Chapter 7

University-Industry Research Arrangements in Biotechnology

"The interaction of industry with the universities is essential to provide an effective exploitation of the research base. This partnership is critical to our national well-being in an increasingly competitive world marketplace."

White House Science Council
A Renewed Partnership, 1986

"There is justifiable concern that the time may be passing when an individual can produce significant discoveries without outside support and present them as pure gifts to society. "

Carnegie Institute
Annual Report of the Staff: The Program in Science Policy 1980-1981, 1982

"To the long familiar military-industrial complex a fraternal twin has been added: an academic-industrial complex through which American and multinational corporations siphon the publicly created resources of our universities and thereby convert publicly financed research into private gain. "

Leonard Minsky
"Greed in the Groves: Part 11"
The NEA Higher Education Journal, 1984

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INTRODUCTION

The joint funding, performance, and application of scientific work by academic and nonacademic interests is not new (9)11)18,32). Yet in recent years, the rapid proliferation of collaborations in biological research, involving partnerships between universities, industry, and government, has greatly extended the frequency, scope, and visibility of such activities. Attempts to commercialize biological techniques have occurred at an accelerated rate when compared to other fields, involving a much broader spectrum of expertise in its participants, and presenting a greater range of commercial application than discoveries in most other disciplines.

Intellectual capital is the mainstay of biotechnology firms, which, to date, have had little else to market. The importance of the university scientist to commercial biotechnology has been well established. Industrial sponsorship of university research in biotechnology yields substantial benefits to the firms involved. Per dollar invested, industry-supported university research in biotechnology is generating four times as many patent applications as is other company research; 41 percent of the companies investing in university-based research have derived trade secrets from that work (6).

Approximately 46 percent of biotechnology firms support biotechnology research in universities. During 1984, the last year for which data are available, the average Fortune 500 company involved in biotechnology planned to spend $1.1 million on university-directed research, while the average non Fortune 500 company planned to spend $106,000. All totaled, in 1984, biotechnology companies in the United States spent about $120.7 million in grants and contracts to universities. The percentage of industrially sponsored university-based research in biotechnology is approximately 16 to 24 percent; higher than the average 4 tos percent spent on overall industry-sponsored campus research (3,6).

Although an increasing number of biotechnology companies are strengthening their in-house research capabilities, available evidence suggests that the private sector will continue to seek the cutting edge provided by the Nation's universities. Direct industry support for all campus research has increased in constant dollar terms every year since 1970. Between 1981 and 1984, this increase was 8.5 percent annually (22). Even with these increases, industry funding remains small compared to government support of biotechnology research on the Nation's campuses.

The nature of university-industry biotechnology research arrangements appears to be changing. At an April 1987 OTA workshop on this topic, industry representatives predicted that few companies will invest large sums in universities for long periods for directed research in biotechnology, as was done by Monsanto at Washington University (35). As predicted in the 1984 OTA report on *Commercial Biotechnology,* an increasing number of university-industry arrangements in biotechnology are developing as consulting and contract research rather than long-term research partnerships (36). The predicted time course required to meet industrial expectations of university research requires more pragmatic collaborative arrangements than in the past.

Early concerns about collaborative research arrangements in biotechnology, particularly those involving universities and industry, were focused primarily on issues of academic freedom, proprietary information, patent rights, and other potential conflicts of interest among collaborating part-

ners. As these research arrangements have evolved, and experience has grown, some of the most worrisome difficulties have been resolved, or never realized.

Concerns remain, however, about the subtle impacts of these collaborative arrangements. It is possible that university-industry relationships could adversely affect the academic environment of universities by inhibiting free exchange of scientific information, undermining interdepartmental cooperation, creating conflict among peers, or delaying or completely impeding publication of research results. Furthermore, directed funding could indirectly affect the type of basic research done in universities, decreasing university scientists' interest in basic studies with no potential commercial payoff (3,4,6). In addition, complex and subjective concerns remain about the effectiveness of these arrangements in meeting the needs of participating institutions, and the ability of these new partnerships to stimulate innovation and improve America's competitiveness in biotechnology.

This chapter analyzes the structure, scope, potential problems, benefits, and outcomes of collaborative research arrangements in biotechnology. It focuses primarily on U.S. university-industry research collaborations. (See ch. 4 for collaborations involving State governments; ch. 5 for collaborative arrangements within industry.)

TRENDS IN UNIVERSITY-INDUSTRY RESEARCH IN BIOTECHNOLOGY

During the 1970s, several key factors in the university environment converged to stimulate increasing interest on the part of academic faculty and university administrators in seeking nontraditional funding sources. First, in many fields, research costs were exceeding the available funds from traditional sources–government funding, university budgets, and private foundations (11). Such cost increases have been especially prevalent in fields that require large-scale, technologically advanced equipment and instruments and, consequently, the involvement of larger numbers of technicians with diverse skills (9). Construction grants, as well as direct Federal nondefense R&D support, have fallen annually (37) providing impetus for the university to seek more industrial funds.

