agreements being formulated and the differences across agencies make it difficult to describe a single set of universal standards.

Results of Review of Sponsored Research Agreements, Bayh-Dole Objectives, and Issues

I would like to turn now to NIH's review of 375 sponsored research agreements in the context of the policies and objectives of the Bayh-Dole Act.

In general, our review confirms that, for the most part, the Bayh-Dole Act is working well. According to Dr. Healy's June 17 testimony before Congressman Wyden's committee, the Scripps-Sandoz Agreement is an anomaly in many respects because, "it deviates from many of the principles of the Bayh-Dole Act and also impinges on the freedom of scientific inquiry." The results of NIH's review tend to support Dr. Healy's statement.

In essence, the Bayh-Dole Act allows our grantee institutions to obtain title to inventions made under NIH funding agreements, such as contracts or grants. The central policies and objectives of the Act are to:

- Promote free competition and enterprise;
- Encourage maximum participation of small business firms;
- Stimulate U.S. industry;
- Promote utilization;
- Protect government rights;
- Promote collaborations between industry and nonprofit organizations; and
- Minimize administrative costs.

"Academic research freedom" is conceptually a bit more abstract and not statutorily defined. However, sociologist Robert Merton has identified four commonly accepted norms that seem to guide the behavior of research scientists:

1. Universalism;
2. Communism;
3. Disinterestedness; and
4. Organized skepticism.

As described by Professor Rebecca Eisenberg of the University of Michigan, "'universalism' means that the truth of claimed observations should be determined based on impersonal criteria without regard to the *identity* of the scientist who makes the observation. . . 'Communism' means that scientific findings are a product of *social collaboration* and should be available to the scientific community. . . 'Disinterestedness' means that scientists should seek *truth* rather than seeking to further their own interests . . . [and] 'Organized skepticism' means that the scientific community should subject the claims and beliefs of its members to empirical scrutiny before accepting them as true." Unreasonable restrictions on the dissemination of research results, collaboration with other scientists, or consulting are inconsistent with these widely accepted norms. So too is undue

control by the industrial partner over the research mission and direction of the research institution.

Let me now share with you some of the highlights from our review as they relate to the objectives of the Bayh-Dole Act. While our main objective was to collect and review agreements comparable in size and scope to the proposed Scripps-Sandoz agreement, we also received a sampling of smaller-scale or project-specific agreements which we decided to review as well.

Free Competition and Enterprise—Size and Scope

As just noted, a key objective of the Bayh-Dole Act is to promote free competition. Therefore, the *scope* of a sponsored research agreement—the potential extent of the industrial partner's right to the research of a grantee institution—was one of the first criteria on which we judged the sponsored research agreements, as well as the closely related criteria—duration and amount of industrial support.

Of the 375 agreements we reviewed, approximately 331 or 88 percent were smaller agreements or what we called "project-specific" agreements—that is, agreements limited in scope to a particular project, restricted research field, or the work of two or less scientists. Forty-four or 12 percent of the agreements were "large" agreements—that is, agreements covering the intellectual output of an entire institution, or major components of an institution, such as departments, centers, and large laboratories. We were concerned that these agreements would reflect some of the problems of the Scripps-Sandoz agreement. However, the vast majority of these 44 large agreements restricted the industrial partner's intellectual property rights to particular research projects or to discrete fields of research.

We also found that approximately 72 percent of all the agreements were for three years or less, and that 85 percent of all the agreements were for 5 years or less. In terms of funding, about half of the agreements were for $150,000 or less, and less than 2 percent of the agreements were for more than $5,000,000. Roughly 95 percent of the project-specific agreements were for $1,000,000 or less. At $300 million, the proposed Scripps-Sandoz agreement was almost three times the size of the second largest agreement.

Preference for Small Business—Fair Access

Another important objective of the Bayh-Dole Act is to "encourage maximum participation of small businesses in federally supported research." The Act requires that, "except where infeasible, the licensing of subject inventions shall be given to small businesses."

Although sponsored research agreements by definition are not licensing agreements, in most cases licensing rights are promised in advance to the sponsoring company. Therefore, this preference for small business should be considered by grantee institutions when negotiating sponsored research agreements.

We estimate that approximately 167 or 45 percent of the sponsored research agreements we reviewed were with small businesses.

U.S. Manufacturing—Preference for U.S. Industry

The Bayh-Dole Act also requires that grantee institutions shall not "grant to any person the exclusive right to use or sell any subject inventions in the United States unless such person agrees that any products embodying the subject invention will be manufactured substantially in the United States." A waiver of this requirement can be obtained from the funding agency. Again, this requirement applies only to exclusive licensing arrangements made by grantee institutions, once something has been invented. However, a grantee institution should also consider this requirement when negotiating a sponsored research agreement.

Although inconclusive, one indication of whether a grantee might have considered this requirement in its negotiation is the nationality of its industrial partner or where the entity is incorporated.

Approximately 13 percent of the agreements reviewed were with entities incorporated outside the United States, whether or not they had U.S. subsidiaries. The other 87 percent of the agreements were with "domestic" companies, which includes U.S. subsidiaries of foreign companies. Several of the agreements mentioned the possibility of obtaining a waiver of the U.S. manufacturing requirement from the Federal Government, but the proposed Scripps-Sandoz agreement had a clause that appeared to require a much higher level of advocacy by the grantee institution.

Utilization and Availability—Protecting Government's Rights

Another objective of the Bayh-Dole Act is to promote utilization and availability of federally funded inventions and to ensure that the Government obtains sufficient rights in inventions to meet the needs of government and to protect the public against nonuse or unreasonable use of inventions. Unusual influence, control, monitoring, and approval by an industrial partner over the NIH grantee could also interfere with the Government's rights and its ability to protect the public against nonuse or unreasonable use.

Not only did the Scripps-Sandoz agreement require the institution to advocate a waiver of the U.S. manufacturing clause on behalf of its industrial partner, it was the only agreement giving the

industrial partner seats on the institution's board of directors; giving the industrial partner the right to review invention disclosure reports before they were submitted to the NIH; and giving the industrial partner the right to remove a research project from a grantee's laboratory prior to completion and transfer the project to its own facilities anywhere in the world.

Research Freedom

The NIH's last general area of concern was whether the proposed Scripps-Sandoz agreement and others like it might unduly restrict scientific freedom and the dissemination of research results. We found again that the Scripps-Sandoz agreement was unusual in this respect because it was more restrictive overall than the other agreements in the review. Generally, we found that grantee institutions seemed to be as concerned as the NIH about research freedom and dissemination of research results. For the most part we did not find unreasonable restrictions, publication delays, or constraints on university researchers from consulting or collaborating with other parties. Furthermore, the vast majority of the agreements did not provide for the kind of pervasive control over the research mission and direction, as did the proposed Scripps-Sandoz Agreement.

Some Conclusions

Through this review and analysis, the NIH has gained a better understanding of the enormous diversity of sponsored research agreements and a better appreciation for their complexity and uniqueness. We have also identified certain issues requiring agency clarification so that the interactions that our grantee institutions have with industry will continue to be productive.

Clearly, as we have heard from Drs. Goldhammer and Lamont-Havers, there are advantages to both industry and universities of entering into sponsored research agreements. However, there are also risks. Generally, grantee institutions should be concerned if a sponsored research agreement has any of the following characteristics:

- Unreasonably *decreases or delays* the dissemination of research findings;
- *Sacrifices control* over research direction/mission;
- Creates situations where grantee institutions are *overly* financially *dependent* on a company;
- *Jeopardizes* the institution's tax-exempt status;
- *Generally overreaches*;
- Results in *conflicts of interest* or conflicts of commitments;
- *Overly restricts* researchers and post-docs in their ability to share ideas and scientific information with others;
- *Adversely affects* or *compromises* the research environment at the institution; or
- *Violates the Bayh-Dole Act* in fact or in principle.

There are no cookie-cutter agreements, nor should there be. The organizations and situations involved in sponsored research agreements are often unique, requiring delicate balancing of risks and benefits by the parties involved. In our review of sponsored research agreements, we found that although certain factors weigh more heavily than others, no one factor or provision caused grave concern. Rather, the juxtaposition of multiple problematic factors or clauses in an agreement sometimes tipped the scale in favor of the interests of an industrial partner, at the expense of the research institution or public, thus upsetting an otherwise fine balance.

In general, the NIH has found no marked trend per se towards the large-scale or megadeals. On the contrary, we found that smaller-scale or project-specific agreements tended to be less problematic than some of the larger-scale agreements, mostly because the access to federally funded research was limited and the industrial partner did not gain any unusual or undue control over the research institutions or their researchers.

However, as we have heard, there does seem to be a policy void in this area. Important questions remain unanswered, questions that will be the focus of the remainder of this meeting. In a dynamic, multifaceted, multinational marketplace, if the United States is to remain a world leader in technological and scientific innovation, the public and private sectors must work together to find answers to these questions, to identify new means, within the confines of the law, to foster rapid development and commercialization of useful products, and to encourage U.S. industrial and small business growth, while at the same time protecting taxpayers' investment and safeguarding the principles of scientific integrity and academic freedom.

Note: Dacia Clayton, Esq. (OGC/NIH) presented this information at the University of Washington's University-Industry Collaboration Symposium on October 26, 1993.

Appendix C

Discussants

Case Studies

Discussants

The following individuals presented short, fictional case studies, which were based on existing sponsored research agreements and illustrated important issues of concern under the Bayh-Dole Act:

Susan E. Cullen, Ph.D.
Associate Vice Chancellor for Research
Professor of Molecular Microbiology
Washington University in St. Louis
St. Louis, MO

Donald Drakeman, Ph.D.
President and CEO
Medarex
Princeton, NJ

Joshua A. Kalkstein, Esq.
Senior Corporate Counsel—Research
Legal Division
Pfizer, Inc.
Groton, CT

Sandra Shotwell, Ph.D.
Director, Technology Management
Oregon Health Sciences University
Portland, OR

Case Study 1

INDUSTRIAL SUPPORT OF RESEARCH IN UNIVERSITIES: RISKS AND BENEFITS TO THE UNIVERSITY, BUSINESS AND THE TAXPAYER

The Case of the Clumping Platelets

Primary Reviewer: Dr. Susan E. Cullen, Associate Vice Chancellor for Research and Professor of Molecular Microbiology, Washington University in St. Louis

Concerned over chronic unemployment and the erosion of its industrial base, the government of a midwestern state has created a **Biomedical Industrial Development Authority (BIDA).** The **BIDA** has seed money from the state, but is funded principally by contributions of $50,000 from each of 30 local and national biomedical companies. The major purpose of the fund is to promote academic-industrial cooperation that will result in the transfer of biomedical technologies from the universities to companies, thus creating new economic opportunities for residents of the state. The **BIDA** can make small grants to universities to support particular projects for short periods of time. However, the expectation is that one of the 30 companies sponsoring the work will pick up and support research that has genuine commercial promise.

Professor Guy L. Less (known to his students as Professor G) at the Missagain State University has been working for a decade on the mechanism by which platelets are activated to clump together and begin the process of clotting in blood vessels. His work and that of his lab have been supported by multiple grants—totalling many millions of dollars—from the National Heart, Lung and Blood Institute (NHLBI) of the National Institutes of Health. Over the years, Professor G has discovered several enzymes that seem to play a role in modulating the activity of intermediaries in the platelet activation process. Until recently, he has never filed invention disclosures with the university research office, since he was unaware that any of his work was patentable.

His practice has been to publish his research results promptly, and not worry about the commercial consequences. In the last three years, however, Missagain State has created an Office of Technology Affairs (OTA) with the purpose of promoting the commercialization of research findings. The head of the office has visited with Professor G, and urged him to disclose any potentially valuable findings to the OTA, so that patent applications can be filed. The director of the OTA has told Professor G that a researcher has an obligation to do everything he can to promote the use of his federally funded research results, and commercialization of his findings is the surest way to accomplish this goal. It may also provide Professor G with

some additional funding from industrial sources to support his lab.

Since he has always done well in the peer review process, Professor G wasn't initially very interested in such support, bu he does feel an obligation to help with the application of his laboratory's findings. As a result, he has filed several invention disclosures with the Office of Technology Affairs. Tw of these are for substances that inhibit enzymes that promote th activation process and one is for a core research tool.

Then, to his great surprise, Professor G finds that one of his major grants comes in just below the payline for the NHLBI. This creates a short-term funding crisis in his lab, and Professor G, desperate for help, consults the OTA. In response, the OTA puts Professor G in touch with **BIDA**. **BIDA** invites Professor G to make a presentation to its Science Advisory Board, which represents the research directors of the companies supporting the Authority. As a precaution, the OTA files patent applications on Professor G's recent disclosures in order to protect any intellectual property that may be revealed during consultations with **BIDA**.

During the presentation to **BIDA**, the research director of Xpectsalot, Inc. notes the relevance of Professor G's investigation to a line of work they are pursuing. Located in close proximity to Missagain State, Xpectsalot is a mid-sized, privately-held, biotechnology company that has been trying to find an inhibitor of platelet activation that can be used to guard against reocclusion of coronary arteries after angioplasty. The Company's scientists have identified one of the enzymes that Professor G found, but not the inhibitors he has been working with. At the urging of Xpectsalot, **BIDA** makes a one-year grant to Professor G to tide him over while he reapplies for funding. Xpectsalot then approaches Professor G independently about working together to explore the mechanism of action, potency, toxicity, and potential efficacy of his inhibitors. They are also interested in any other work he may be doing that could be relevant to platelet activation.

With the help of the OTA, Missagain State negotiates a research and licensing agreement (the "Agreement") which grants Xpectsalot an exclusive license to the inhibitors and research tool for which Missagain State has filed patent applications and to "any other intellectual property concerning inhibition of platelet activation that may result from work done in Professor G's laboratory." No geographic or specific fields of use are specified. In return, Xpectsalot agrees to provide Missagain State U with $200,000 a year for three years to support work on platelet activation and inhibition, with five one year options to renew the research component of the Agreement at the Company's discretion. The Agreement also establishes a five member Joint Scientific Review Counsel controlled by Xpectsalot, to select additional projects to be funded and review Professor G's work

under the Agreement. Under the Agreement, Professor G cannot consult or collaborate with other nonacademic third parties and must obtain the Company's written permission to collaborate with other academic parties. The Agreement further requires Professor G and anyone working under or with Professor G, including graduate students and post docs, to sign the Company's standard confidentiality or nondisclosure agreement and to send all proposed publications to Xpectsalot for approval prior to publication.

Although not formally part of the Agreement, in the spirit of the collaboration, Professor G routinely allows scientists sent over from Xpectsalot to serve mini-fellowships in his lab and makes regular presentations of his lab's work to Xpectsalot's scientific staff. In return, the research director of Xpectsalot provides Professor G and his students with liberal access to Xpectsalot's computer modeling expertise.

Several additional patent applications result from Professor G's work which are considered to be under the original research and license Agreement. Although it was not a part of the original Agreement, Xpectsalot agrees to pay the patent costs as long as it gets full control over the prosecution.

As time goes on, Professor G's relationship with Xpectsalot blossoms. He derives more than three-quarters of his support from this industrial source (Professor G continues to receive a small grant from NHLBI). Under nondisclosure agreements, Xpectsalot has shared considerable proprietary information with Professor G and other individuals in his lab, including graduate students. Upon the direction of the Joint Scientific Review Counsel, Professor G becomes more and more involved in the isolation of other inhibitors and their testing for safety and toxicity in animals. He consults to Xpectsalot and sits on their science advisory board. Several of his graduate students go to work for Xpectsalot, but one who wants to work for another biotech company is limited in his employment choice because of the confidentiality agreement with Xpectsalot. Many of the researchers working at Xpectsalot in the platelet activation area have passed through Professor G's lab for mini-fellowships. One hundred new jobs have been created by Xpectsalot and the company has recently been hailed by Big Bucks Magazine as one of the fastest growing, up-and-coming businesses in America.

After seven years, the first commercial product based on Professor G's work comes to market. Missagain State University, Professor G's lab, and Professor G share equally in the resulting 1% royalty stream of $20,000 a year. With the success of its first niche-market product, therapeutic products in the pipeline, and its high quality scientific staff, Xpectsalot, is acquired by a multinational pharmaceutical chain named Tuffchoice, Ltd., and moves out of state. The unexpected FDA approval of another company's alternative therapy causes Tuffchoice to reorient its

product strategy and research focus, and the Agreement with Missagain and Professor G is not renewed, much to Professor G's dismay. Xpectsalot's former research director, now a V.P. at Tuffchoice, has told Professor G that the parent company is not interested in developing the therapeutic product further even though Professor G thinks it will be more effective that the competitor's product. He also told Professor G that Tuffchoice's licensing group has no time or resources to market the core technology for sublicensing. Professor G's confidentiality obligations to Xpectsalot extend indefinitely beyond the term of the Agreement.

Completely distraught at this turn of events, Professor G contemplates a career change. Secretly, he thinks about applying to law school and going to work for Congressman Phil A. Buster.