Second, increasing Federal budget deficits, soaring inflation, and the change of Administration in 1981 signaled the possibility of some changes in Federal support for university research, which many scientists and university administrators feared would result in drastically cut budgets (11,17).

During this same period, American industry was becoming increasingly aware that its traditional position of "technological supremacy" was being challenged on a variety of fronts, and that its competitive edge in many sectors was in jeopardy (7,28,30). The growing consensus that competitiveness was linked to innovation, and that university research and technology transfer played a critical role in the Nation's ability to compete, led business to show greater interest in creating and strengthening its own connections with the academic community (12).

The putative decline of U.S. industrial competitiveness and productivity soon became a topic of intense public concern, affecting Federal, State, and local politics (11). The assumption that strengthening the links between industry and university research could improve America's economic malaise gave impetus to a variety of new government policy initiatives over the last decade. These included:

- The Patent and Trademark Amendments Act of 1980 (Public Law 96-517), which included changes in Federal patent laws relating to universities. The act changed the presumption of title in inventions made with Federal funds from the government to universities, small businesses, and nonprofit institutions regardless of which agency's funds had been used to make the invention.
- The Stevenson-Wydler Technology Innovation Act of 1980 (Public Law 96-480) to promote cooperative research and technology transfer.

- The 1981 Economic Recovery Tax Act (ERTA) (Public Law 97-34), which provided a 25 percent tax credit for increases in company R&D expenses over and above base-year R&D expense levels and for the contribution of research equipment to universities. Recent revisions of the tax laws have preserved this favorable tax treatment for industrial support of university research, though the benefits are somewhat reduced (8). Under ERTA, limited partnerships formed for the purpose of supporting R&D were also eligible for favorable tax treatment. Many biotechnology companies increased their funding of university research through research and development limited partnerships (RDLPs) (19). (See ch. 5 for further detail.)
- Relaxation of antitrust regulations through the National Cooperative Research Act of 1984 (Public Law 98-462), in part to facilitate research collaborations among previously competitive industrial firms.
- Federal funding for university-industry cooperative programs and projects, for example through the National Science Foundation.
- Growth of State economic development programs that provide incentives to promote university-industry cooperation. (See ch. 4 for further discussion of State programs.)

This confluence of events and policies increased the interest of universities, industry, and government in activities pertaining to partnerships between academia and business in all fields of science. Interest in collaborative research arrangements in biotechnology has been keen because of the potential impact of the resulting products and processes of biotechnology on a diversity of industrial sectors, a multitude of existing and newly proposed Federal and State funding initiatives in this area, and an unprecedented influx of investment capital.

The trend toward academic and business partnerships in biotechnology is expected to continue. However, the growth rate may or may not maintain the pace witnessed in recent years. in part, the rate of future growth will depend on decisions that have yet to be made by industry and on the future availability of trained scientists with significant track records to demonstrate commercial potential.

Some commentators feel that industry will not continue to rely on universities for some of the production-oriented work, and that business is already conducting most of the purely developmental research in house (2,14). Scale-up issues may differ significantly from R&D issues and may be best handled in house. These shifts of resources will obviously change the nature of the collaborative efforts. Concerns about protecting proprietary research may also force industrial firms conducting more development and product-oriented research to work in house in lieu of contracting that portion to the universities. It is likely that new trends in university-industry arrangements will be seen first in the field of pharmaceuticals, with less developed areas of industrial application, such as agriculture, lagging behind. Participants in the April 1987 OTA workshop agreed that industries will continue to rely on universities for cutting-edge research, technical breakthroughs, and support for individual projects, the outcomes of which will result in potential new projects and increased sales (35).

TYPES OF COLLABORATIVE RESEARCH ARRANGEMENTS IN BIOTECHNOLOGY

University-industry research collaborations in biotechnology and in other fields encompass a diversity of approaches. The particular type of interaction that collaborating partners choose depends on their goals and institutional characteristics (27). The relevant factors include:

. company: the size, structure, and profitability of the company, the nature of its business, and the progressiveness of its research program;
. *university:* the type, size, and financial health of the university, the relative size and stat-

ure of its science and engineering programs, and the orientation of its research and researchers; and
- externalities: geographic location, proximity of the collaborating institutions, regional and state economic development initiatives, the location of university alumni in key industrial positions, and the migration of university faculty to industry and vice versa.

Since 1980, many researchers have attempted to develop topologies to categorize the kinds of university-industry interactions that exist. Some of these are generic to all fields (26)27); other categorization schemes are specific to biotechnology (13)18)21,36). However, with so many radically different models all passing under the same general rubric of "research collaboration," it may never be possible to adequately encompass the field in a simple set of categories (31).

One categorization scheme for biotechnology research relationships is shown in table 7-1.

Table 7-1.—Types of University-Industry Research Arrangements in Biotechnology

Between university and firm
- Industry-supported university research: cooperative research programs; jointly run research facilities
- Organized consulting arrangement
- Industrial liaison programs
- Company equity held by university
- University-owned science parks
- Equipment donations by firm
- Company licensed patent owned by university
- Joint commercial ventures
- Consortia

Between *faculty members and firm*
- Research grants and contracts
- Faculty members as principal officer in firm
- Faculty member on firm's Board of Directors or Science Advisory Board
- Exclusive or non-exclusive consulting with industry
- Full-time summer employment
- Company equity held by faculty member

Between *trainees and firm*
- Training grants or scholarships
- Direct support of trainee's research
- Trainee salary support, summer or academic year
- Exclusive or non-exclusive consulting
- Informal collaboration

SOURCE: Adapted from D. Blumenthal, M. Gluck, S. Epstein, et al., *University-Industry Relationships in Biotechnology; Implications for Federal Policy,* DHHS Grant #100A-83, submitted to the Office of the Assistant Secretary for Planning and Evaluation, National Institutes of Health, U.S. Department of Health and Human Services, Bethesda, MD, Mar. 20, 1987.

Research Consortia

Biotechnology consortia have been developed by some university-based biotechnology centers to promote technology transfer and raise additional capital. Consortia may include either one company and several universities, several companies and one university, or several companies and several universities. Companies often represent widely differing aspects of the technology in question (e.g., large-scale and small-scale applications). Research tends to be basic with little direct attention to commercialization, but with the implicit or explicit assumption that commercial applications will eventually be available for member companies to pursue independently. Federal or State Government funds often supplement industry funding of these consortia.

Pennsylvania State University, for example, has had 20 sponsoring industries for a cooperative program in recombinant DNA technology and has attracted several industrial sponsors for its Biotechnology Institute. The Center for Biotechnology Research, sponsored by Engenics Corp. (a spinoff of Stanford University) involves six other companies, Stanford University, the University of California, and the Massachusetts Institute of Technology. The University of Wisconsin Biotechnology Center Biopulping Consortium is described in box 7-A. The Midwest Plant Biotechnology Consortium, a group of 15 universities and 30 companies with an interest in plant biotechnology, is described in chapter 10.

Service Facilities

Service facilities are university-based operations that provide, for a fee, the use of equipment, facilities, or expertise to either industry or university scientists. They permit universities to make considerable capital investments in buildings and equipment based on the potential earnings that can be generated through user fees. The Wisconsin Biotechnology Center, the Center for Advanced Research in Biotechnology (CARB) of the Maryland Biotechnology Institute, and the Center for Biotechnology at SUNY Stonybrook are examples of service facilities.

Box 7-A.—The University of Wisconsin Biopulping Consortium

In April 1987, the University of Wisconsin's Biotechnology Center and the U.S. Department of Agriculture's Forest Products Laboratory joined to develop a biopulping research consortium. Boise Cascade Corp., Celulosa Puerto Piray SA of Argentina, Consolidated Paper, Inc., Dow Chemical Co., Great Northern Nekoosa Corp., James River Corp., Mead Corp., Potlatch Corp., Procter & Gamble Co., Sandoz Chemicals Corp., Scott Paper Co., Spout-Bauer, Inc., and Weyerhaeuser Co. each contributed $15,000 annually during an initial 5-year period to support the project. The Biotechnology Center will join the 13 founding companies as the fourteenth contributor to the project.

The biopulping process has the potential to improve on present mechanical and chemical methods by reducing energy, capital costs, and environmental treatment requirements. The process would use enzymes from a naturally occurring white rot fungus known as *Phanerochaete chrysosporium* to separate lignin from cellulose in a selective manner. When dilignification with fungi is combined with mechanical pulping, energy consumption drops by 25 percent. The consortium's initial research is focusing on whether this process can adapt to large-scale pulp production.

Corporate sponsors will have access to the research on an ongoing basis through an information service, a yearly symposium, and direct interaction with staff members. Industry sponsors are expected to play an important role in both identifying needs and transferring the technology to onsite applications.

SOURCES: *Pulp and Paper Week*, Apr. 6, 1987; and J. Kelley, University of Wisconsin Biotechnology Center, personal communication, 1987.

Photo credit: University of Wisconsin-Madison

The Protein/DNA Sequence/Synthesis Facility at the Biotechnology Center of the University of Wisconsin-Madison.