How could Missagain State U have structured a better deal for State and for Professor Guy L. Less? What went wrong?

Case Study 2

INTERNATIONAL ASPECTS OF TECHNOLOGY COMMERCIALIZATION

The Case of the Sniffily Nose

Primary Reviewer: Mr. Joshua A. Kalkstein, Esq., Senior Corporate Legal Counsel-Research, Pfizer Inc.

In 1992, scientists at Mega Grant University (MGU), funded by a large NIH grant, isolated a receptor in human nasal mucosa that most common cold viruses use when infecting mucosal cells. MGU filed for a patent on the receptor and granted an exclusive license to Sneeze Away MiniPharm, a small Oregon company formed with venture capital primarily for the purpose of commercializing this discovery. Sneeze Away scientists have completed determination of the receptor's structure and are now developing drugs to block it. However, by summer 1993, funds to continue this promising research ran out. In late 1993, Sneeze Away signed a contract with the U.S. subsidiary of XenoPharma, a large foreign pharmaceutical manufacturer. This contract gives Sneeze Away stockholders a handsome return on their investment and commits Xeno to establish a state-of-the-art research facility in Xenoland to complete research and development (R&D) of a cold medicine to be marketed under the trade name Never Drip. It also gives the principal Sneeze Away scientists large shares of Xeno stock along with stipends and housing necessary for them to work with Xeno scientists in Xenoland to complete the development of Never Drip. In return, Xeno will receive the majority of Sneeze Away stock, acquire property rights in all Sneeze Away's patents, and rights under the original license from MGU. Sneeze Away will continue working on a couple minor research projects, but will mainly work with Xeno USA on marketing and distribution of Never Drip. For the most part Xeno U.S.A. does no manufacturing or research and in addition from serving as a U.S. distribution center for its parent, it will oversee the reorganization of Sneeze Away.

Just after signature, the contract was leaked to the Portland Inquirer, which published a sensational report concluding that this contract is yet another example of:

> "the systematic plundering of America's taxpayer-financed science-base by wealthy foreign companies, whose home governments are content to let U.S. taxpayers finance the bulk of the world's basic research, knowing that foreign companies can pick up promising results at pennies on the U.S. taxpayers' dollar."

The national media and Congress have taken considerable interest in this agreement, since it now appears that Never Drip will

become one of the best-selling medicines in the world. The Chief Executive Officer of Sneeze Away defended the agreement noting that, of all offers of financing that his company received, not only was Xeno's the most generous, but also Xeno is in the best position to rapidly complete R&D on a cold medicine and to market it on a world-wide scale. He points out that the contract specifically requires Xeno to file an application for FDA approval within one year, a guarantee no other company could match. This is a particularly important point since each year considerable money and job time is lost to the common cold. Furthermore, rapid commercialization of Never Drip would help to alleviate serious public health problems associated with complications arising from the common cold experienced in particular by the elderly and children.

Some members of Congress are saying that the contract violates the spirit, if not the letter, of the Bayh-Dole Act and regulations, because an invention derived from NIH-funded research has been effectively sublicensed to a company that will manufacture that invention outside the U.S. for sale in the U.S. market. Sneeze Away's lawyers respond:

- There is no invention yet (the final patent for Never Drip has not been issued), therefore Bayh-Dole does not apply.

- Even if Bayh-Dole applies, it applies only to the initial grant recipient, MGU. Sneeze Away is a licensee, not an <u>assignee</u>, of MGU. Therefore the following key provision in the Bayh-Dole regulations does not apply:

  > Neither the contractor [i.e., MGU] nor any assignee will grant to any person the exclusive right to use or sell any subject inventions in the United States unless such person agrees that any products embodying the subject invention or produced through the use of the subject invention will be manufactured substantially in the United States.

  In other words, licensees of MGU, such as Sneeze Away, are not covered by the substantial-U.S.- manufacture requirement and can sublicense to whomever they please.

- Even if the Bayh-Dole Act does apply to MGU's license to Sneeze Away, Xeno's acquisition of the right to use the cold virus receptor is not a <u>grant</u> under the provisions of Bayh-Dole. Xeno is purchasing a controlling interest in Sneeze Away, and therefore any licenses Sneeze Away holds naturally will come under the control of Xeno, even in the absence of a formal sublicensing agreement.

- Furthermore, Never Drip will incorporate not only discoveries made by MGU scientists funded by NIH grants, but also by Sneeze Away scientists funded by venture capital. In view of

the important contributions by Sneeze Away scientists, it would be unfair to insist that the preference for U.S. manufacture requirement apply in this case.

- Sneeze Away made reasonable efforts to find an investor that would manufacture in the U.S. but no such investor could match Xeno's ability to rapidly commercialize Sneeze Away's research.

- Even if Xeno U.S.A does no manufacturing or research in the U.S., its U.S. operations provide important alternative economic benefits through substantial job creation. Should increased U.S. jobs or other substantial economic benefits be considered by a funding agency when determining whether the U.S. manufacturing requirement has been satisfied?

Many members of Congress are asking why Bayh-Dole should contain a loophole permitting companies that sublicense patents derived from federally-funded research or that acquire such patents through corporate-buy outs to evade the preference-for-U.S.-manufacturing provision. They also want to know whether NIH or MGU should have known in advance of the Xeno-Sneeze Away agreement and whether NIH or MGU could have done anything to prevent it.

One particularly outspoken critic, Senator U. S. First, has obtained documents indicating that Minnesota Materials, Inc. (MinneMate) proposed a partnership with Sneeze Away which would have allowed R&D on Never Drip to continue, with reasonable assurance that clinical trials would begin within two years. MinneMate is a small business which does all of its R&D and manufacturing in Minnesota. However, 11 percent of its stock is owned by the Minnesota-born widow of a Polish nobleman. This stockholder has become a Polish citizen and now lives in Warsaw.

Senator First also is criticizing negotiations between MGU and Xeno on an agreement under which Xeno would contribute $5 million annually over five years for research on treatment for Alzheimer's Disease to MGU's renowned but financially strapped neuroscience department. In return, Xeno would have first rights of refusal to license any discoveries related to Alzheimer's Disease made by MGU neuro-scientists. However, Xeno would not be able to delay publication of research findings by more than two months, and MGU researchers would be free to collaborate with scientists from other outside institutions, so long as they did not circumvent the first-right-of-refusal agreement. Both MGU and Xeno want this deal to go through. MGU has not been able to find a U.S. company that is willing to make an equivalent investment in its neuroscience department. Xeno anticipates a number of breakthroughs from this collaboration which it can rapidly commercialize. Senator First found out about this proposed agreement from a press released issued by MGU and has requested an explanation from MGU's primary funding agency, NIH.

Feeling vulnerable to Senator First's attacks, Xeno is suggesting it can renegotiate its contract with Sneeze Away so that Sneeze Away will be responsible for packaging and marketing Never Drip for the North American market. Although this would shift Sneeze Away's focus from R&D, it would allow it to hire a work force of approximately 2000 sales agents, managers and blue collar workers. Xeno has even hinted that it might build a plant in the U.S. to produce Never Drip pills. However, the pharmaceutical chemicals for this plant would be imported from Xenoland and the highly automated plant would employ only 50 U.S. technicians. A Xeno spokesperson explained that, unlike some other international pharmaceutical companies, Xeno believes that it should continue to conduct most of its development work and chemical manufacturing in its home laboratories, at least for the near future. This will ensure efficiency and adequate quality control.

Senator First has introduced legislation that would require NIH to track all patents, including licenses and sublicenses of such patents and their commercial use, derived in any part from NIH grants or contracts. Any transfer to a foreign-controlled company with little R&D or manufacturing presence in the U.S. would be prohibited, unless the transferor demonstrates that no other company could reasonably commercialize the patented technology, or the transferee demonstrates that its use of the technology would enhance the U.S. technology base. Other members of Congress suggest that a transfer tax of 30% be levied on the value of technology transferred to companies with little R&D or manufacturing presence in the U.S. This, they maintain, would ensure that such companies pay their fair share of taxes to support the research whose results they purchase, but would not prohibit such transfers.

Other members of Congress oppose these proposals as protectionist and administratively burdensome. Many wonder whether there is any objective evidence that the U.S. should be concerned about transfer of some NIH-funded technology to "foreign" companies. They advocate that, before considering any changes in current law, the U.S. should find out what proportion of sponsored research agreements involve technology transfers to a foreign-controlled corporation, and of these, what percentage involve technology transfers to companies with minimal R&D or manufacturing presence in the U.S.

ISSUES FOR CONSIDERATION

On the basis of your current industry, academic or government perspective, please comment on the following issues presented by this case:

1. Do you agree with the analysis of Bayh-Dole set forth by Sneeze-Away's lawyers, particularly its limitations when applied to this type of situation?

2. Concerning what constitutes "substantial manufacturing in the U.S." under Bayh-Dole, do you think that the revisions proposed by XenoPharma in its contract with Sneeze Away would satisfy (a) the letter, and (b) the overall objectives of Bayh-Dole?

3. In this example, many members of Congress refer to companies with "little R&D or manufacturing presence in the U.S." as companies deserving stricter scrutiny when purchasing publicly-financed technology. Is this an appropriate criterion? What criteria, if any, might be better? What institution or agency should decide when such a criterion applies?

4. Is "foreign control" an appropriate criterion to use in deciding whether certain corporate purchases of publicly-funded technology deserve strict scrutiny? If so, what should constitute "foreign control"? U.S. Department of Commerce guidelines classify as "foreign-controlled" any company, at least 10 percent of whose's voting stock is held by a single foreign person. Is such a definition appropriate in the case of MinneMate?

5. Sneeze Away's lawyers raise the issue of the commingling of NIH and privately supported inventions in a single commercial product. How should such commingling be handled under Bayh-Dole? i.e., should a patent for a commercial product that is only partly derived from an NIH-supported patented invention trigger the Bayh-Dole U.S. manufacturing requirements?

6. The proposed agreement between the MGU neuroscience department and XenoPharma raises the issue of commingling of research funds by an NIH grantee. What degree of commingling should trigger the Bayh-Dole U.S. manufacture requirements? What, if any, guidelines should there be to prevent or keep track of commingling of government and industry funds in

sponsored research projects? Would such guidelines be practical?

7. What is your assessment of the various Congressional proposals to deal with the issues raised in this case; specifically:

   a. active patent tracking (by whom?),

   b. prohibition of technology transfers to companies lacking a substantial scientific or technical presence in the U.S,

   c. a transfer tax,

   d. before taking any other measures, determine what proportion of technology transfer agreements involve foreign-controlled companies or companies without a substantial scientific or technical presence in the U.S.

8. a. Do you believe that the Bayh-Dole preference for U.S. manufacturing should be extended to cover situations such as Xeno-Sneeze Away?

   b. If so, who should decide when this provision is triggered: the NIH grantee, NIH, another U.S. Government agency?

   c. Would your answer to (a) be any different if there had not been commingling of inventions financed by private funds and an invention financed by NIH?

   d. Who should determine if Sneeze Away made reasonable efforts to meet the Bayh-Dole substantial-U.S.-manufacturing requirement?

Case Study 3

FAIR ACCESS TO FEDERALLY FUNDED TECHNOLOGY, MONITORING UTILIZATION, AND PROMOTING COLLABORATIONS

The Case Of The Enzymatic Dilemma

Primary Reviewer: Dr. Sandra L. Shotwell, Director of Technology Management, Oregon Health Sciences

Prof. Nigel Eve (known to his friends as "Ny") and his postdoctoral fellow Sophocles Isticate at the Nerdhouse Institute of Technology ("NIT") have discovered and isolated a new enzyme MyT606 which appears to be implicated in the progression of multiple sclerosis. Although the exact mechanism of this enzyme is not yet known, it is hypothesized that inhibitors of this enzyme could be useful in slowing the progression of the disease. The work was supported under an NIH grant to NIT, which is located in Hoboken.

Ny Eve and Soph Isticate have submitted a manuscript describing the MyT606 to the Journal of Biochemical Research and have been told that it will be published in about two months. Dr. Isticate suggested to Prof. Eve that they contact the Technology Licensing Office (TLO) at NIT and consider filing a patent application. The TLO informed the authors that the technology looked interesting and that the TLO would consider filing a patent application on MyT606, but that their patent budget is very limited and they were concerned that the utility of the enzyme has not been proven. Dr. Isticate reminded the TLO that the manuscript was about to be published, and that foreign patent rights would be lost unless a patent application was filed soon—or the manuscript withdrawn.

Prof. Eve, meanwhile, is interested in cloning the enzyme and investigating its mechanism of action, but his current grant cannot support the additional technician needed to do the cloning. Dr. Isticate's postdoctoral fellowship has come to an end and he has accepted a job at Bigco Pharmaceutical Corporation, a New Jersey-based pharmaceutical company which was recently acquired by Hellenic Industries, a multi-national based in Athens, Greece. Hellenic has provided $100 million to Bigco to build a research facility in Newark, New Jersey. Dr. Isticate is hoping to continue his research in multiple sclerosis at Bigco's laboratories. He is a Greek citizen and finds the connection with the "home office" to be an additional attraction of his employment.

Under a confidentiality agreement, the Technology Licensing Office at NIT has discussed the new enzyme with MiniPharm, a venture-capitalized startup specializing in degenerative diseases. The connection came about when the business

development manager from MiniPharm visited the NIT TLO in search of new technologies for MiniPharm. The MyT606 disclosure had come into the TLO the day before, and seemed relevant. MiniPharm indicated interest in licensing the technology, but they are not sure that they have the resources to support three years of research in Prof. Eve's laboratory. They have invited Prof. Eve to join their Scientific Advisory Board, a position that would give him stock options. However, Prof. Eve is aware that NIT policy prohibits a faculty member from accepting research support from a company in which he owns equity.

Another disclosure of the invention was made by Dr. Isticate in a seminar he presented to Bigco as part of his job interview. He was not certain whether this seminar was "closed" or "confidential", but he does know that some scientists from Hellenic headquarters were there. Although the seminar itself was general and would not affect foreign patent rights regarding the enzyme isolation, Dr. Isticate discussed further details (in Greek) with some of the Hellenic scientists during a dinner following the seminar. Bigco has now indicated that they would be interested in a collaboration between Dr. Isticate (now at Bigco) and Prof. Eve at NIT. They would consider supporting the research program at NIT.

Both Bigco and MiniPharm stated that an exclusive license would be necessary if they were to invest the resources needed to further develop the technology. As a term of its sponsored research agreement Bigco has also asked for an assignment of title to any invention made under the support agreement. They would also like NIT to agree to get a waiver of the U.S. manufacturing requirement of the Bayh-Dole Act for future inventions.

The NIT Technology Licensing Office and Prof. Eve are facing several dilemmas:

1. The TLO patent budget is too tight to allow them comfortably to file a patent application when they are not sure that they will have a licensee. Yet if they don't file soon, they will lose foreign patent rights—unless they delay publication.

2. Prof. Eve finds a relationship with MiniPharm to be an attractive proposition. Their scientists are highly qualified and their management is "firmly committed" to the field. Dr. E. Preneur, their CEO, states "Unlike at Bigco, this wouldn't be just one project on our research and development agenda—it would be THE flagship project of the company."

3. The TLO notes, however, that MiniPharm only has about half a million dollars in the bank, and although the venture

capitalists are promising "a second round of funding—sometime soon," nothing is assured.

4. The Director of the Technology Licensing Office also worries that the technology was not widely publicized—it hasn't been published yet, and BigCo and MiniPharm each learned about it essentially "by accident".

5. Although BigCo is an American Company, its new "parent" is Greek.

6. Pro. Eve is urging speed, particularly in getting funding—or at least a license—so that the cloning can begin—before he is "scooped" by a scientist at Stanford who, he knows, is hot on the trail of this enzyme.

7. Prof. Eve would also enjoy the possibility of working with BigCo. since this would allow him to continue his very satisfying relationship with Soph Isticate.

What to do???

Case Study 4

PREFERENCE FOR SMALL BUSINESS, FREE COMPETITION AND FREE ENTERPRISE

The Case of the Sleeping Giant

Primary Reviewer: Dr. Donald L. Drakeman, President, Medarex

Mega Corp., a Fortune 500 conglomerate, has a highly successful pharmaceuticals division based on skyrocketing sales of Mega-doze, a sleeping "patch" based on the soporific qualities of patented molecules derived from recycled issues of the federal register. Mega-doze, which causes instantaneous deep sleep while activating the brain functions responsible for keeping the eyes open and nodding the head thoughtfully at periodic intervals, has become a billion dollar product with celebrity endorsements from the Speaker of the House, the entire federal judiciary, and many corporate executives.

Mega Corp. has decided to designate $100 million for novel neurological research over the next five years. Rather than establish an internal research program, Mega's representatives have approached the Sleep Neurology Unified-research Zone (SNUZ), a multi-disciplinary research institute with an annual budget of $50 million, half of which comes from NIH grants and the remainder through the university with which SNUZ and its faculty are affiliated. In return for its $20 million per year commitment, Mega has demanded a right of first refusal to obtain an exclusive license to all technology developed at SNUZ during the five year period, whether or not the technology was funded by Mega. If Mega does not exercise this right, SNUZ is then free to license the technology to third parties, but must first offer the proposed license to Mega (right of second refusal).