- In Wisconsin, the Biotechnology Center operates a number of pay-back facilities. If a startup firm needs a monoclinal antibody, it can be made at the Center for a fee, avoiding for the firm the cost of investing in equipment necessary for monoclinal production. The Hybridoma Facility offers three options to clients desiring hybridoma production, screening, cloning, or antibody production—full service, self service (inexperienced), and self service (experienced), Another facility offers services in protein purification and obtains equipment through shared equipment grants. A Plant Cell and Tissue Culture Facility offers instruction, protoplasm isolation and plating, media preparation, anther culture, and long-term storage of plants in test tubes. Additional facilities include the Transgenic Mouse Facility, the Protein/DNA Sequencing/Synthesis Facility, and the Biocomputing Facility.
- At CARB, advanced computer graphics capabilities and x-ray crystallography equipment will be available for companies willing to pay for structure analysis in protein engineering and rational drug design.
- At the Center for Biotechnology at the State University of New York at Stonybrook, service facilities are provided by the Hybridoma Center, the Center for the Analysis and Synthesis of Macromolecules, and the Center for Radioligand Synthesis and Spectroscopy.

POTENTIAL BENEFITS OF UNIVERSITY-INDUSTRY COLLABORATION IN BIOTECHNOLOGY

Historically, the potential for new economic and social benefits from scientific research has helped scientists secure funding and, at times, social stature for their work (9). More recently, scientific research-especially collaborative research between industry and universities—has been targeted as one of the critical elements in stimulating technological innovation, enhancing industrial competitiveness, and in achieving sustained economic growth and development, both regionally and nationally. In fact, nearly every statement on America's current economic predicament cites the university as the source of new scientific and technological breakthroughs, and university-industry partnerships as the vehicle through which sustained economic recovery will be achieved (18).

Whether university-industry collaborations can make good on these claims has yet to be determined. To date, there have been no rigorous, empirically based, national studies of the outcomes of these collaborative arrangements. Part of the problem is that many of these collaborations are too new to assess. OTA recently sponsored one of the few studies of the outcomes of collaborative research arrangements in advanced materials, information technology, and biotechnology (31). The findings of that study suggest that commercial outcomes—products and processes—have been fairly limited to date, and that outcomes are heavily contingent on how the collaboration is structured and managed.

One survey of industrial firms with university-industry research relationships in biotechnology asked respondents for their list of perceived benefits of collaboration (3)4). Factors perceived by 50 percent or more of these industrial respondents as benefits "to a great or some extent" (in order of priority) were:

- the likelihood of the collaboration resulting in product or process licenses;
- the ability of the company to keep current with important research;
- reduction in costs of mounting R&D programs in a new field;
- enhancement of the firm's public image; and
- training and staff development for company scientists.

From the university perspective, some benefits cited in another study include:

- . improvement in the level of research and training in applied science;
- transfer of technology to industry and greater relevance to society; and
- assistance in offsetting uncertainties of Federal R&D support (13).

Except for expectations of the profound commercial potential for biotechnology-related products in a variety of sectors (e.g., agriculture, chemicals, pharmaceuticals), many of the benefits cited are similar to ones described as motivators in other fields of science.

Benefits for the Universities

Money, in a variety of guises, could be a primary benefit to the university of industrial sponsorship of research: money for research, the opportunity for equity participation, limited investment in physical plant and facilities, and the associated added income for faculty, Further, inflation in the late 1970s and the fear that current support for basic research would be cut forced many universities to tap several sources for funding and equipment. Ninety percent of the universities responding to a recent survey report receiving some industrial funds to conduct research in biotechnology (3,4).

Evidence suggests, however, that large capital infusions, such as those which occurred between Hoechst and Massachusetts General Hospital, may be the exception rather than the rule. In 1984, 60 percent of industrially funded biotechnology projects at universities were funded at less than $50,000,20 percent were funded for $50-100,000, and only 20 percent were funded for over $100)000 (6).

Furthermore, it is not clear that the financial benefits to universities, other than direct support itself, have been realized, Eighty nine percent of

the sampled universities realized at least one patent from biotechnology research over the past 5 years, but substantial income from licenses is rare, and earnings fail to exceed the cost of administering the patents and licenses. In addition, few universities own equity in any biotechnology company owned or founded by their faculty, and even fewer reported any substantial appreciation in such holdings (6). It seems unlikely, therefore, that university-industry relationships in biotechnology have or will significantly meet the unmet capital needs of universities.

The real benefit from university-industry research collaborations could be the capacity to do things neither partner could do alone. Industry may provide critical leverage to university applications to Federal and private funding agencies. For many university scientists, industrial sponsorship provides the added excitement and prestige that comes from working on truly cutting-edge scientific research and entering into long-term agreements with industry (2)24). Collaborations with industry may also help the university retain faculty members who might otherwise leave, and to attract new faculty and students. Industry collaborations may allow smaller, less prestigious universities to build their research base and to offer training opportunities for students. Since many of the small, less well known universities often have trouble gaining access to research funds at the National Institutes of Health and elsewhere, the use of industrial capital to build their research capability would offer great benefit.

Benefits for Faculty

In a survey of over 1,200 faculty members conducted at 40 major U.S. universities, approximately 47 percent of biotechnology faculty reported consulting with an outside company, and 8 percent reported holding equity in a firm whose products or services are directly related to their own university research. The survey also revealed that biotechnology researchers with industrial support publish at higher rates, patent more frequently, participate in more administrative and professional activities, and earn more than colleagues without such support **(6).**

Table **7-2** summarizes the responses of biotechnology faculty, with and without industry support, to questions of the perceived benefits of university-industry collaborations **(6).** The table shows that the majority agreed that such arrangements involved less red tape than does Federal funding and increased the rate of practical applications from basic research. The table also illustrates some interesting differences between biotechnology faculty with industrial support and those not receiving funding from this source.

Benefits for Students

Although the literature on the effects of university-industry collaborations in biotechnology is replete with anecdotes about the problems such relationships can cause for graduate and post-doctoral training, one study found that students do not feel that their training is being short-changed or that the quality of their educational experience is being compromised (10). In fact, the students surveyed generally felt that “the benefits outweighed the risks.” There is no evidence to date suggesting that students working in labs with industrial support are getting less guidance or receiving insufficient faculty attention. Compared to colleagues without industrial support, biotechnology faculty with industrial support seem to spend comparable amounts of time each week with graduate students and postdoctoral fellows (3)4).

Industrial sponsorship can provide increased fellowship opportunities and more employment opportunities for students when they graduate. Not everyone taught can or wishes to go into academic science. The results of a 1985 survey of personnel needs in biotechnology firms conducted by the Institute of Medicine and the American Society for Microbiology revealed that there has been a substantial increase in the number of scientists employed in the biotechnology industry since 1983 (16). (See ch. 8 for further discussion of personnel and training.)

In addition, exposure to industrial projects can provide students with the opportunity to conduct more research, gain knowledge of industrial applications, and learn how to test hypotheses. Students funded by private firms maybe more likely than those without industry connections to report patents resulting from their research (3). Those students are often offered permanent po-

Table 7-2.—Benefits of University-Industry Collaborations Reported by Biotechnology Faculty

Question	"To some extent or to great extent" (%) Industry support	No industry support
To what extent does industry research support:		
• Involve less red tape then federal funding	76	51'
• Increase the rate of applications from basic research	67	52'
• Provide resources not obtainable elsewhere.	63	36'
. Enhance career opportunities for students	60	43'
• Enhance scholarly productivity	41	20'
• Produce patents that increase university revenues	41	33

[a]Significantly different from faculty with Industry support ($p < 0.01$).

SOURCE: D. Blumenthal. M. Gluck, K.S. Louis, et al. "University y-Industry Research Relations in Biotechnology: Implications for the University," *Science* 232:1361-1366, June 13, 1966.

sitions because of their familiarity and experience with industrial research problems (l).

Benefits for Industry

A **1984** survey of biotechnology companies revealed that the investments these companies were making in university research seemed to be yielding substantial benefits to the firms involved (3,4). Per dollar invested, university research generated more patent applications than company research. Whether these patent applications will result in marketable products or processes and profits for the sponsoring firms has yet to be determined. Collaborative research with universities constitutes a relatively small part of most firms' R&D investment, generally less than 10 percent. For an important minority, such collaborations constitute a significant part of their research (6).

Clearly the commercial potential in biotechnology-related processes and products is one of the primary benefits that industry perceives it will gain through university-industry research collaborations, but it is not the only one that industry values. Industry has to master this technology to do its own research. Collaborations with universities permit industry to buy in at a relatively low cost, without having to recreate the resources and talent already available in academia. Academic-business research relationships allow businesses to tap otherwise inaccessible brainpower, increasing their competitive edge. Thus, collaborations enable industry as well as universities to accomplish tasks neither could tackle alone.

POTENTIAL PROBLEMS OF UNIVERSITY-INDUSTRY COLLABORATION IN BIOTECHNOLOGY

Concerns about the commercialization of academic biomedical research probably reached a zenith around 1981, about the same time that the House Committee on Science and Technology convened its first hearing on the subject (33). The hearings focused on two major issues: whether university-industry research relationships violated scientific and academic freedom and responsibilities, and whether these relationships best served the interests of the American public.