A year ago, several local venture capitalists founded Maximum Intelligence Network, Inc. (MINI), intending to take advantage of MINI's close proximity to the neurological research at SNUZ to develop into a major biotechnology company specializing in IQ-enhancing agents that work during various sleep cycles. MINI's ten employees often retain SNUZ researchers as consultants and MINI has entered into a $100,000 agreement under which it sponsors research at SNUZ. In return, MINI has a right of first refusal to obtain a license for the exclusive rights to technology it has funded; the license terms are to be negotiated in good faith by MINI and SNUZ when the right of first refusal is exercised.

The SNUZ administration has also been approached by two full-time SNUZ faculty members who have recently established The Institute for Never-ending Youth (TINY), a for-profit venture seeking to commercialize the researchers' recent discovery of the brain cell

receptor stimulated by rock music videos (which they have dubbed the MTV receptor). Funding for this work has come exclusively from NIH grants. TINY's founders believe that they can develop a genetically engineered product that will activate this receptor resulting in the same general effects as Mega-doze but which will also cause the user to develop a youthful disposition. TINY seeks to obtain from SNUZ an exclusive license to any MTV receptor-related products developed either in the researchers' SNUZ laboratories or in the small lab TINY intends to open across the street. The researchers have offered SNUZ ten percent of the equity in TINY. (They believe the equity is worth well over $2 million and possibly as much as $20 million based on Wall Street's interest in neuroscience companies, although TINY is unlikely to be able to sell stock to the public for several years, if at all.) The remainder of TINY's equity would be owned by the researchers and by their financial backers who have agreed to provide seed capital to TINY if the company successfully acquires the exclusive rights to the MTV receptor-related products. TINY has also offered SNUZ a 5% royalty on any product sales. The researchers want all of their MTV receptor research excluded from the Mega deal.

Mega Corp. has approached SNUZ with a proposal to exclusively license the MTV receptor and related products in a separate transaction from the five year funding program. Mega has offered a cash payment of $100,000 plus a 5% royalty. Mega is also balking at having any SNUZ research excluded from its multi-year right of first refusal.

You are a member of the SNUZ board of trustees. You have been advised by the administrative staff that:

> 1. The Bayh-Dole Act states that "It is the policy and objective of the Congress to promote the utilization of inventions arising from federally supported research or development; to *encourage maximum participation of small business firms in federally supported research and development efforts*; to promote collaboration between commercial concerns and nonprofit organizations...; [and] to promote the commercialization and public availability of inventions made in the United States...."
>
> 2. The Code of Federal Regulations provides that recipients of federal research grants are "expected to use efforts that are reasonable under the circumstances to attract small business licensees. *They are also expected to give small business firms ... a preference over other applicants for licenses ....[But these rules are] not intended, for example, to prevent non-profit organizations from providing larger firms with a right of first refusal or other options in inventions that relate to research being supported under long-term or other arrangements with larger companies.*"

3. The Mega deal will allow SNUZ to become the world's leading soporific research institute, a veritable sleeping giant, although the institution is otherwise in sound financial condition and does not require the Mega deal for survival or to fund on-going research.

4. Mega is only interested in providing the $100 million funding if it can "leverage" its investment by acquiring access to SNUZ's NIH-sponsored research.

5. If the Mega deal goes forward as originally outlined, the venture capitalists are likely to shut down MINI, and Tiny will never get off the ground.

6. The SNUZ faculty are fairly evenly divided among the following groups:

a. Those who oppose all corporate relationships (including Mega, MINI and TINY) as inherently corrupting of the pure research environment.

b. Those who believe that the Mega deal will threaten their own lucrative consulting relationships with industry.

c. Those who welcome the Mega funding as an opportunity to dramatically expand SNUZ's scope and research base.

d. Those who, like TINY's founders, have a personal interest in starting a biotech company to commercialize their research, and are nervous about becoming unduly entangled in the Mega deal.

e. Those who seek to have these technology transfer issues decided by the NIH instead of the SNUZ administrators (which, they believe, will be unduly influenced by financial opportunities), despite protests from SNUZ administration who cite the following provision of the Code of Federal Regulations to support their position that NIH does not have standing to make or influence the decisions:

> Small business firms that believe a nonprofit organization is not meeting its obligations [to provide a preference for small businesses] may report their concerns to the Secretary. To the extent deemed appropriate, the Secretary will undertake informal investigation ... and, if appropriate, enter into discussions or negotiations with the nonprofit organization to the end of improving its efforts in meeting its obligations under the clause. *However, in no*

event will the Secretary intervene in ongoing negotiations or contractor decisions concerning the licensing of a specific subject invention.

7. MINI has urged SNUZ to turn down or restructure the Mega deal because its broad right of first refusal (1) will discriminate against MINI and other small companies contrary to the intent of the Bayh-Dole act, (2) conflicts with MINI's own right of first refusal agreement, and (3) may preclude SNUZ from relationships with other biotechnology companies that may offer a combination of stock, license fees, royalties and sponsored research that could be more financially attractive than the Mega deal.

8. The TINY faculty members have asked SNUZ to turn down the Mega deal and Mega's MTV receptor proposal because they believe that a small biotechnology company dedicated to a limited number of products is more likely to successfully commercialize a particular product than a large conglomerate. The faculty members argue that even though large companies may have greater resources, they also have many competing projects seeking capital; accordingly, a company like Mega might neglect or abandon a project like the MTV receptor (especially if it would replace a successful existing product) purely for strategic reasons despite the medical value of the product.

You must decide what to do about the multi-year Mega proposal as well as how to handle the competing offers from Mega and TINY for the MTV receptor.

Appendix D

Public Comments

Public Comments

Some individuals and representatives of organizations addressed the Panel during the Forum's public testimony session, in addition to providing written comments. Four witnesses provided written comments only.

William H. Beers, Ph.D.
Senior Vice President
The Scripps Research Institute
La Jolla, CA

Christopher J. Doherty, Esq.
Washington Director
New England Biomedical Research Coalition
Washington, DC

Marvin E. Ebel, Ph.D.
Associate Dean, Graduate School
Acting Director, Research Services
University of Wisconsin–Madison
Madison, WI

Lester B. Salans, M.D.
Vice President
Sandoz Research Institute and Sandoz Pharmaceuticals Corporation
East Hanover, NJ

Written Comments

Council on Governmental Relations
Washington, DC

Warren Cheston, Ph.D.
Director, External Affairs
The Wistar Institute
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January 15, 1994

Panel of the Forum on Sponsored
Research Agreements
c/o Ms. Peggy Schnoor
National Institutes of Health
Shannon Building, Room 218
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Panel Members:

I am writing on behalf of The Scripps Research Institute to express its views on the issues identified in the agenda of the Forum on Sponsored Research Agreements scheduled for January 25-26, 1994. As one of the world's largest nonprofit biomedical research organizations not affiliated with a university, Scripps has a unique perspective on the issues raised in the agenda. Scripps welcomes the opportunity to share that perspective with you.

We will address in turn each of the five issues identified in the agenda:

Issue 1 -- The Scope and Size of Sponsored Research Agreements

Over the years, Scripps has entered into many sponsored research and licensing agreements of many types. Scripps trusts that others will submit comments addressing the merits of project specific agreements as well as other types of arrangements. Because larger-scale funding and licensing agreements have been particularly important to Scripps, we focus our comments on agreements of that type.

Scripps has had large-scale funding and licensing agreements for over a decade -- with Johnson & Johnson

since 1982 and with PPG Industries since 1984. Based on our substantial experience with such agreements, we can report that they offer significant benefits to the public by, among other things:

-- expanding the funding available for scientific research;

-- increasing the breadth and diversity of such research, for example by enabling research for which NIH or project specific corporate funding might not otherwise be available;

-- facilitating funding requests for specific research projects, thereby expediting the pace and level of research initiatives;

-- promoting the exchange of ideas across departmental and laboratory boundaries;

-- promoting collaborations among researchers in basic and applied fields;

-- providing for the infrastructure needs of America's research institutions, thereby enhancing their capability and vitality;

-- providing training and employment opportunities for new scientists, technicians and support staff; and

-- expediting the identification, development and commercialization of promising technologies.

These benefits, in turn, increase the likelihood that the scientific research of today will lead to the life-saving products of tomorrow.

The following are some of the particularly important reasons why large-scale funding and licensing agreements serve the public interest:

1. Large-Scale Agreements Are Investments in the Future of Independent Research Institutes. NIH grant funding for basic biomedical research has not kept pace with expanding research opportunities, and in any event, cannot meet the infrastructure needs of independent research institutes. As a result, institutes like

Scripps must seek stable sources of substantial additional funding -- to recruit scientists to achieve the intellectual critical mass necessary to launch new research programs, to train young scientists, to purchase state-of-the-art equipment, to pursue research that would not be funded by the Government, and otherwise to support their missions. Project specific agreements certainly provide important funding, but unlike large-scale agreements, they do not support these long-term institutional needs of independent research institutes.

2. Large-Scale Agreements Foster Cross-Fertilization. When different companies enter into project specific agreements with individual laboratories or departments of a research institution, walls of secrecy are erected among the researchers, restricting the free exchange of ideas, data and information. Agreements cutting across departments promote the cross-fertilization of research and ideas.

3. Large-Scale Agreements Promote Productive Collaborations Between Academia and Industry. One of the policy objectives of the Bayh-Dole Act is "to promote collaboration between commercial concerns and nonprofit organizations." 35 U.S.C. § 200. By providing an institutional framework for scientists from each sector to share ideas and perspectives on subjects of common interest, large-scale agreements help achieve this objective. The relationships fostered by large-scale agreements have given Scripps' scientists access not only to the scientists and research programs of corporate sponsors, but in some cases, to essential biological materials that would not otherwise be available to academic researchers.

4. Large-Scale Agreements Help Ensure that Inventions are Utilized. Congress' overriding goal in enacting the Bayh-Dole Act was to ensure that Government-funded inventions actually are used. Large-scale licensing agreements provide an efficient mechanism for transferring basic innovations to a capable commercial company for development. Such a mechanism increases the number of valuable new biomedical products available to the public.

We have heard the concern expressed that large-scale agreements could permit one company to

monopolize the scientific output of a research institute. However, existing law requires companies licensing inventions under large-scale agreements to commercialize the inventions to which they obtain exclusive licenses. Because no company has the money or the expertise to commercialize all of the many discoveries made by an institute like Scripps, most discoveries remain available for commercialization by others. Thus, notwithstanding Scripps' large-scale agreements, Scripps also has licensing or collaborative agreements with some 50 small companies.

Given the advantages of large-scale agreements, it is not surprising that regulations of the Department of Commerce, which has the exclusive authority to promulgate generally applicable regulations implementing the Bayh-Dole Act, specifically permit granting "a right of first refusal or other options in inventions that relate to research being supported under long-term or other arrangements." 37 C.F.R. § 401.7(a).

Scripps is well aware that large-scale agreements may not be appropriate for all NIH grantees. But we believe that they are uniquely appropriate for grantees like Scripps, whose needs differ in many respects from the needs of others. Like all grantees, of paramount importance to Scripps is the academic freedom of its scientists to pursue their research ideas. Nothing must interfere with an individual scientist's ability to determine the course and scope of his or her research, to publish the results, and to engage in the free exchange of information and ideas among colleagues.

But an independent research institute like Scripps also seeks to satisfy a number of institutional objectives, such as the following:

-- having stable sources of funding, in amounts large enough and for periods long enough to plan for future research and to respond to the rapidly changing needs and priorities of public health and biomedical research;

-- having the freedom to make independent decisions on the allocation of financial resources among institutional needs and specific research projects;

-- having efficient mechanisms for the prompt consideration of funding requests for specific projects;

-- promoting interdisciplinary research and the exchange of ideas throughout the institute; and

-- having efficient mechanisms for the licensing and commercial development of inventions.

The NIH grantee community is very diverse, and the importance of these objectives -- and any other objectives one might identify -- necessarily will vary among NIH grantees. For example, some research institutions receive funding from state governments, others from private endowments, still others from tuition. Scripps cannot rely on such support for all of its funding, and therefore must look elsewhere for long-term financial support.

The diversity of the NIH grant community is one of its great strengths, in part because it allows grantees to approach important problems in different ways and from different perspectives. That diversity should not be jeopardized by guidelines that treat all grantees as though they are alike. It is vital that any NIH guidelines for sponsored research agreements provide grantees sufficient flexibility to structure arrangements that reflect their divergent needs.

Issue 2 -- The U.S. Manufacturing Requirement, Preference for U.S. Industry, and Foreign Access

Congress has concluded that certain products of Government-funded inventions should be manufactured substantially in the United States. 35 U.S.C. § 204. Scripps certainly endorses that policy, as it directly produces manufacturing jobs in the United States.

The preference for U.S. industry reflected in the manufacturing requirement of the Bayh-Dole Act does not, however, mean that NIH grantees should only collaborate with, and accept scarce research funding from, companies headquartered in the United States. Such a limitation would serve only to deprive the grantee community of

resources, and the public of the benefits of expanded scientific research opportunities.

In addition, in the current pharmaceutical market, headquarters location does not seem a particularly useful criterion for distinguishing potential licensees. The pharmaceutical industry today is truly an international enterprise, with almost all companies having a significant presence in the United States, regardless where their headquarters might be.

In making policy with respect to such companies,

> [T]he United States wants [multinational enterprises] to conduct business here and interact with local firms in ways that generate and retain wealth and quality jobs within its borders. . . . [T]his translates most immediately into high-wage, high-value jobs for Americans, indigenous technology development, advanced manufacturing that draws on local talent, an expanding tax base, and ultimately, generalized economic well-being.

Office of Technology Assessment, U.S. Congress, Rep. No. OTA-ITE-569, Multinationals and the National Interest: Playing by Different Rules 2-3 (1993).

NIH should not seek to limit the types of companies with which the grantee community can establish funding and licensing relationships. If anything, NIH should encourage firms with headquarters abroad to increase their activities in this country, including by collaborating with and taking licenses from NIH grantees.

Issue 3 -- The Utilization of and Licensing Requirements for Inventions Made with Federal Funding

Scripps believes that the public interest generally is best served when new biomedical products are made available to the public as a result of Government-funded research, regardless of considerations such as the size of the company that developed and manufactured them and whether that company is headquartered abroad. Indeed, utilization of

Government-funded inventions is the primary policy objective of the Bayh-Dole Act. 35 U.S.C. § 200.

Consistent with that objective and existing law, grantee institutions should require exclusive licensees to make good faith efforts to achieve practical application of inventions made with Government funding. Licensees who do not do so should not be permitted to retain their exclusive rights. This requirement has to be managed flexibly, however, and determinations have to be made based on a wide variety of relevant circumstances. There is no single set of standards that would properly govern the level and timing of efforts to develop such inventions. That is why government regulations prescribing utilization requirements in detail are likely to be too inflexible. Fortunately, the march-in rights the Government already has under 35 U.S.C. § 203 are a powerful guarantor that inventions will be developed, and are probably sufficient to ensure compliance by licensees.

Because the Government already has sufficient means to promote commercialization of Government-funded inventions, the details of licensing transactions are best left to the parties rather than prescribed by regulation. Government-managed technology transfer before the Bayh-Dole Act involved extensive delays, offered few incentives to commercialization, and rarely resulted in marketable products. Congress intentionally reassigned the responsibility for transferring particular technologies developed with Government support from the Government bureaucracy to grantees and their private sector partners in the marketplace. Additional regulation of licensing would be a step backwards.

Similarly, given the uncertain nature of basic scientific research and the likelihood of unexpected developments, it usually is not practicable to incorporate precise licensing terms such as benchmarks into sponsored research agreements with upfront licenses. In such circumstances, it is probably sufficient to impose a generalized obligation on licensees to make good faith efforts to achieve practical application of inventions. Indeed, this appears to be the reason for the policy followed by NIH itself in its CRADA agreements; even though NIH will grant a CRADA partner the first right to obtain a

license to a subject invention, NIH normally does not try to determine precise licensing terms until later.

Issue 4 -- The Preference for Small Business

Scripps believes that the small business licensing preference is important, and it has long been Scripps' policy to collaborate with and grant licenses to small businesses.

Scripps' experience shows that large-scale funding and licensing arrangements are not inconsistent with this policy. No company has the money or the expertise to commercialize all of the many discoveries made by an institute like Scripps. Thus, even where an institute enters into a long-term exclusive licensing arrangement with a larger company, most discoveries remain available for commercialization by others.

This is illustrated by Scripps' experience with Johnson & Johnson. Although Johnson & Johnson has a first right to license Scripps' discoveries, the number of development projects for which Johnson & Johnson has actually acquired rights is less than the number of technologies Scripps has licensed or has sought to license to others, and Scripps currently has licensing or collaborative agreements with some 50 small companies.