By the time the Committee convened its second set of hearings, nearly one year later, some of the initial controversy had subsided (34). Then Congressman Gore said in his opening remarks: "We do not view such agreements as bad per se, but rather as a development that needs to be examined in detail." However, this kind of detailed examination has not taken place. With the exception of a few isolated studies, little evidence exists to either substantiate or refute the largely rhetorical claims of those who feel great harm is being done to academic science as a result of the new "university-industrial complex."

In one study of university-industry research interactions, the scientists and administrators surveyed raised a variety of concerns (26). Most of

the issues were not mentioned more than 25 percent of the time by either company or university representatives, although academic respondents clearly raised more concerns about the research interactions than their industrial counterparts. Both parties expressed concern about basic vs. applied research. About 23 percent of university representatives raised concerns about academic freedom. None of the other issues—adverse impacts on research quality, credibility, continuity, and the commingling of funds—appeared to be of major concern to either industry or university respondents.

In general, the perception of potential problems that can result from university-industry collaborations in biotechnology does not differ from that seen in other fields. However, the degree and frequency with which problems are occurring is perceived to be intensified in biotechnology, perhaps because of the accelerated proliferation of these partnerships in a relatively short time.

Problems for Universities

Comments from analysts of university-industry collaboration about the problems universities are experiencing in collaborative arrangements range from "the problems are many" to "the problems have been beat to death." At issue is whether and to what degree universities should remain detached from the world of business. (Some question whether this idealized (or idolized) kind of academic environment ever existed at all.) Yet regardless of viewpoints, observers interviewed by **OTA** seemed to agree that universities are indeed being changed by their research relationships with industry.

one frequently cited problem concerns secrecy. Some analysts maintain that colleagues cannot exchange information, despite its intellectual potential, because of its commercial value. Others argue that a delay in publication of six months makes little difference and that trade secrets tend to be on the production side, not the basic research side. Some contend that as corporations bring development-oriented activities in house, the secrecy issue will diminish on the campus. But in one study, 25 percent of industrially supported biotechnology faculty reported that they have conducted research that belongs to the sponsor and cannot be published without prior consent; and **40** percent of faculty with industrial support reported 'hat their collaboration resulted in unreasonable delays in publishing (3). When research approaches the point of publication, the company may request that certain pieces of information be withdrawn because they may reveal a trade secret, such as the composition of a buffer, or formulation of a pharmaceutical compound.

Several commentators interviewed by OTA expressed concern about interdepartment and intradepartment competition for scarce resources and the potential imbalances in resource allocation that university-industry collaborations can cause. The possibility was raised that this competition would cause some fields within the university to atrophy. For example, a $32 million Biological Sciences Complex at the University of Georgia apparently has drawn funds, and criticism, from other instructional programs.

Problems for Faculty

The potential problems for universities and faculty members engaged in collaborative arrangements include:

- impacts on the university's research agenda, such as the potential for professors to orient their research toward products that could have commercial value or the shifting of research to accommodate corporate sponsors;
- conflicts of interest, such as the use of university equipment for private gain or the shift of time away from university responsibilities;
- exploitation of students as inexpensive labor or outright neglect of students by faculty who become increasingly involved in commercial projects; and
- interruptions in the free flow of information and materials among colleagues because of patent-induced publication delays, trade secrets, and other proprietary inhibitions—the "publish or profit" problem **(18).** Faculty with industry funds are much more likely than other biotechnology faculty to report that their research has resulted in trade secrets and that commercial considerations have influenced their choice of research projects (3).

Table 7.3.—Risks Reported by Biotechnology Faculty

Question	"To some extent or to great extent" (%) Industry support	No industry support
To what extent does industry research support pose the risk of:		
• Shifting too much emphasis to applied research	70	78[a]
Ž Creating pressures for faculty to spend too much time on commercial activities	68	82[b]
• Undermining intellectual exchange and cooperating activities within departments.	44	68[b]
• Creating conflict between faculty who support and oppose such activities	43	61[b]
Ž Creating unreasonable delays in the publication of new findings.	40	53[b]
Ž Reducing the supply of talented university teachers.	40	51[a]
• Altering standards for promotion or tenure	27	41[b]

[a]Significantly different from faculty with industry support ($p < 0.05$).
[b]Significantly different from faculty with industry support ($p < 0.01$).

SOURCE: D. Blumenthal, M. Gluck, K.S. Louis, et al , "University-Industry Research Relations in Biotechnology: Implications for the University, " Science 232.1361-1366. June 13, 1986

None of these problems, however, is unique to university-industry collaborations. The quest for grants, prizes, and status has often led to secrecy before research results are published.