The small business licensing preference never was intended to preclude institutions from entering into beneficial long-term relationships with larger companies. See 37 C.F.R. § 401.7(a). By their nature, small businesses often are unable to provide independent research institutes with the substantial amounts of general funding over long periods that they need in order to achieve institutional objectives. This is one of the reasons that Scripps cannot rely too heavily on small businesses for the licensing of Scripps' inventions.

Another reason is that developing pharmaceutical products requires huge financial resources and a very long lead time. As a result, there is a substantial class of discoveries that few if any small companies are likely to have the ability to commercialize. Senator Dole anticipated this when the small business licensing

preference was added to the Bayh-Dole Act, commenting that in many cases licensing to small businesses "will not be feasible either because no small businesses are interested or because those that are may lack the resources necessary to bring the invention to the market." 130 Cong. Rec. S14,142 (daily ed. October 10, 1984).

Scripps believes that the public interest generally is best served when new biomedical products are made available to the public as a result of Government-funded research at the earliest possible date. Thus, licensee size should be considered along with other relevant factors in making licensing decisions, but generally should not be determinative.

Scripps would like to take this opportunity to identify an issue that is an increasing source of concern to it and likely to other research institutions: In the course of negotiating licensing agreements with commercial companies, and small businesses in particular, it has become apparent that licensees believe that access to the research scientists who invented the technology is as important as the license to the technology itself. Without the opportunity to consult with those scientists, the commercial companies fear that their efforts to develop and commercialize the technology will not be successful.

As an academic institution, Scripps will not commit its scientists to work on projects outside Scripps. Any such consulting agreement must be negotiated directly between the commercial company and the scientist.

The refusal of the research scientist to consult with the commercial company often renders the technology difficult or impossible to license. On the other hand, the agreement of the research scientist to provide consulting services or even take an equity position in the company creates a potential conflict of interest situation for Scripps.

We would welcome NIH's guidance on reconciling the objectives of utilizing Government-funded inventions and giving a licensing preference to small businesses with the need to avoid conflicts of interest.

Issue 5 -- Research Freedom

Maintaining the academic integrity and freedom of its scientists is the cornerstone of any research institution and a paramount objective of Scripps at all times. Scripps does not believe that any industrial partnership can succeed unless scientists are free to determine the course and scope of their research, to publish the results of their research, and to exchange ideas and information with colleagues. Neither Scripps nor any other research institute would survive for long if it compromised the academic freedom of its faculty.

Because academic freedom is so essential to the health of a research institute, primary responsibility for maintaining it necessarily must reside with the research institutes who accept corporate funding. NIH's role in ensuring academic freedom should be to continue its practice of awarding grants based upon scientific merit and peer review, including review of published research results.

The agenda of the Forum specifically asked about restrictions on consulting and publishing. Scripps believes that corporate sponsors of research have a legitimate interest in protecting their proprietary position. For that reason, and to avoid conflicts of interest, scientists performing research sponsored by a corporation reasonably may be precluded from performing substantially similar work for other commercial entities.

Scripps is commonly asked to agree to some form of pre-publication review in sponsored research agreements, because corporate sponsors want to ensure that public disclosure of inventions will not result in the loss of patent rights. Scripps understands the rationale for such requests, and attempts to respond to them in a manner conducive to the investigator's right promptly and fully to publish research results. Scripps often avoids the need for pre-publication review by ensuring that patent applications protecting the subject matter of the publication are filed promptly. Because this is not always practicable, Scripps has generally been willing to agree to pre-publication review provisions, so long as they are narrowly tailored and

provide for the shortest delay consistent with the preservation of patent rights.

In practice, Scripps has not found pre-publication review requirements to be problematic. Indeed, to the best of our knowledge, there has never been an instance where a requirement of pre-publication review has precluded a Scripps scientist from publishing a paper when he or she wanted to do so and in the form originally proposed.

Conclusion

If there is a common thread that runs through our comments, it is that NIH's efforts to provide guidance to its grantees should not instead serve to fetter them. The United States remains the world leader in biomedical research because of our pluralistic research community. NIH grantees constitute an exceptionally broad array of research organizations, each with its own special needs and perspectives.

Just as the Government does not dictate what research should be done, or how it should be conducted, neither should it dictate what research collaborations and licensing arrangements should be permitted or how they should be structured. We are in the midst of explosive advances in biomedical technology. There are unparalleled opportunities for scientific breakthroughs if our intellectual resources can be matched with funding and licensing opportunities. We cannot afford to foreclose those opportunities with a set of one-size-fits-all guidelines that disallow collaboration, funding and licensing arrangements just because they don't follow a customary or pre-approved mold.

We urge the Panel to ensure that any guidelines it recommends be crafted broadly and flexibly enough to permit grantees to continue to tailor their arrangements to their particular needs and circumstances -- so that scientific research will continue to flourish and the public will continue to benefit.

* * *

We at Scripps hope that our comments are useful to NIH as it proceeds to develop guidelines in the important area of sponsored research agreements. We appreciate the opportunity to comment on these issues and look forward to attending NIH's Forum.

Sincerely,

William H. Beers, Ph.D.
Senior Vice President

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(617) 277-5020

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NEW ENGLAND BIOMEDICAL RESEARCH COALITION
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January 24, 1994

VIA FEDERAL EXPRESS

Ms. Peggy Schnoor
National Institutes of Health
Shanon Building
Room 218
9000 Rockville Pike
Bethesda, Maryland 20892

Dear Ms. Schnoor:

The New England Biomedical Research Coalition is an affiliation of New England hospitals, research institutions and biotechnology firms organized to identify and pursue its members common interests. This letter presents the Coalition's general comments on technology transfer for the upcoming Forum on Sponsored Research Agreements Perspectives, Outlook and Policy Development.

This Forum coincides with the beginning of an historic debate in America on the costs of its health care system. It thus offers a well-timed opportunity to focus on how technology transfer programs like the Bayh-Dole Act (the "Act") are working well; for example, by improving the cooperation of industry, university and government in biomedical research. Of course, once we identify these successes we should agree not to "fix" what does not need repair.

One clear measure of the Act's success is the effect it is having on the movement of innovations from university laboratory to market place. For example, between 1980 and 1990 the percentage of total U.S.-origin patents granted to universities more than doubled, from 1% to 2.4%. In this same period, the number of applications for patents by universities on NIH sponsored inventions increased more than 300%. With respect to licensing, universities granted over 1300 new licenses to technology developed in their laboratories in 1992 alone. These licenses are benefitting both universities and the general economy. In 1989 and 1990, 35 major universities granted 197 exclusive licenses and earned more than $ 29.3 million in

royalties. A recent survey by the Association of University Technology Managers identified $ 9 billion in product sales and 53,000 jobs arising from university licenses.

Critical to this success is the Act's careful system of incentives. Universities may retain patent title to technology developed through federally funded research; investors can get exclusive licenses to that technology; and, inventors retain the right to royalties on their work. Thus, each of these parties is given a direct stake in the best development of the new technology. Such a system has been key to getting new technology into the marketplace.

Also critical to the Act's success is its policy of preserving academic freedom and independence. Early on, some saw the Act as a potential threat to academic freedom. In this view, research support agreements between universities and industry would distort research priorities with commercial goals. Today, it is clear that the Act works because it gives universities freedom to manage inventions within broad parameters. Thus, universities can fine-tune the terms of their commercial relationships to protect against distortion of academic priorities.

The success of the Act does not mean there is no room for improvement. For example, comprehensive technology agreements that give exclusive access to an institution's full range of research may not do enough to guarantee commercial development of all that research. Perhaps such agreements should include an incentive to "use it or lose it," and thus discourage the failure to develop valuable research. This would do more to avoid the risk that important innovations might languish unused because of the very agreements intended to promote their development.

In addition, one of the Act's biggest successes -- getting industry involved in the funding of basic research -- threatens to become one of its biggest problems. The Act has contributed to a significant increase in the funding of university R&D by industry. In the past decade, industry support of university research grew faster than did any other source of funding. Since 1971, the portion of U.S. industry R&D expenditures going to academic institutions has nearly doubled. The problem this provokes is government scrutiny and interference with the funding arrangements it set out to encourage. However, universities must remain free to negotiate agreements that attract industry funding, or the funding will disappear.

In order not to drive away such funding, government oversight of these agreements must reflect certain basic principles. First, basic research does not pay for itself. As federal funding for such research declines, universities must retain the flexibility to negotiate agreements that attract industry funds. Second, innovations do not reach the marketplace by themselves; industry must be able to profit from bringing them there or they will not arrive. Government must not deny business that incentive to take substantial risks that only comes from commensurate financial returns. Third, when taxpayers' enjoy a return on their investment in basic research, the form of that return is the availability of innovative technologies and products. This is the kind of return Congress identified in its own catalogue of the benefits of technology and industrial innovation: "improved standard of living, increased public and private sector productivity, creation of new industries and employment opportunities, improved public services and enhanced competitiveness of United States products in world markets." This is the interest -- getting new products to market -- that should animate oversight of these agreements.

Finally, the current administration has repeatedly emphasized its commitment to bringing government and business together to improve the competitiveness of American industry. Technology transfer in biomedical research is one area that should not be left outside of this broad commitment. Indeed, as the American people and their leaders ponder ways to make health care coverage more affordable and available they should consider the recent explosion of new medical knowledge emanating from the nations collaborative enterprise of government, university and private research laboratories.

Sincerely,

Christopher J. Doherty

Christopher J. Doherty

CJD/mfd

January 21, 1994

STATEMENT BY MARVIN E. EBEL
ON BEHALF OF THE UNIVERSITY OF WISCONSIN-MADISON
FOR THE NIH FORUM ON SPONSORED RESEARCH AGREEMENTS
JANUARY 26, 1994

My name is Marvin Ebel. I am Associate Dean of the Graduate School and Acting Director of Research Services at the University of Wisconsin-Madison. I would like to make some comments on a growing problem in our relationships with private contributors to our research, based on our recent experience in negotiating agreements with the private sector.

I commend NIH for creating this forum, and addressing significant issues on technology transfer and developing relationships with private industry. I invite Panel members to consider that Material Transfer Agreements, in addition to Sponsored Project Agreements, must be negotiated in order to carry out many projects in the biomedical sciences.

We all recognize that the free exchange of scientific materials, as well of scientific information, is a cornerstone for building success in modern biological research. We also recognize that licensing, whether or not the material is patented, is an effective way to commercialize the development of new biological materials. When a company supplies such material to an investigator at another institution or company, it is reasonable that the recipient use the material solely for research, not commercialization. A conflict arises, however, when we consider new but derivative materials produced in the course of that research. The supplier of the original material may claim, and indeed may have a legitimate need for a license, perhaps even an exclusive license, for the use of the derivative material. The receiver of the original material, i.e., the developer of the new material, also has legitimate interests in the derivative material, since it represents the product of that individual's own research.

The situation becomes very complicated when the research of the recipient is sponsored by the federal government. Then the Bayh-Dole act, in the case of patentable materials, or federal policy in other cases may either require that the government receive a royalty-free license to use of the material, or else allow the government to file for a patent when the institution decides not to take title to an invention. Additionally, NIH policy is that in general materials developed with grant funds shall be made available to the scientific community. These requirements can be in direct conflict with the need, or at least the desire, of the provider to receive an exclusive license to the derivative material.

Each of the conflicting requests can be justified. If the derivative is a trivial extension of the original material, or a trivial replacement of it, then rights in the original material lose their value unless strong control is placed on the distribution and licensing of the derivative. Conversely, if the derivative has required considerable original research, then the inability of the researcher to commercialize the development may inhibit the development and use of important new materials.

Middle ground must clearly be found. However, negotiating agreements which strike that middle ground can be time-consuming and frustrating, especially for the investigators who are waiting to begin the next round of crucial experiments. I know of no simple solution to the problem.

However, the development of a standard material transfer agreement could provide a major simplification to the negotiations, especially if NIH would strongly encourage its use. Such a standard agreement should recognize the need of institutions to have unrestricted rights to publish results of their research, as well as to use derivative materials for educational purposes and to continue promising lines of research. Commercialization rights should be shared with the provider of the original material, based on the relative contributions of the two entities to the developed property. Failure to provide some commercial rights to the investigator and the institution will result in such material going into the public domain, with the attendant loss of incentives for improvement of the material.

As a first step to such a standard agreement, guidelines as to when derivative material ceases to be derivative (perhaps after x years?) would be helpful, as would any scheme to define joint rights in derivatives, perhaps on a sliding scale.

At the University of Wisconsin-Madison, we are requested to sign over 10 such Material Transfer Agreements per week. While many can be worked out relatively easily, some require extensive negotiation, and in a few cases, we have been unable to accommodate the needs of the source and our legal responsibilities to the federal government.

I am convinced this is a major challenge in the development of modern biomedical research.

STATEMENT

SUBMITTED FOR THE RECORD

BY

SANDOZ PHARMACEUTICALS CORPORATION
EAST HANOVER, NEW JERSEY

ON
SPONSORED RESEARCH AGREEMENTS
BETWEEN
FEDERALLY-FUNDED GRANTEE INSTITUTIONS
AND
INDUSTRIAL SPONSORS

BEFORE THE

AD HOC GROUP OF CONSULTANTS TO
THE ADVISORY COMMITTEE TO THE DIRECTOR

NATIONAL INSTITUTES OF HEALTH

JANUARY 25-26, 1994

SANDOZ PHARMACEUTICALS CORPORATION ("SANDOZ") IS PLEASED TO SUBMIT THIS STATEMENT TO THE ADVISORY COMMITTEE IN ITS CONSIDERATION OF ISSUES RELATING TO RESEARCH COLLABORATIONS BETWEEN FEDERALLY-FUNDED RESEARCH INSTITUTIONS AND THE PRIVATE SECTOR.

SANDOZ HAS A LONG-STANDING COMMITMENT TO RESEARCH AND DEVELOPMENT (R&D) IN THE UNITED STATES AND ABROAD AND WE HAVE CONTRIBUTED SUBSTANTIALLY TO THE NATION'S WELL BEING THROUGH OUR SUPPORT OF BASIC AND APPLIED BIOMEDICAL RESEARCH AND TRAINING.

THE BAYH-DOLE ACT OF 1980

CONGRESS ENACTED THE BAYH-DOLE ACT IN ORDER TO STIMULATE INDUSTRIAL INNOVATION, TO DECENTRALIZE TECHNOLOGY TRANSFER, AND TO ELIMINATE ADMINISTRATIVE BURDENS THAT HAD HAMPERED DEVELOPMENT OF NEW TECHNOLOGIES IN THE PAST. THE LAW SEEKS TO INVOLVE PRIVATE INDUSTRY IN THE INNOVATIVE RESEARCH PROCESS WITHOUT MICRO-MANAGEMENT BY THE GOVERNMENT.

THE CASE FOR INDUSTRIAL SPONSORS' PARTICIPATION IS MORE COMPELLING TODAY THAN IN 1980. ACCORDING TO REPRESENTATIVE RON WYDEN: "FEDERAL RESEARCH SUPPORT IS DECLINING, AND; AS A RESULT, DRUG COMPANIES, FEDERAL RESEARCH LABS, AND PRIVATE UNIVERSITIES AND NON-PROFITS ARE PUTTING TOGETHER DEALS TO FILL THE FINANCIAL GAP." (OPENING STATEMENT, JUNE 17, 1993, HEARING BEFORE THE HOUSE SUBCOMMITTEE ON REGULATION, BUSINESS OPPORTUNITIES AND TECHNOLOGY, PAGE 1.) THE BUDGET DEFICIT HAS CURTAILED PUBLICLY-FUNDED SUPPORT FOR R&D AT OUR NATION'S RESEARCH INSTITUTIONS, AND GOVERNMENTAL SUPPORT WILL BE INSUFFICIENT TO CARRY AMERICA INTO THE TWENTY-FIRST CENTURY. PRIVATE INDUSTRY MUST FILL IN THE

GAPS. WITHOUT HELP FROM THE PRIVATE SECTOR, GRANTEE INSTITUTIONS AND THE FEDERAL GOVERNMENT CANNOT DEVELOP PROMISING NEW TECHNOLOGIES OR TRANSLATE THE KNOWLEDGE GAINED FROM BASIC RESEARCH INTO NEW TREATMENTS FOR DISEASE.