In addition, university-industry collaborations could cause imbalances of faculty, students, and space, shake public confidence, and jeopardize government funding (25). Furthermore, collaborations could threaten the scientist's objectivity, although there is no hard evidence that academics with industrial ties are in fact less objective in their judgments, or less interested in scientific truth (20,21,29). Table 7-3 presents the risks reported by biotechnology faculty with and without industrial support.

The most frequently cited problems for faculty involved in collaborative research relationships with industry are the potential conflicts inherent in having mixed allegiances. The danger is that faculty will spend a disproportionate amount of time on applied research and commercial interests. Industry supports research that is more likely to be applied.

Faculty members with industry support are more than four times as likely as faculty without industry support to report that their choice of research topics has been influenced by the likelihood that the results would have commercial application (6). Although companies may selectively support faculty whose research has commercial potential, biotechnology faculty with or without industry support seem to feel that industrial support does shift research in applied directions.

Critics of the university's involvement in industrially oriented research are concerned that the more one engages in outside commercial activities, the less one devotes to university responsibilities. However, one study seems to suggest the opposite (3,4). Biotechnology faculty with industrial support exhibit enhanced productivity in several areas, including university activities, and show no significant declines in teaching time. Teaching time may not be an appropriate measure of the effects of commercial activities, since the content and quality of that teaching, and the material contained in the coursework itself, may be more relevant.

problems for Students

In a recent survey of students, over 25 percent either received direct support from industry for their research (12 percent) or worked in labs of investigators who received industrial funds (an additional 15 percent) (6). There is a great deal of discussion, but little reported in the literature, about the effects of university-industry relationships on students and postdoctoral fellows. The fear that students could be exploited by commercial priorities or the pecuniary interests of their professors, and that their education and training may be compromised, was often expressed in OTA interviews with academic scientists.

One study (10) adds some empirical data to an area in which the only evidence of problems for students to date has been in the form of newspaper articles and anecdotes. The study surveyed

693 graduate students and postdoctoral fellows at six research-intensive U.S. universities, assessing the effects of industry-sponsored university research in the life sciences, and more specifically in biotechnology. The study revealed that students with industrial support published about a third fewer papers, reported more significant delays in publication, and reported inhibitions in discussing their work with colleagues more frequently than their peers. Some students and fellows with industrial support must work on projects chosen by industry, or provide other services to their industrial sponsors. Industry-sponsored research tends to be more applied, which may, in part, explain the lower rate of publication.

Problems for Industry

Industry would appear to face few problems from university-industry research collaborations. obviously, if an agreement is not viewed as successful, a company can elect to discontinue support. The major concern of industry could be whether these academic-business partnerships in biotechnology will result in the revolutionary new products and processes currently envisioned.

Exclusivity is an expectation of firms sponsoring collaborative research. The scientist's or university's ability (or willingness) to grant exclusivity may be a point of contention. Furthermore, since many parties could be involved in the collaboration, the designation of rights may become more complex. As projects come to fruition in multi-party collaborations, who negotiates the **contract with industry, who holds the contract, and how property rights are assigned will be major issues facing industry, as well as all parties involved.**

One particularly problematic scenario involves a consortium involving Federal, university, and industrial funds. As a result of the collaboration, a company could gain title to patents based wholly or partly on Federally funded work. Existing law requires that patents resulting from Federally funded research in universities be owned by the university or the Federal Government (if the university has an institutional patent agreement with the granting agency). Thus, if the university permits patent title to the company, it could be in violation of the law. Self-interest on the part of the university may be the best protection against such a violation given the logical desire for the university to retain patent ownership.

Findings from a 1986 industrial survey (3,4) suggest that companies sponsoring university research also perceive potential risks in university-industry relationships. Problems perceived by over 20 percent of the firms as a potential risk "to a great or some extent" were:

- poor payoff in marketable products (62 percent);
- loss of proprietary information (58 percent);
- excessive monitoring and controlling effort (42 percent); and
- university withdrawal from the relationship before the firm receives anticipated benefits (21 percent).

VARIABILITY IN THE BENEFITS AND PROBLEMS

Many of the researchers and commentators who discuss the benefits and the problems of university-industry research collaborations in biotechnology often speak as if academia and business were monolithic entities. obviously, this is not the case. Universities vary enormously in their structures, values, objectives, orientations, and responses toward collaborative research. The diversity of U.S. industrial firms on these dimensions is probably even greater. Consequently, the type of university-industry research arrangement that works for an Eastern Ivy League university may be very different from one that fits a land grant college in the South or the Midwest; the motivations and expected outcomes of a large multinational corporation that collaborates with a university—such as Monsanto's agreement with Washington University—undoubtedly would vary greatly from those of a start-up venture like Embryogen and its relationships with Ohio University. Because these differences may affect the benefits and problems experienced by collaborating

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partners, analysts must go beyond the generalities and document some of these variations.