BECAUSE THE ACT HAS ENCOURAGED INDUSTRY AND ACADEMIA TO COLLABORATE IN THIS FASHION, IT HAS PRODUCED TANGIBLE BENEFITS FOR THE AMERICAN CONSUMER IN THE FORM OF NEW TECHNOLOGIES AND INNOVATIVE CHANGES TO EXISTING PRODUCTS. EVEN WHEN THESE FRUITS OF BASIC AND APPLIED RESEARCH ARE NOT REALIZED, THE KNOWLEDGE THAT IS GAINED CONTRIBUTES SIGNIFICANTLY TO THE ADVANCEMENT OF THE SCIENTIFIC FIELD (AERONAUTICS, AGRICULTURE, HEALTH CARE, ETC.) IN WHICH THE RESEARCH IS CONDUCTED. AS A RESULT, THE ACT HAS ENSURED THAT AMERICAN TAXPAYERS' INVESTMENT IN GRANTEE INSTITUTIONS IS AUGMENTED -- AND DEVELOPMENT ACTIVITIES ARE COMPLEMENTED RATHER THAN DUPLICATED -- SO THOSE INSTITUTIONS CAN CONDUCT PIVOTAL RESEARCH WHICH THEY COULD NOT OTHERWISE AFFORD.

"FOREIGN" ACCESS TO THE FRUITS OF FEDERALLY-FUNDED RESEARCH

THE ONGOING DISCUSSIONS CONCERNING COLLABORATIVE AGREEMENTS HAVE BEEN SOMEWHAT CLOUDED BY QUESTIONING THE ROLE OF FOREIGN COMPANIES IN THIS AREA.

WHILE SANDOZ' PARENT IS, INDEED, A SWISS COMPANY, OUR PRESENCE IN THE UNITED STATES IS DECIDEDLY AMERICAN. SANDOZ WAS INCORPORATED IN NEW YORK STATE IN 1919. THE SANDOZ COMPANIES NOW EMPLOY ABOUT 12,000 PEOPLE IN THIS COUNTRY, AND SANDOZ EMPLOYEES WILL BE FOUND IN EVERY ONE OF THE 50 STATES. SUBSTANTIAL SANDOZ FACILITIES ARE LOCATED IN 11 STATES. ALL OF THE BUSINESS

ENTITIES ARE AMERICAN COMPANIES, AND THE VAST MAJORITY OF OUR EMPLOYEES AND TOP EXECUTIVES IN THIS COUNTRY ARE AMERICANS. NOT ONLY DO WE PAY SUBSTANTIAL CORPORATE TAXES, BUT OUR U.S. PAYROLL RESULTS IN ADDITIONAL TAXES TO THE FEDERAL AND STATE GOVERNMENTS OF WELL OVER $100,000,000.

WHILE AT HARVARD, LABOR SECRETARY ROBERT REICH JOINED MANY LEADING ECONOMISTS IN MAKING A PERSUASIVE CASE THAT THE LOCATION OF A CORPORATION'S HEADQUARTERS IS FAR LESS IMPORTANT THAT ITS COMMITMENT TO CREATING AND MAINTAINING HIGH-WAGE, HIGH-SKILLED JOBS IN THE UNITED STATES. IN "WHO IS US?," REICH POINTS OUT THAT, "OWNERSHIP OF THE CORPORATION IS PROFOUNDLY LESS RELEVANT TO AMERICA'S ECONOMIC FUTURE THAN THE SKILLS, TRAINING, AND KNOWLEDGE COMMANDED BY AMERICAN WORKERS -- WORKERS WHO ARE INCREASINGLY EMPLOYED WITHIN THE UNITED STATES BY FOREIGN-OWNED CORPORATIONS." SANDOZ' CORPORATE NATIONALITY IS LESS IMPORTANT THAN THE BENEFITS WE PROVIDE OUR EMPLOYEES, OUR CUSTOMERS, AND THE U.S. ECONOMY. IN PRESIDENT CLINTON'S OWN WORDS (AS STATED IN HIS INAUGURAL ADDRESS), "THERE IS NO LONGER A CLEAR DIVISION BETWEEN WHAT IS FOREIGN AND WHAT IS DOMESTIC." IN SUM, SCIENCE KNOWS NO BOUNDARIES.

EVEN IF DISTINCTIONS BETWEEN FOREIGN AND DOMESTIC COMPANIES COULD BE DRAWN, THERE IS ABSOLUTELY NO REASON TO DISCRIMINATE AGAINST FOREIGN COMPANIES IN ANY FASHION, PARTICULARLY SINCE THE BAYH-DOLE ACT DOES NOT DO SO. THE ACT PERMITS, AND INDEED ENCOURAGES, FOREIGN COMPANIES TO DEVELOP PROMISING TECHNOLOGIES -- IF THEY AGREE TO SUBSTANTIALLY MANUFACTURE RESULTING PRODUCTS IN THE UNITED STATES. THIS IS THE PREFERRED RESULT AND ONE WHICH SANDOZ ENDORSES.

THE NEED FOR EXCLUSIVE LICENSING OF FEDERALLY-FUNDED RESEARCH

PRIOR TO BAYH-DOLE, THE FEDERAL GOVERNMENT HAD A POLICY WHICH DISCOURAGED THE GRANTING OF EXCLUSIVE LICENSES. THE OBSTACLES CREATED BY THAT POLICY BECAME VIRTUALLY INSURMOUNTABLE. THE HISTORICALLY LOW RATE OF UTILIZATION OF GOVERNMENT-OWNED INVENTIONS WAS IN LARGE PART DUE TO "RESTRICTIVE GOVERNMENT POLICIES AND PRACTICES -- PARTICULARLY... THE PRACTICE OF NOT GRANTING EXCLUSIVE LICENSING." (GAO REPORT NO. 85-94, AUGUST 29, 1988). BECAUSE OF THOSE PAST POLICIES, THE RESULTS OF BASIC RESEARCH FUNDED BY THE FEDERAL GOVERNMENT WERE JUST NOT BEING MADE AVAILABLE TO THE AMERICAN PUBIC.

THE PROMISE OF EXCLUSIVITY EMBODIED IN THE ACT IS FUNDAMENTAL TO INVESTMENTS IN BIOMEDICAL RESEARCH, WHERE LICENSEES MUST INCUR SUBSTANTIAL RISKS, SPEND MANY YEARS OF INTENSE EFFORT, AND FACE STAGGERING COSTS PRIOR TO THE COMMERCIALIZATION OF A NEW PRODUCT. INDUSTRIAL SPONSORS SIMPLY MUST BE GIVEN A SUFFICIENT INCENTIVE TO JUSTIFY INVESTING IN HIGH-RISK DRUG DEVELOPMENT. CONGRESS HAS CLEARLY DETERMINED THAT EXCLUSIVITY FOR A LIMITED TIME PROVIDES THE CRITICAL INCENTIVE TO INVEST THE HUGE RESOURCES REQUIRED TO BRING A NEW DRUG FROM THE DISCOVERY STAGE, THROUGH CLINICAL TRIALS, AND HOPEFULLY, TO THE AMERICAN CONSUMER.

THE IMPORTANCE OF ACADEMIC FREEDOM IN DEVELOPING FEDERALLY-FUNDED RESEARCH

SANDOZ IS COMMITTED TO ACADEMIC FREEDOM. THAT IS WHY WE HAVE ENTERED INTO NUMEROUS RESEARCH AGREEMENTS IN WHICH WE COOPERATE WITH GRANTEE INSTITUTIONS. THE PRINCIPLES OF ACADEMIC FREEDOM THAT GUIDE THOSE INSTITUTES ENCOURAGE AND SAFEGUARD AN ENVIRONMENT IN WHICH SCIENTISTS ARE FREE TO CONDUCT RESEARCH THAT STIMULATES THE MOST SOPHISTICATED AND CREATIVE BIOMEDICAL RESEARCH IN THE WORLD, TODAY. SANDOZ BELIEVES THAT EVERY EFFORT MUST BE MADE TO PRESERVE THAT ATMOSPHERE. TOGETHER WITH OUR GRANTEE INSTITUTIONS WE HAVE TAKEN EVERY STEP TO ENSURE THAT NO FACET OF OUR AGREEMENTS COMPROMISES THE RIGHT OF SCIENTISTS TO PURSUE THEIR OWN IDEAS. THE RELATIONSHIP OF SANDOZ WITH, AND SUPPORT OF, ACADEMIC INSTITUTIONS DO NOT, IN ANY WAY, JEOPARDIZE TRADITIONAL ACADEMIC BEHAVIOR AND STANDARDS.

CONCLUSION

HEART DISEASE AND CANCER, THE TWO LEADING CAUSES OF DEATH AMONG AMERICANS, ARE EXPECTED TO ACCOUNT FOR ONE-FIFTH OF OUR COUNTRY'S EXPECTED TRILLION DOLLAR HEALTH CARE BILL THIS YEAR. GOVERNMENT HEALTH COSTS FOR ALZHEIMER'S DISEASE -- WHICH DEVASTATES FOUR MILLION AMERICANS AND COSTS $100 BILLION EACH YEAR -- ARE EXPECTED TO INCREASE DRAMATICALLY AS THE POPULATION AGES. THE IMPACT OF AIDS UPON OUR SOCIETY IS ALSO DRAMATIC IN TERMS OF HUMAN SUFFERING AND HUGE EXPENDITURES.

THE ONLY DIRECT WAY TO IMPACT THESE AND OTHER HEALTH PROBLEMS IS TO DELIVER, AS QUICKLY AS POSSIBLE, THE BENEFITS OF TECHNOLOGICAL BREAKTHROUGHS TO THE PATIENT. SUCH A DELIVERY

SYSTEM MUST INVOLVE THE GREATEST UNIVERSITIES AND RESEARCH CENTERS IN THE WORLD, WHICH ARE LOCATED IN THE UNITED STATES. THEY LEARNED THEIR LESSONS EARLY, NAMELY, THAT THE KEY TO TECHNOLOGY DEVELOPMENT IS TO TRANSFER NEW IDEAS FROM THE RESEARCH LAB TO THE MARKETPLACE IN AN EFFICIENT MANNER. DURING THE PAST DECADE, GOVERNMENT BEGAN TO LEARN THAT LESSON AS WELL. AND, AS A RESULT OF THE BAYH-DOLE ACT, GRANTEE INSTITUTIONS -- AS WELL AS THE FEDERAL GOVERNMENT -- HAVE BECOME OBLIGATED TO PROMOTE THE COMMERCIALIZATION OF INVENTIONS DEVELOPED WITH FEDERAL SUPPORT.

WHILE IT CANNOT BE MEASURED WITH SCIENTIFIC PRECISION, IT IS BEYOND DOUBT THAT THE BROAD SPECTRUM OF COLLABORATIVE RESEARCH PROMPTED BY THE ACT HAS SOWN THE SEEDS FOR MANY THERAPEUTIC BREAKTHROUGHS SUBSEQUENTLY DEVELOPED BY THE PHARMACEUTICAL INDUSTRY. IN THE FINAL ANALYSIS, IT IS THE AMERICAN PUBLIC THAT BENEFITS FROM INDUSTRY-SPONSORED RESEARCH AGREEMENTS. AS THE MYSTERIES OF HUMAN BIOLOGY ARE UNCOVERED AND NEW PREVENTIVE AND THERAPEUTIC STRATEGIES ARE DEVELOPED, THE INVESTMENT IN COLLABORATIVE RESEARCH YIELDS GREAT RETURN BY IMPROVING THE HEALTH STATUS OF AMERICANS AND MILLIONS OF PEOPLE AROUND THE WORLD.

THIS MEANS, OF COURSE, THAT THE GOVERNMENT'S AND THE GRANTEE'S OBLIGATIONS DO NOT TAKE PRECEDENCE OVER THEIR RESPONSIBILITY FOR ASSURING THE PROPER USE OF FEDERAL FUNDS, PROTECTING THE PUBLIC INVESTMENT IN BIOMEDICAL RESEARCH, AND SAFEGUARDING THE PUBLIC INTEREST. NEVERTHELESS, CONGRESS HAS MANDATED THAT AGENCIES SUCH AS NIH SUPPORT A VIGOROUS TECHNOLOGY TRANSFER PROGRAM THAT STRIKES A REASONABLE BALANCE BETWEEN

PROTECTION OF THE PUBLIC INTEREST AND SUCCESSFUL COMMERCIALIZATION OF IMPORTANT NEW INVENTIONS. FORUMS SUCH AS THIS, WHICH THE ADVISORY COMMITTEE HAS CONVENED, ARE INDICATIVE OF THAT SUPPORT.

SANDOZ BELIEVES THAT THIS DIALOGUE CAN RESULT IN AN INCREASED CONCENTRATION OF EFFORTS BY ALL PARTIES INVOLVED IN THIS SYNERGISTIC PARTNERSHIP -- GOVERNMENT, INDUSTRY, AND ACADEMIA -- TO PROMOTE TECHNOLOGY TRANSFER WITHIN THE EXISTING STATUTORY FRAMEWORK. IF, HOWEVER, TODAY'S DISCUSSIONS SIMPLY RESULT IN INCREASED EFFORTS TO MICRO-MANAGE THE INNOVATIVE PROCESS, MUCH OF THE PROGRESS SINCE 1980 WILL BE UNDONE. IN THE ABSENCE OF NEW POLICY CHOICES AND THE ENACTMENT OF NEW LEGISLATION BY CONGRESS, SANDOZ BELIEVES THAT WE SHOULD FOSTER AN INNOVATIVE RELATIONSHIP BY WORKING WITHIN EXISTING POLICIES.

SANDOZ LOOKS FORWARD TO CONTINUED DIALOGUE WITH THE COMMITTEE, THE NIH, AND POLICYMAKERS ON THESE IMPORTANT AND CHALLENGING POLICY ISSUES.

COUNCIL ON GOVERNMENTAL RELATIONS
One Dupont Circle, Suite 425 Washington, D.C. 20036 (202) 331-1803 FAX: (202) 331-8483

STATEMENT BY

THE COUNCIL ON GOVERNMENTAL RELATIONS

PRESENTED TO THE NATIONAL INSTITUTES OF HEALTH

JANUARY 25 - 26, 1994

SPONSORED RESEARCH AGREEMENTS: PERSPECTIVES, OUTLOOK AND POLICY DEVELOPMENT

National Institutes of Health
Forum on Sponsored Research Agreements:
Perspectives, Outlook and Policy Development

The Council on Governmental Relations (COGR), an association which comprises 137 of the leading research universities in the United States, is pleased to submit a statement for the record, as NIH convenes the Forum on Sponsored Research Agreements: Perspectives, Outlook and Policy Development. COGR deals extensively with policies and technical issues involved in the administration of federally sponsored programs at universities, and is keenly interested in the spectrum of issues reflected in the Forum agenda. We commend NIH for planning and facilitating a needed government/university/industry dialogue, and for opening this dialogue with a thoughtfully prepared agenda.

We understand that the purpose of the Forum is to provide recommendations that will be used in NIH's development of general principles to guide grantee institutions as they negotiate research-support agreements with industrial sponsors. The Forum agenda, contributions by the several outstanding speakers and panelists, and public comments should yield a rich body of material useful to that purpose.

Beyond the Forum proceedings, COGR is pleased to contribute to the material you will consider a set of two recently printed documents. One is a guide to the Bayh-Dole Act and its implementing regulations. The other is a set of twenty questions and answers on university technology transfer practices. Taken together, these documents serve as a primer on the subject, and speak directly to many of the topics and issues mentioned in the Forum agenda. These materials, combined with the government/university/industry dialogue facilitated by the Forum and the findings from the NIH survey of commercialization agreements, should provide an informed basis for the guidelines you contemplate. COGR looks forward to further opportunities to participate in formulating and refining those guidelines.

Since their inception, universities have been engaged in technology transfer through their traditional activities of teaching, research and publication. In recent years, universities have become increasingly aware of the commercial potential of these research findings, and have placed greater emphasis on transfer of technologies through patenting and licensing of inventions to the private sector. These efforts have been encouraged and underpinned by the Bayh-Dole Act and other closely related legislation. These laws were enacted by Congress to increase U.S. commercial innovation, productivity and competitiveness in the marketplace by stimulating commercialization of inventions resulting from federally funded research and development.

The results have been very favorable, and the cumulative base of technology transfer knowledge, experience and capability now in place promises even more impressive results in the future than have been seen to date. The laws and the public policies they reflect are sound. We are glad to see the Forum aimed at guidelines that will further enhance application of these laws and policies. We strongly disagree with those who suggest that the Bayh-Dole Act has outlived its usefulness. In a 1989 survey reported by the National Science Foundation, which included 76 major American firms in seven manufacturing industries, executives

stated that a substantial portion of new products and processes introduced between 1975 and 1985 depended upon academic research and development. They explained that these products either could not have been developed in the absence of recent academic research or were developed with very substantial aid from recent academic research. This is testimony to the ongoing cooperation between universities and industry, which is vital to U.S. international competitiveness and which government policy should continue to nurture.

We appreciate this opportunity to comment, and look forward to further opportunities in the future to assist NIH in development of its guidelines for research agreements between NIH grantees and industrial sponsors.

FORUM ON SPONSORED RESEARCH AGREEMENTS
January 26, 1994
Session IV

Statement of the Wistar Institute

Warren Cheston, Ph.D., Director, External Affairs

The Wistar Institute wishes to express its strong support of the past and current efforts of the National Institutes of Health to involve its grantee institutions in the transfer of the results of NIH supported research to the commercial sector resulting in products for the improvement of the public health. We believe that this tri-partite effort among the grantee institutions, NIH, and the commercial sector has had extraordinary success.

Wistar's experience working with NIH in this effort began in the late 1960s. As the result of NIH supported research, Wistar had developed two viral strains potentially useful for the production of vaccines against rubella and human rabies. Under Letters of Determination entered into between Wistar and the Assistant Secretary for Health, Wistar was granted rights to patent these strains and to license them to vaccine manufacturers in the United States and Europe. These vaccines became accepted throughout the world and remain the primary vaccines against these diseases. Three companies market rabies vaccines and over 10 market rubella vaccines based on these Wistar strains. As a beneficial side effect, until the Wistar patents expired in the late 1980s Wistar earned royalties from the sales of these vaccines by the manufacturers. Annually these royalties were a significant part of Wistar's operating income. Consistent with Wistar's obligation under the Letters of Determination, all this income was used in direct support of Wistar's research program, supplementing NIH supporting grants. This represents a "no-lose" situation for all involved: Wistar, NIH, the vaccine manufacturers, and, importantly, the general population not only of the United States but also of other countries throughout the world.

Because the Letter of Determination was a cumbersome mechanism to involve NIH grantee institutions in the transfer of government-owned technology to the commercial sector, the Institutional Patent Agreement (IPA) was developed by which the grantee institutions and the Assistant Secretary for Health entered into a contract specifying the terms under which the Federal Government's rights to interventions were transferred to the grantee institutions. Wistar was awarded such an IPA, by which the rights to a number of patents involving inventions developed in the late 1970s and early 1980s were conveyed to Wistar. The IPA and the governmental policies and procedures evolving out of the Bayh-Dole Act and successor legislation have been the basis for Wistar's successful technology transfer

program. This program continues to generate a significant part of Wistar's operating income. Once again, all participants in this enterprise benefit by enlightened Federal policies and, equally important, wise implementation of these policies by NIH.

Wistar recognizes that there has been criticism of NIH because of alleged improprieties of some NIH grantees in their management of the rights granted to them by NIH. There has been a call for more detailed oversight by NIH of grantee institutions in the management of these rights. We at Wistar realize that such an increase in oversight may be required to satisfy those whose confidence in the probity of the not-for-profit sector in managing what is public property may not be particularly high. If such changes in NIH's method for dealing with its grantees turn out to be inevitable, we are optimistic of the likely effects of such changes on NIH's goals in working with its grantees and, through them, the for-profit sector to maximize the public benefit to be derived from intellectual property generated by NIH funded research. We would appreciate the opportunity to participate in a dialogue with NIH in its areas of concerns, sharing our experience over the past two decades.

Fundamentally, Wistar believes that much of the success of the past through the mechanisms of the Letter of Determination and the Institutional Patent Agreement rests in the flexibility these mechanisms provided to grantee institutions in negotiating contracts with companies in the commercial sector. Each party to such a contract hopes to achieve certain goals in the contract negotiation. The limitations placed on the abilities of grantee institutions to develop acceptable compromises based on the Letters of Determination, Institutional Patent Agreements, and policies evolving from the Bayh-Dole Act have been real and of consequence. To mention just a few: the "march-in-rights" reserved by the Federal Government and the "made primarily in the United States" concept have both been of concern to commercial entities, especially when such an entity has its main focus outside the United States. Wistar's experience has been that when the public need for such restrictions and limitations has been explained, even the most unsophisticated company is willing to accept such restrictive covenants in their contracts with NIH grantee institutions. Any alteration in the way that NIH provides oversight to grantee institutions to whom government patent rights have been transferred should be based on public policy concerns whose logical basis is clear and easy to convey to those companies who will potentially develop and market products based on these government patent rights.

Finally, a few comments are in order on the effects of technology transfer partnerships between NIH and its grantees that have evolved in the past decades. It is impossible to overstate the positive effect on The Wistar Institute of the income stream that has resulted from this partnership. Such an unrestricted income stream has enabled Wistar to significantly supplement the funds it derives from peer-review sources. Its

impact is enhanced because of its unrestricted nature and, therefore, may be freely allocated by Wistar's director to satisfy the highest priority internal needs. For example, it is a resource for the younger scientists prior to their generation of peer-review support and for older scientists who wish to venture into new fields.

In addition, the concept of directly affecting the public health through the commercialization of inventions resulting from basic research continues to be a stimulating factor to a segment of Wistar's scientific staff. This stimulus has been possible through the enlightened policies on inventorship rights adopted by the Federal Government and, particularly in Wistar's case, by NIH.

As the ability of NIH to fund research proposals deemed worthy by peer-review diminishes, institutions such as Wistar have increased their technology transfer efforts to generate an alternative stream of income. The 1993 survey by the Association of University Technology Managers shows that the technology transfer efforts of U.S. universities and hospitals generated over $215 million in royalty income during FY 1992. Much of that income has gone to the support of biomedical research. Since Wistar is neither a university nor a hospital, it was not included in this survey. If it had been, it would have ranked 12th among universities and, if normalized to the size of research support received from the Federal Government, it would have ranked 3rd in the royalties earned in FY 1992. From these figures alone, it is quite clear why Wistar is concerned about NIH policies with respect to implementation of the Bayh-Dole Act.

H.S. LEAHEY
PRESIDENT
ASSOCIATION OF UNIVERSITY
TECHNOLOGY MANAGERS (AUTM)

BACKGROUND

Since the passage of the Bayh-Dole Act in 1980 (PL 96-517) the granting of title to inventions to non-profit recipients of US government research funding has produced unprecedented access of research results to US-based companies. Because of this change in federal policy and increasing competitive pressures on a global basis, industry looks to the research community as a source of new technology, forging partnerships that encourage investment in new technology and the transfer of that new technology to industry for the development of products benefiting society.

In an attempt to provide data that are vital to understanding the benefits of non-profit technology transfer programs to society AUTM, sponsored its first technology transfer survey of North American non-profit research institutions.

SURVEY RESULTS

The AUTM members responding represented 112 US universities and hospitals, 10 Canadian universities and hospitals and 8 other organizations, including research institutes, patent management firms and government laboratories.

Phase I of the Survey is complete and the raw data with FY 91 and FY 92 results has been distributed to AUTM members. This survey shows that the nonprofit research community is now actively engaged in technology transfer.

In FY 92, the respondents :

granted 1,731 licenses, including 371 licenses to startup companies;
reviewed 7,604 invention disclosures;
filed 3,251 patent applications;
managed 3,177 active licenses earning royalties.

In addition, the study confirms that licenses to US-based companies, foreign companies and small business are consistent with the earlier GAO sponsored studies.

Phase II of this study has begun and will include an statistical analysis of the data aimed at creating "metrics" or standards of measurement for licensing activities. These data will be presented to the membership at the AUTM Annual Meeting in Phoenix, AZ in February, 1994.

Phase I of a second study, the AUTM Public Benefits Survey, is now complete and the data includes specific examples of products on the market, companies created, and licenses granted to small companies. While anecdotal, this study will provide additional insight into the benefits of technology transfer.

Finally, AUTM is providing seed funding for several leading economists to meet with AUTM members to discuss a project that would evaluate the economic impact of technology transfer on society. Specifically AUTM wishes to collect data on the impact of licensing on job retention and creation.

BENEFITS TO SOCIETY

It is the belief of AUTM that, dollar for dollar, investigator-based research is the best investment the government can make. These funds are used by universities and medical centers to advance scientific knowledge, educate students, train an advanced work force, and improve the standard of living for the public.

The benefits resulting from the protection intellectual property and the transfer of this knowledge to industry include the development of new products, the investment of private funds resulting in the creation of high quality jobs, and the payment of taxes on a broader sales base, providing a direct reimbursement of the government's investment in research.

AUTM endorses NIH's efforts to give guidance to the research community in their relationships with industry. Such guidelines are necessary to remind recipients of Federal research support of their responsibilities as stewards of public funds. These guidelines should require the development of policies at each research institution that emphasize the use of electronic databases to announce availability of license rights; grant license preferences for US manufacturers, especially small businesses; submit annual Federal invention utilization reports; avoid unmanageable conflicts of interest and abuse; and protect academic freedom.

AUTM's survey results show that Bayh-Dole is working well, and that Federal grant and contract recipients are generally conscientious about their stewardship responsibilities. AUTM members look forward to reviewing the draft guidelines and making detailed suggestions. Thank you.

ABOUT AUTM

AUTM was formed in 1974 as a nonprofit professional and educational society and assists its members with programs on:

Organization of Technology Transfer Offices;
Professional Development;
Management of their stewardship responsibilities to research sponsors;
Advancement of their public service mission, including economic development.

AUTM has over 1100 members with about one-half representing approximately 260 US and Canadian non-profit research institutions; and one-half comprising representatives of small, medium and large technology-based businesses, venture capital firms, government research laboratories, government agencies, especially economic development agencies at the federal, state and local levels, and patent management firms.

AUTM membership has grown at rates exceeding 20% per year congruent with the rise in awareness that technology transfer is a valuable competitive weapon in a challenging global economy.

Jack L. Tribble, Ph.D.
Patent Counsel

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CONFIRMATION

January 14, 1994

Ms. Peggy Schnoor
NIH
Shannon Building, Room 218
9000 Rockville Pike
Bethesda, MD 20892

Dear Ms. Schnoor:

This is in response to the notice of December 30, 1993, 58 Federal Resister 69369 seeking comments on the various topics for discussion at the Forum on Sponsored Research Agreements: Perspectives, Outlook and Policy Development. We will not ask for time to speak at the January 26, 1993 meeting but do request that this letter be placed in the record as the Merck & Co. position regarding the licensing of inventions made with Federal funding which can be used for research purposes.

Over the years Merck has completed numerous transactions with academic institutions receiving NIH funding which required licensing to be carried out under the Bayh-Dole Act, 35 USC §§ 200-212 (Act). A trend has recently emerged in which the availability of federally funded inventions is being restricted and is impeding the advancement of biomedical science within the U.S.

The stated intent of the Act is to assure that the patented results of federally funded research be made broadly and rapidly available for all scientific investigation irrespective of the objectives of the research and the terms under which licenses are granted for the sale of products under the patents. Merck supports the licensing of patented inventions for research use separately from licensing for commercial development of products for sale. Research use as used herein, refers to biological or biochemical compounds or processes that are useful for drug discovery and excludes the use of those compounds that can be used specifically as therapeutic agents. Examples of research tools include cDNA clones, receptors, monoclonal antibodies, transgenic animals and other inventions that can be used for drug discovery. While it

may be appropriate to license development products exclusively, the exclusive licensing of materials for research, i.e. research tools, limits scientific advancement. Merck is aware of a number of situations where federally supported inventions have not been made available to qualified scientists able to utilize the technology for research purposes. In some cases research licenses are not available at any price.

It is recognized that one purpose of the Act is to permit government funded patentees to grant exclusive licenses for the commercialization of products. This purpose can be accomplished and at the same time the broader intent of the Act be met, i.e., that inventions be utilized as broadly as possible. Accordingly, it is Merck's position that a federally funded patentee should grant non-exclusive licenses for research tools independent of licenses for products for sale.

A policy that promotes open and broad access of research tools discovered under federally funded research programs, under a non-exclusive license, would foster competition among commercial laboratories to discover and ultimately develop human health products, thereby meeting the Congressional intent of the Act. Therefor, NIH should develop and implement a clear statement of policy that promotes the non-exclusive licensing of basic research tools to academic and commercial laboratories for research purposes.

Sincerely ,

Jack L. Tribble, Ph.D.
Patent Counsel

cc: Mr. Paul D. Matukaitis, Director of Patents
Dr. Benjamin Shapiro, Executive Vice President, World Wide Basic Research

Appendix E

Background Leading to the Forum

TASK FORCE ON THE COMMERCIALIZATION OF INTELLECTUAL PROPERTY RIGHTS FROM NIH-FUNDED EXTRAMURAL RESEARCH

DRAFT REPORT

MAY 25, 1993 MEETING

Invited Participants

NIH Task Force Meeting
May 25

David Blumenthal, Chief, Health Policy Research and Development Unit, Massachusetts General Hospital

James Burris, Associate Dean for Research Operations, Georgetown Medical Center

Stan Heimberger, Publisher, *Clinical Therapeutics* and *Current Therapeutic Research, Clinical and Experimental*

Susan Kramer, Director, Department of Cell Analysis, and Head, Research Contracts and Reagents Program, Genentech

Ronald Lamont-Havers, Deputy Director for General Affairs, Cutaneous Biology Research Center, Massachusetts General Hospital

Lou Lepene, Vice President for Business Development, Interneuron

Malcolm Moore, Professor of Cell Biology and Head, James Ewing Laboratory of Developmental Hematopoiesis, Memorial Sloan-Kettering Cancer Center

Lita Nelsen, Director, Technology Licensing Office, Massachusetts Institute of Technology

INTRODUCTION

The NIH Task Force on the Commercialization of Intellectual Property (task force) convened on May 25, 1993 the first of two advisory meetings to learn the views of representatives from the university and industry communities regarding technology transfer and related issues. The perspectives gained from these two communities will be considered by the task force as it prepares a report for the NIH director in response to a request from Representative Ron Wyden, chairman of the Subcommittee on Regulation, Business Opportunities and Energy of the House Committee on Small Business. Representative Wyden's inquiry stems from his review of a pending comprehensive technology transfer agreement between Sandoz, a pharmaceutical corporation based in Switzerland, and the not-for-profit Scripps Research Institute in San Diego, California, which received $61.2 million for research from NIH in fiscal year 1992.

The May advisory meeting was arranged as an informal roundtable discussion, allowing five representatives from academic institutions and three from companies in the private sector to discuss candidly their views on technology transfer arrangements at their own institutions and elsewhere. More than a dozen officials from NIH also participated in this dialogue. Sandy Chamblee, who chairs the task force, presided over the meeting.

CONSIDERATION OF THE SCRIPPS-SANDOZ AGREEMENT

Although elements of the Scripps-Sandoz agreement were introduced as part of the discussion during the May meeting, most participants expressed discomfort at trying to analyze that agreement when detailed information about it is not available. NIH officials have discussed the agreement with representatives from Scripps. However, neither they nor the non-NIH participants at the May meeting are familiar with the details of that pending agreement.

Nonetheless, the outlines of the proposed Scripps-Sandoz agreement, which has been described in the news media, helped to frame many of the issues for discussion. Perhaps more than any single detail, the broad scope of that agreement appears to be most troubling—a case where the sheer reach of its provisions seems to have led to a qualitative difference from other such partnerships, one participant observed.

Although certain provisions in the Scripps-Sandoz agreement appear to be objectionable, the size and sweep of this agreement amount to a mitigating factor, several participants noted. Thus, it appears unlikely that very many other corporations will be capable of proposing such undertakings with not-for-profit research institutions and, similarly, few of the latter organizations are likely to find such corporate partners—

particularly if the agreements between them continue to trigger congressional and administrative inquiries.

Perhaps more to the point, such large-scale partnerships seem to represent the research world's equivalent of very special "love affairs." The so-called "mega" deals tend to arise when individual corporate and research-institution representatives discover one another on professional common grounds, see opportunities for special synergy, and propel their respective institutions into establishing a broad partnership. Although such large-scale agreements appear to be rare events, they sometimes grant a great deal of valued freedom to the investigators at the recipient institution whose work is being supported.

CONSENSUS VIEW IS THAT OVERALL SYSTEM IS WORKING

In the course of the discussion, participants at the May meeting identified certain themes regarding technology transfer arrangements on which there is wide general agreement. Foremost, representatives from both academic institutions and industry say that current efforts to transfer federally supported basic biomedical research into practical benefits for the United States—in terms of developing and producing new drugs or other clinical treatments—are working very well. Thus, considerable care is needed not to harm a system that is performing satisfactorily and meeting its mandated goals.

This cautionary note—the need to exercise care to preserve a working system—is particularly important during the current period when the pharmaceutical-biotechnology industry appears to be in a state of considerable flux. Health care reform, rapidly changing technologies, new and reemerging diseases, continuing shifts in demographics, and internationalization of research in general and of the industry in particular are among the factors that are changing the character of the health care industry as a whole and the pharmaceutical and biotechnology components of it in particular. Any attempt to regulate a component practice, such as technology transfer, of this larger enterprise will need to be considered within the context of the broad changes occurring in the industry.

At the early phase of negotiations when a particular technology transfer agreement is first being contemplated, relationships between the potential partners are apt to be fragile. Forcing them to comply with an elaborate or rigid set of federally determined rules could prove unwieldy and perhaps disastrous, several meeting participants noted. If the system were to become more bureaucratic than it already is, many university-based researchers may simply refuse to participate—a refusal that would tend to slow the conversion of research into useful technologies.

A reasonable safeguard might be to insist on disclosure and some form of review for large-scale agreements of the sort similar to the one between Sandoz and Scripps. Thus, for institutions such as Scripps that receive substantial support from Federal sources, some form of public review may help to alleviate abuses and protect against public concerns. However, participants emphasized, it would not make sense to subject small- or mid-scale arrangements to such reviews, as it would discourage partnerships from being formed. The existence of such agreements should be acknowledged, but details about them are considered proprietary, participants pointed out.

DIFFICULTIES IN ASSESSING A HIGHLY VARIED SYSTEM

The consensus view of the meeting participants that the current technology transfer system works did not amount to a blanket approval of all practices within the current process for converting basic biomedical research findings into clinically useful products. None of the participants tried to argue the system has been optimized or that abuses never occur. Indeed, no one at the advisory meeting considered it now possible to judge rigorously the overall performance of the U.S. system for technology transfer—if, indeed, it can be called a "system" at all. One participant pointed out that empirical evidence on which such judgments could be based is scanty at best. Although systematic surveys are under way, the analysis of the data now being collected has not begun.

In general, predicting financing trends in biotechnology is difficult. Thus, asserting that the large-scale agreement being contemplated by Scripps and Sandoz represents a "trend" is problematic at best. In any case, most participants consider the evidence for such a trend very doubtful. As a corollary to that belief, meeting participants argue that it does not make sense to try to regulate general practices based on exceptional cases such as the Scripps-Sandoz partnership appears to represent.

From anecdotal experience, which is plentiful, participants agree that the technology-transfer system is anything but uniform in profile. As one participant noted, the system is "cranky but effective." Its success rests largely on a Federal policy decision dating back to the post-World War II period to invest heavily in basic, untargeted biomedical research. The success of that policy continues to prove solid and Federal support for biomedical research "needs to continue," participants agree.

However, now and during at least one earlier period since World War II, doubts have been cast on the reliability of that Federal support system. Those periods of funding uncertainty or decline have been marked by upheavals among university researchers as they have had to scramble for alternative sources of funding. Thus, for example, during the mid-1970s, when Federal support for biomedical research stagnated, university investigators turned to

industry for the first time on a large-scale basis, and this practice became integrated into the system because it was viewed as a necessary stabilizing force. In recent years, as NIH budgets once again have stagnated, university researchers have come under renewed pressure to seek out alternative sponsors from both domestic and foreign sources in the private sector, participants noted.

Meanwhile, during this same period, other developments have encouraged closer ties between university-based researchers and industry. For instance, by the 1980s, with the coming of age of broadly applicable technologies that arose from that basic research, new means to realize useful products were proving profitable. At least to some observers, that profitability is another indication of the system's overall success, at least as measured by standard criteria in a market-driven economy. From a public policy standpoint, however, the challenge is to discern the point at which private sector profits cease to be perceived as acceptable and begin to appear exploitative.

Just as NIH has supported highly diversified biomedical research undertakings throughout the country, so many institutions encourage research faculty members to pursue their own research interests and to forge their own alliances to further that research. Indeed, suggested one meeting participant from the technology transfer department of a leading U.S. university, diversity also characterizes the system of contracts and alliances that results from these investigator-driven efforts. Thus, even within a single institution, the terms of technology transfer agreements tend to be very different from one another. Although the view that each agreement is unique admittedly is extreme, it points to the extraordinary variety that exists throughout the system. Significantly, many participants—but not all of them—are convinced that such diversity acts as a safeguard against abuses.

Although the number of biomedically related technology transfer agreements between universities and companies has multiplied rapidly during recent years, the funds transferred from industry into research institutions because of those arrangements still represent a relatively small fraction of overall research budgets for academic and similar not-for-profit institutions. Moreover, although a handful of high-profile technology transfer programs at specific institutions have resulted in some spectacular economic successes, many and perhaps most of those programs apparently are not yet breaking even. This economic reality—that promising research may not fulfill commercial expectations or, at least, may take years to produce a net return on investment through royalties for the research institution—is considered another long-term safeguard on the integrity of academic institutions within the system.

Another key point that is little appreciated: technology transfer is by no means a one-way process. Thus, not all the flow of information and materials is from NIH and universities to industry. For instance, not only do companies publish many of their research findings to make them rapidly accessible to the wider research community, but in some cases, companies also supply valuable reagents and knowhow to researchers at universities and at NIH—sometimes in the absence of arrangements that include clearly delineated proprietary benefits for the companies.

IDENTIFYING RISKS, BENEFITS OF TECHNOLOGY TRANSFER AGREEMENTS

The participants at the May advisory meeting identified several risks as well as benefits to current technology transfer programs at universities and other not-for-profit research institutes. In the course of identifying the risks in these programs, participants emphasized that none of those risks can be considered so large as to overwhelm the benefits. The crucial question is more a matter of determining a fair balancing of benefits among private and public sector collaborators as well as the public at large.

For example, there is a risk that provisions in technology transfer agreements may decrease or delay the dissemination of research finding. Participants acknowledge the fact that potentially useful biomedical research developments sometimes are "deep-sixed" by companies and agree that such instances are deplorable.

After establishing a collaborative effort with an industrial partner, a not-for-profit institution can become "overly dependent" on industrial sources of funding, which "don't last forever." Moreover, too good a patent or too rigid a licensing program can spell future trouble for an institution. For instance, if a patent covers what proves to be lucrative technology, the university may be required to spend considerable sums in attorneys' fees to protect its financial interests in proceedings within the Patent and Trademark Office or in court.

Another peculiar risk to efficient technology transfer is embedded in provisions of the Bayh-Dole Act. Those provisions establish for Federal agencies a right to royalty-free use of products emanating from federally sponsored research. Some university representatives cite these provisions to explain why they avoid technology transfer agreements from inventions in defense-related research programs, for which the Government might be the principal consumer. In such instances, the potential for payback royalties to the university are essentially nullified. What impact these provisions may have on biomedically related research and attendant technology transfer agreements is not yet known, although the congressional Office of Technology Assessment is investigating this matter.

Although the fear of the U.S. pharmaceutical-biotechnology industry losing its competitive edge to foreign companies was considered as an economic risk, industry representatives at the meeting pointed out several difficulties in evaluating this issue. One difficulty comes from the increased problem in distinguishing national from truly foreign and from international corporations. If a "foreign" company supports U.S. research and then also manufactures its products in a U.S. facility and employs U.S. citizens, the seeming risk to the domestic economy is minimized by these arrangements. Moreover, the sponsorship of clinical trials outside the United States in Europe and Japan also can serve the best interests of U.S. consumers. In any case, if a useful drug becomes available to the American public, then a clear benefit has been realized from the Federal basic research investment—regardless of what corporate entity is making the product.

Even granting some tangible basis to the economic concerns that arise from too great a dependence on foreign investments to develop U.S.-initiated basic research findings, most times a university simply has no choice when it comes to identifying a corporate collaborator, pointed out a university representative. Although most parties would prefer to structure alliances not to rely so heavily on foreign investors, domestic partners often may not be available.

Typically, only a single partner emerges as a potential sponsor for a particular research program, meaning the technology transfer project often has only that one chance to be funded. Moreover, even if the initial agreement is developed between a university and a domestic corporate sponsor, a small undercapitalized company may eventually release its license to a foreign corporation, sometimes without permission or the foreknowledge of the university researchers. In any event, trying to regulate these transactions to reduce this risk appears problematic, several participants noted.

One objectionable element of the Scripps-Sandoz agreement is an apparent provision that greatly broadens the scope of Sandoz's access to research findings obtained by Scripps investigators. The concern is that Sandoz will claim exclusive rights to technology and knowhow developed with substantial help from other resources, including funding from NIH. All the participants considered this provision, if accurately described, unacceptable. The idea that a corporate sponsor can buy all rights to all technology developed at an institution, even when it continues to receive considerable support from Federal sources, "won't pass the 'smell test' of public policy," said one participant from a university-based hospital.

However, university participants noted that large-scale agreements, including the one contemplated between Sandoz and Scripps, as well as agreements that are much smaller in scope,

run into a problem that is commonplace in virtually any research project or program—namely, how internal boundary lines are determined. Frequently, a project may have several sponsors, and it is difficult in most cases to determine whose funds supported which developments within a project or program. When things go well, ambiguous boundaries can work to benefit the public. For example, corporate sponsors can better marshall their resources and more effectively convert research developments into products, university participants say. On the other hand, the practice can be portrayed in a negative light, as companies "skimming the cream."

Determining in a generic fashion how boundaries should be drawn is very difficult, if not impossible, participants said. Most of the time, agreements between research institutions and corporate sponsors are developed at an early stage of research when the full potential of the project or program cannot be described. Thus, if multiple sponsors are supporting the program and its scope is broad and fundamental, the commercial outcomes are not likely to be predictable. Absent such particulars, it is necessary to fall back on common sense rather than some regulatory scheme to assure that the outcome is fair.

DEFINING THRESHOLDS OF ACCEPTABLE CONDUCT

May meeting participants attempted to outline a set of generally acceptable standards that any university or similar research institution would likely insist on meeting when it establishes technology transfer agreements with corporate partners. The following set of guidelines is observed by one prominent U.S. university that sponsors a wide range of technology transfer agreements.

- There should be no restrictions on who may visit university laboratories or confer with faculty.

- The time period in which a particular corporate sponsor enjoys exclusive rights to develop basic research should be limited. Thus, if that sponsor is not interested in certain findings, then other potential sponsors should be allowed ready access to them so that the development can be pursued.

- Investigators are allowed to publish or otherwise disseminate their findings rapidly, with an allowance made to file patent applications.

- Investigators have authority over what research is conducted in their laboratories; that is, they should not be forced into doing projects that do not fulfill the usual criteria they may set.

- The institution owns all patents, but it will grant exclusive licenses.

- Corporate partners that license technology and develop products for commerce agree to indemnify the university from any lawsuits that might arise from such commerce.

- Overhead rates are uniform throughout the institution.

Other participants noted additional safeguards that are valuable, perhaps essential, elements of technology transfer agreements. For instance, even when a particular arrangement is large-scale and specified over a multi-year period, it is important that it not grant comprehensive exclusive licensing rights to a single entity when, in fact, research is being sponsored by several or many entities. To do otherwise is tantamount to converting a not-for-profit research institution into a research-contract agency.

Another safeguard, which some not-for-profit institutions already insist on, is to require that faculty receive a substantial proportion of their overall research support from peer-reviewed sources.

TASK FORCE ON THE COMMERCIALIZATION OF INTELLECTUAL PROPERTY RIGHTS FROM NIH-SUPPORTED EXTRAMURAL RESEARCH

DRAFT REPORT

JUNE 9, 1993 MEETING

Invited Participants

NIH Task Force Meeting
June 9, 1993

Stephen J. Banks, President, BCM Technologies, Inc., Baylor College of Medicine

Karen Holbrook, Associate Dean of Scientific Affairs, University of Washington

Michael R. Koch, Associate Director of Corporate Licensing and Development, Hoffman-LaRoche

Cornelius Pings, President, Association of American Universities

Carol Tracy, Director, Office Technology Transfer, Georgetown Medical Center

Michael Williams, Vice President for Neurological Research, Abbot Laboratories

INTRODUCTION

The NIH Task Force on the Commercialization of Intellectual Property (task force) convened on June 9, 1993 the second of two advisory meetings to air the opinions of representatives from the university and industry communities regarding technology transfer and related issues. The perspectives gained from these two communities will be considered by the task force as it prepares a report for the NIH director in response to a request from Representative Ron Wyden, chairman of the Subcommittee on Regulation, Business Opportunities, and Energy of the House Committee on Small Business. Representative Wyden's inquiry stems from his review of a pending comprehensive technology transfer agreement between Sandoz, a pharmaceutical corporation based in Switzerland, and the not-for-profit Scripps Research Institute in San Diego, California, which received $61.2 million for research from NIH in fiscal year 1992.

Like the May advisory meeting, the June meeting was arranged as an informal roundtable discussion. Five representatives from academic institutions and two from companies in the private sector discussed their views on technology transfer arrangements. Two of the academic participants work for an organization that represents leading U.S. universities in Washington, DC, and tries to develop general policy guidelines for its affiliates. In addition, more than a half-dozen officials from NIH participated in this dialogue. Sandy Chamblee, who chairs the task force, presided over the meeting.

CONSIDERATION OF THE SCRIPPS-SANDOZ AND OTHER AGREEMENTS

Although elements of the Scripps-Sandoz agreement were introduced as part of the discussion during the June meeting, participants spent little time analyzing it in detail. In fact, several participants dismissed this and other such large, blanket agreements between corporations and research institutions as "aberrations . . . not a trend." Moreover, although definitive figures are not available, participants agreed that the contribution of corporations to support university-based research is considered to be small compared to overall Federal spending.

One participant from a large pharmaceutical corporation used even blunter terms to describe large-scale agreements between corporations and universities or other research institutions, saying that such arrangements are "idiotic and unproductive." He says that most large drug companies "don't do them because it's a waste of money." Instead of developing blanket agreements, his company is "concerned with smaller interactions with universities involving technology that meshes with our strategic goals." He also criticizes attempts by universities to seek such arrangements by marketing their technology through newsletters and brochures, suggesting that companies are more likely to

identify specific programs or investigators and then develop very focused agreements. "It's a buyer's market," he pointed out.

Participants suggest that university-corporate technology transfer agreements other than the pending Scripps-Sandoz agreement deserve consideration. Because some of these arrangements embody important safeguards and appear to work very well whereas others appear to be misguided, analysis of carefully selected cases may reveal general lessons that could be applied more widely when agreements are being worked out in the future.

For instance, one participant pointed to the long-standing agreement between Massachusetts General Hospital and Shiseido of Japan as "one of the best partnerships" between a large company and a NIH-supported academic institution. Importantly, the partnership appears to emphasize basic research and training of visiting Japanese researchers rather than specific technology goals.

Not all attempts to develop such partnerships can be expected to succeed. "Successful agreements often need to be nurtured over many years, not made overnight," said a university-based participant. She and her colleagues recently learned that careful nurturing cannot always overcome "cultural" differences between would-be partners. Thus, her university negotiated with representatives from a non-U.S. company for many months before breaking off those negotiations because the company "wanted too much." Among those unacceptable demands, the company tried to place too many restrictions on university researchers—for example, insisting that they give up established collaborative or consulting relationships with other companies. The non-U.S. company also wanted to set up a one-on-one management structure, bringing its own people into the university to work with each of the major research groups that were designated for the new center; this proposal was also deemed intrusive and therefore unacceptable.

CONSENSUS VIEW IS THAT OVERALL SYSTEM IS WORKING

Participants at the June meeting identified certain general themes regarding technology transfer arrangements. First, the system, which is characterized by a high degree of diversity, seems to be expanding. Some universities have had programs for many years, whereas others are relative newcomers but are energetically working to improve relations with industry. The general expectation is that improved relations will lead to small- and mid-sized partnerships rather than "mega" deals.

"We have an eye on commercialization of technologies, and we're trying to find support from whatever sources we can," said a representative from a private university with limited experience in this area. "Interactions with industry are very important." At this stage, officials at the university are encouraging

interactions with both large and small as well as foreign and domestic companies, although the expectation is that domestic companies are more likely to enter agreements.

Second, representatives from universities or university-affiliate organizations as well as from companies do not want to see NIH or other Government agencies impose elaborate new restrictions on these partnerships. "We're dealing with small increments of technology," said a representative from a private university, and the system "is working quite well." Another participant pointed out that there is "great anxiety" in the university community that an "elaborate code" leading to increased "bureaucratic tyranny" might be introduced. "These are legitimate issues" for NIH to examine and for institutions to think about, he said, "but I don't think there is a need for an elaborate set of rules. For one thing, our campuses are too diverse."

Company representatives also do not want to see elaborate new restrictions imposed on the present system. "Each collaboration is a unique transaction," said a representative from a multinational pharmaceutical corporation. Thus, imposing restrictions on technology-transfer partnerships, particularly by trying to set front-end price restrictions on ensuing commercial products, will "undermine" the entire effort, he asserted.

Other specific restrictions that have been proposed, such as prohibiting exclusive licensing agreements, also are deemed unworkable, according to industry participants. "It would leave lots of technology in limbo . . . or rotting away because of legal barriers," said one representative from a pharmaceutical company. "Companies accept incredible levels of risk" when they decide to develop a commercial product, a representative from another pharmaceutical company said. The company representatives also noted that current estimates for product development costs woefully understate the investments needed; the latest figures appear to be $800 million in aggregate costs per licensed product instead of $300 million. With such development costs to be met, the transfer of technology needs to be expedited, not faced with additional hurdles, they argued.

Third, uncertainty about whether NIH will continue to encourage universities (as it has seemed to do in recent years) to develop partnerships with industry has academic officials perplexed. At the same time there is low or no Federal budget growth—a circumstance that also encourages universities to seek support from the private sector. Unless current Federal budget trends change, the academic community will have nowhere else to turn if NIH policies further restrict alliances between university researchers and industry.

NIH officials said that, although the need to "protect the Government's investments" is recognized, general agreement over policies in this area has not yet been reached. At NIH, there is

"interest" in NIH and companies jointly supporting research projects at universities. Some small NIH-supported programs are designed to do just that, but they are still too new to evaluate fully.

CERTAIN CONSTRAINTS DEEMED NECESSARY

Amid these two generally accepted themes—that universities are increasingly developing working ties with industry and that the imposition of restrictions would stifle these useful developments—meeting participants also acknowledged the need to safeguard certain practices in these relationships. "Common sense" should dictate where to draw the line, said a participant from the university community.

"We need to pay attention to what universities are there for—basically, teaching and research and sometimes the delivery of health care." He added, "Universities should cooperate in the commercialization of technology, but that doesn't mean we should do it. Let businesses do business." He and others favor agreements between university and corporate sponsors that are on a relatively small scale but do not specify commercial products—that is, agreements that support basic research in a commercially relevant area, but are not product development projects per se. Most participants agreed that blanket agreements claiming exclusive rights to all potentially commercial discoveries from a research group are not appropriate. "We can give companies a window to knowledge," one participant said. "I'd never promise to give away the university's intellectual property before it's developed," said another representative from the university community.

A participant from a pharmaceutical company expressed similar sentiments from a different perspective: "Most of the time, we try to let the science drive the system." That is, university and corporate collaborations often get bogged down in elaborate negotiations aimed at assuring either party's rights in extreme situations, losing sight of what the collaborative effort really is intended to accomplish. "We end up fighting with our own lawyers . . . We've got to get back to trust." This loss of trust can be "detrimental" to research when it leads more and more researchers to withhold their materials from circulation, thereby slowing down scientific progress, he added.

If universities and companies can keep their respective roles in mind, it follows that universities need to practice care so as not to "sully the academic research atmosphere," said a participant from the university community. For example, policies about publishing research findings "cannot be all over the map," he asserted. "We need to establish a narrow band of acceptable [practices]." Similarly, university researchers need to be free to discuss their findings at conferences; constraints on that

freedom for the purpose of preserving patent rights can be minimized by speeding up the writing of patent applications.

Very importantly, these freedoms should extend to graduate students and postdoctoral fellows, whose training and early career development could otherwise become seriously jeopardized. Several participants expressed deep concern that researchers at an early stage of their careers could be channeled into a "two-tier system," with some of them doing proprietary research at lucrative rates and others doing basic research and being paid on a lower scale.

A participant from a state-supported university noted that her institution has not developed uniform rules for constructing agreements with industrial partners. Moreover, it allows considerable freedom to faculty members to take equity positions, receive consultant fees, and sit on corporate boards. However, it has strict guidelines governing the training of graduate students. For example, they stipulate that graduate students cannot conduct proprietary research as part of dissertation projects.

Another participant from the university community pointed out that limits also need to be applied to faculty members. For example, proposals for certain kinds of technology transfer schemes need to be rejected sometimes "because they won't work." It is also important that institutions, not individual faculty members, retain ownership of intellectual property—with appropriate arrangements made to reward individual inventors through royalty agreements, he said.

Another meeting participant said that it is standard practice at his (private) university for the institution to retain ownership of intellectual property. Another restriction imposed on faculty members at his institution is that only administrators, not faculty, are permitted to negotiate agreements with companies.

Regardless of these safeguards, the institution finds itself in a fluid state, a university representative noted. In the biomedical research area, familiar boundaries once set by scientific disciplines are tending to break down, as investigators are being urged to conduct interdisciplinary efforts. This boundary confusion is compounded as private corporate support as well as money from citizens' groups (to study specific diseases) is being brought in to supplement Federal funding. In the midst of this "entangled program," companies may seek to commercialize products that arise from research that volunteer organizations have helped to support on behalf of patient groups. It is very difficult to anticipate the allocation of resources, credit, and profits with all these elements at work.

SAFEGUARDS AGAINST CONFLICTS OF INTEREST

Several concerns about conflicts of interest that might arise from technology transfer agreements were aired during the June meeting. For example, faculty members with an equity interest in a pharmaceutical product that their research had helped lead to might be called on to evaluate the safety and efficacy of that product. Some participants argued that barriers that precluded investigators from helping to evaluate products at the clinical level were sufficient protection against such conflicts of interest.

Others argued that disclosure of financial interests was an essential and perhaps a sufficient safeguard. They also argued that eliminating experts from continued participation in research on a product of special interest inflicted its own set of costs. "Disclosure should not mean disengagement," asserted one participant. "No one can risk their credibility" as a scientist, pointed out another participant, suggesting that there are already many quality controls built into the research process.

Some participants pointed to potential problems with conflict of interest at the institutional level. Thus, if a university enters into a broad technology transfer agreement with a company, it may tie technical developments into a less-than-ideal arrangement, thereby hampering commercialization. For instance, the partner company might not have expertise or interest in certain technologies and may choose to stifle their further development. Participants agreed that universities need to discourage agreements that lead to the suppression of technological developments—perhaps by stipulating time limits for exclusive rights.

Another concern arises because of a tendency by some researchers to exaggerate the commercial potential of emerging technologies. For example, a university researcher may enter into an agreement with a company to commercialize his research but also might misuse his expertise and overstate the economic potential of his findings. Such statements might be used to run up the value of stocks. Most participants agreed that regulations enforced by the Federal Securities and Exchange Commission protect the public against this abuse.

Moreover, in cases where faculty members or the universities hold equity positions, it is in their own best interest to "enhance the value" of stocks over the long term. To further encourage this practice, Federal regulations specify extended holding periods before certain classes of stockholders can sell their holdings to protect against abusive insider manipulation of company values. Along these lines, participants from universities and companies also expressed confidence that investors, particularly venture capitalists and institutional

investors, are sophisticated enough to make well-informed investment decisions without additional safeguards.

Copies of the Association of American Universities' "Framework Document on Managing Financial Conflicts of Interest," which was published in May 1993, were made available to participants. Many of them agreed that this document provides a good model for the university community to follow.

TASK FORCE ON THE COMMERCIALIZATION OF INTELLECTUAL PROPERTY RIGHTS FROM NIH-SUPPORTED EXTRAMURAL RESEARCH

DRAFT REPORT

SEPTEMBER 29, 1993

MEETING OF FEDERAL AGENCY REPRESENTATIVES

Federal Agency Participants

Advanced Research Projects Agency
Richard Dunn, General Counsel

Department of Commerce
John Paugh, Director of Office of Technology Commercialization
Richard H. (Dick) Mullens, Deputy Director of Office of Technology Commercialization
John Raubitschek, Patent Counsel for Department of Commerce

Department of Defense (Navy)
Bill Garvert, Deputy Counsel (Intellectual Property)

Department of Energy
Dick Constant, Assistant General Counsel for Intellectual Property
Judd Hightower, Patent Attorney, Deputy Assistant General Counsel for Intellectual Property
Roger Lewis, Director of Office of Technology Utilization

Department of Agriculture
Howard Silverstein, Patent Attorney
William (Bill) H. Tallent, Assistant Administrator
Ann Whitehead, Coordinator National Patent Program

Food and Drug Administration
James L. Tidmore, Director of Division of Contracts and Grants Management

Internal Revenue Service
Beth Purcell, Assistant Branch Chief of Branch 6
Mike Thracher, Assistant Chief Counsel

National Science Foundation
Linda G. Sundro, Inspector General for the Board
Karen Herman, Professional Assistant

Observer—Office of Technology Assessment
Robyn Nishimi, Senior Associate

INTRODUCTION

The NIH Task Force on the Commercialization of Intellectual Property (task force) invited representatives from several federal agencies to a meeting on September 29, 1993. The NIH task force, which is planning a public meeting for November 8-9, 1993, informed the guest participants of that upcoming event and sought their views on technology transfer and related issues. Dacia Clayton, who presided over the meeting for NIH, reminded participants that the purpose of the task force is to develop policy guidelines for technology transfer agreements under the Bayh-Dole Act. This undertaking began, in part, as a response to Representative Ron Wyden, chairman of the Subcommittee on Regulation, Business Opportunities and Energy of the House Committee on Small Business. Representative Wyden's inquiry stems from his review of a pending comprehensive technology transfer agreement between Sandoz, a pharmaceutical corporation based in Switzerland, and the not-for-profit Scripps Research Institute in San Diego, California

CONSIDERATION OF OVERSIGHT, POTENTIAL SANCTIONS

Much of the discussion during the informal meeting at NIH in September revolved around the degree and kind of oversight various federal agencies bring to technology transfer agreements. Attitudes and practices are diverse--a fact that is in keeping with the wide differences in missions of the agencies that sent representatives to the meeting.

Perhaps most striking is the perspective of the Internal Revenue Service (IRS). Although it does not sponsor research and therefore has no direct involvement in developing technology transfer agreements, the IRS has oversight over organizations that are parties to such agreements, including tax-exempt research institutions in the public and private sectors as well as corporations.

In extreme cases, technology transfer agreements could lead to a tax-exempt organization losing that status, according to IRS officials. Although there is no "bright line" where that status can be said to change, agency officials say that a medley of characteristics would need to be analyzed in making such a decision, with a focus on the degree of control that is ceded by the tax-exempt organization to a corporation when the two enter into a technology transfer agreement. Important traits include the degree of exclusivity and how much in the way of future rights are accorded the corporate partner as well as whether the latter obtains membership rights on the tax-exempt institution's board.

In the view of IRS, a violation occurs if the tax-exempt

university or research institution effectively becomes a subsidiary of the company, officials indicate. However, overt violations raise their own difficulties: Because there is only one sanction available to IRS officials--namely, revocation of an organization's tax-exempt status--this penalty is considered too unwieldy and, in most cases, too severe to invoke. Members of Congress have expressed some interest in devising less severe penalties, but so far none is available.

In the absence of usable sanctions, the continuing success of Bayh-Dole requires "delicate balancing," according to officials from the Department of Commerce (DoC). In general, they note, the Bayh-Dole Act mandating technology transfers from federally supported research into the private sector is considered successful. For example, in fiscal year 1993, total royalties reported by U.S. universities amounted to $200 million, a significant increase over comparable periods before the law took effect, officials point out. (That royalty income is tax-exempt to universities, according to an official from the IRS.)

Nonetheless, many observers say the system needs to be reviewed and probably is not working at its optimum. In the interest of adjusting the system, the Department of Commerce is sponsoring a public meeting in October to determine whether any regulatory changes are needed. However, officials say they do not envision the Department taking on a policing or even a central administrative role in this area, preferring instead to leave most matters to the array of federal granting agencies.

One subject to be addressed at the DoC meeting involves technology transfer agreements between universities (and comparable institutions) conducting federally sponsored research and non-U.S. corporations, a subject that is not fully addressed by the Act and associated regulations, officials note. For instance, current rules prescribing preferences for U.S. manufacturers do not cover assigned licenses that are subsequently purchased by foreign entities.

Regardless of this and other unmet concerns, most of the federal agencies that support research seldom, if ever, apply sanctions to their grantees when they enter into technology transfer agreements that could be deemed inappropriate. However, federal granting and regulatory agencies are interested in seeing that grantees are aware of and abide by some common set of standards. Before compliance with standards can be realistically encouraged, both the agencies and the grantees will need to understand more fully just what sorts of agreements are being made and what the standards are. Indeed, some officials argue that many problems can be overcome merely by better educating the entire community engaged in these efforts. Moreover, improved dissemination of information is seen as a preferable solution over a regulatory approach of imposing stringent rules.

The diversity of universities, corporations, consortia, and the kinds of agreements that are being formulated makes it difficult if not impossible to describe a single set of standards, officials from several granting agencies point out. It also complicates matters that federal granting agencies do not appear to subscribe to a set of common standards. Another complication is that at least some universities appear to apply more stringent standards than federal granting agencies may require. However, other universities appear to be ignoring the Bayh-Dole mandate and, for example, may be forfeiting both U.S. and non-U.S. patent rights by allowing their faculty to publish research findings without applying for patents in a timely fashion.

In a sense, the Bayh-Dole act calls upon research-oriented universities to act in their own self-interest, transferring federally sponsored technology into the private sector in return for additional support from their corporate partners. Hence, some university officials have asked NIH not to impose stringent rules or to take on a regulatory role, fearing that attempts to control technology transfer agreements will destroy many of these fragile and typically small-scale relationships with the private sector.

Perhaps it makes sense to rely on general triggers, such as size and scope of proposed agreements, and to examine only those technology transfer agreements that so qualify on a case-by-case basis, participants suggest. Currently, federal officials contend that their authority to undertake reviews before such technology transfer agreements are signed is limited, if it exists at all. Moreover, once a federal grant has been made to an institution, it is difficult to withhold funds as a sanction against an agreement that is deemed inappropriate.

Another potential sanction, referred to as march-in rights because it enables federal agencies to reclaim potentially commercial research findings from a grantee, exists as a threat but appears not to be practiced by any federal agency. Although some agencies now receive reports from grantees that describe whether and how technologies are utilized, typically there is no systematic effort to determine whether the Bayh-Dole mandate is being met. Currently, information that comes to granting agencies is anecdotal, and typically comes in the form of complaints about alleged abuses.

In fact, several federal officials say, their agencies do not have the capacity to undertake this kind of review. The Office of Naval Research (ONR) is an exception, as it has an elaborate system for tracking research it sponsors, particularly that which results in commercializable inventions. However, budget cutbacks threaten this tracking program.

DIVERSITY OF APPROACHES BY FEDERAL GRANTING AGENCIES

Several federal agencies besides NIH are reexamining their technology transfer policies. For example, the governing board of the National Science Foundation (NSF) recently asked the inspector general's (IG) office to examine systematically the technology transfer agreements being made between NSF grantees and corporate sponsors. In the process of that review, NSF officials also will attempt to outline what they consider acceptable principles for such agreements and inform grantees how they can best comply with those principles. In the future, the IG will hold the responsibility to continue tracking technology transfer agreements and to assure that university-based grantees are complying with NSF's recommended practices.

NSF officials acknowledge that support from industry has become an essential component of university-based research. However, unrestricted support is preferred over narrowly restricted funds, and some kind of cap may be needed for targeted research moneys. NSF officials also recommend that steps, such as rapid patent application processing, be taken to minimize periods during which research findings are kept secret. Similarly, assurances are needed so that one company does not license and then squelch a promising technology merely to exclude its competitors from a specific marketplace. And care is needed to assure that federal efforts to promote technology transfer do not lead to serious conflicts of interest at universities and elsewhere.

Officials from the Department of Energy (DOE) say that none of the researchers the agency supports has entered into an agreement that is anywhere near the scale or scope of the Sandoz-Scripps draft agreement that was described in press accounts. DOE-supported researchers and laboratories do enter into technology-transfer agreements with the private sector. However, those agreements usually do not include exclusive licensing provisions, are on a relatively small scale, and honor statutory provisions indicating a preference for U.S. manufacturer of products emanating from the technology development and transfer agreement.

DOE officials note that two kinds of exceptions to the U.S. manufacturing preference have arisen: one, when licensees have been bought out by foreign corporations and, the other, when the licensee turns out to be a wholly owned subsidiary of a foreign corporation. These exceptions represent indirect breaches of Bayh-Dole, and they are cited as potentially troublesome if and when a highly profitable product were to be developed. This loophole has been used by foreign corporations to acquire the licensing rights for several significant non-biomedical technologies, but so far none has led to an astonishing commercial success, officials note.

U.S. Department of Agriculture (USDA) officials say that

researchers they support are reporting inventions more frequently now--about 30 per year--than before Bayh-Dole was enacted, when the rate was more like one per year. Along with this higher invention rate has come growth in the number of technology transfer agreements that are being worked out with U.S. and non-U.S. companies. In some cases, USDA-supported researchers have sought but not found U.S. corporate partners and thus have had to license seemingly commercially valuable technology to foreign firms. Officials say that such licensing agreements typically are made on a non-exclusive basis. Moreover, efforts to secure U.S. developers--whether successful or not--are carefully documented.

Most of these efforts are undertaken on behalf of USDA's intramural research program. The department's extramural research program is relatively small and thus none of its grantees has been subject to a technology transfer agreement remotely like the Sandoz-Scripps arrangement. In any case, no specific set of rules is being applied to the small-scale agreements that are being devised, according to USDA officials.

In this context, the most contentious issue to arise involves plant genome mapping and sequencing efforts, they note. Conflicts center on the inherently contradictory goals embedded in these efforts--one calls for rapidly determining and disseminating genome information, and the other calls for patenting valuable information for useful purposes. The compromise now in place allows university researchers to hold information secret for a prescribed period to allow patent applications to be filed.

The Office of Naval Research looks at technology transfer agreements very much in the context of its defense-related mission. Officials say there are two overriding concerns. One is that ONR not pay twice for the research it sponsors. The second is that a strong domestic industrial base be available to make use of ONR research results. Put bluntly, the Navy and other branches of the Defense Department are interested in assuring that vital products of technology are readily on hand to meet military needs, especially during periods of hostility. This need dictates a clear preference for U.S. corporate partners when making technology transfer arrangements. Other stipulations appear to be of secondary importance.