In a recent OTA study of collaborative research arrangements (31), the particular type of organizational structure was not highly correlated with benefits or outcome measures; the same could be said for problems. What is more likely—although additional research is needed in this area—is that the potential problems for the university and its faculty may be tied to the degree to which a particular arrangement interferes with faculty duties and the level—individual or institutional-at which the agreement is made. From an industrial point of view, benefits are in part tied to these two factors as well, but the direction of the causation is probably reversed.

Variability Among Industrial Partners

It is not possible to explore all the differences among industrial partners that can affect university-industry research collaborations in biotechnology. Furthermore, there are times when the same company enters into different types of agreements with separate universities, each characterized by its own pattern of interactions and outcomes. An example is Monsanto's agreements with Harvard and Washington Universities. One variable may be distinctive in the relationships between universities and businesses—the size of the collaborating partner.

Discussions with industrialists, both large and small, suggest that collaborations with small firms seem to constitute the greatest gamble for universities. Compared to larger firms, small firms are more likely to support faculty with significant equity in their companies, report the use of trade secrets, and fund projects of very short duration.

On the other hand, the financial benefits of relationships with small firms may be considerable. These arrangements seem to produce many more patent applications per dollar invested than do relationships with large firms (3,4). However, the applications for patents held by universities may not produce profitable licenses, and relationships with large companies seem smoother and less complicated with fewer conflicts of interest.

The benefits to individual scientists may be greater with large companies, which are more likely to supply a steady stream of money over the long term (20). However, not all the experts interviewed by OTA perceived small firm collaborations as potentially risky. Much depends on the type of university involved and the way that institution perceives its missions vis-á-vis industry (23). There may be potential risks in collaborating with companies large enough to buy an academic department (14).

Variability Among Sectors or Areas of Research

Little is known about sectoral variations in the nature of university-industry collaborations in biotechnology (e.g., agriculture, chemicals, pharmaceuticals). The major sectoral differences involve orientation and focus: product vs. process. Since companies are most interested in products which can yield the greatest potential gain, the most frequent and intense university-industry research collaborations seem to be taking place in pharmaceuticals. In agriculture, while there are proprietary plants, the research problems are thought to be more complex and the envisioned products more long term. Hence, the degree of collaboration has not been as intense. This is likely to change. In chemicals, where the research is more applied, a large proportion of the research can be done in corporate labs or through consulting, decreasing this sector's dependence on university-industry research relationships.

Some argue that biotechnology firms have already altered the nature of problem selection by academic scientists; problems dependent on the elaboration of technique, not theory, are emphasized. Consequently, in university-industry research relationships, corporations are focusing on the development of biological (e.g., enzymes, pharmaceuticals) because of the likelihood of more rapid commercial payoff. Thus, problems requiring that substantial theoretical obstacles be crossed before technical breakthroughs can be achieved (e.g., the control and transfer of nitrogen fixation in the agricultural sector) are receiving less immediate attention in collaborative research partnerships.

Variability Among Universities in Their Responses to Collaborative Research Arrangements

Just as collaborative arrangements vary tremendously depending on their form, structure, and research area, universities exhibit a great deal of diversity in their responses to the benefits and problems that can result from university-industry research relationships. Differences in response include:

- the amount of time allowed to faculty for outside consulting, or for the management of or involvement in entrepreneurial activities;
- the degree to which faculty can use university equipment, facilities, and staff (including students) in nonacademic, commercial research;
- sanctions against, or incentives for, universities to become financially involved in the start-up or spinoff ventures of faculty (e.g., equity interests in ventures seeded, funding incubator centers);
- whether the university, industrial sponsor, or individual scientists retain intellectual property rights or the exclusivity of such patents, licenses, and trade secrets;
- the amount of time deemed acceptable to delay publications prior to or simultaneous with patent filings; and
- whether university scientists or industrial sponsors (or some combination of the two) set research priorities and the research agenda.

There are few standards in place throughout the academic community on the six dimensions just described. Rather, each institution is meeting the challenge of setting its own boundaries of acceptability in ways that are consistent with its characteristic culture and mission. Some analysts believe that the largest, most prestigious universities must be the ones to stand up to the potential risks of industry-university collaboration and set the standards for other institutions to follow (23).

Too simplistic are assumptions that a continuum can be constructed to characterize the nature of collaborative research arrangements in biotechnology and that problems would intensify as the ties between academia and business intensify. Problems and benefits exist at all ends of the continuum. Furthermore, rather than a linear continuum, there exist multiple axes at any moment in time (e.g., type of arrangement; size of industrial partner; university culture; area of research).

SUMMARY AND CONCLUSIONS

In the long run, the trade-offs made between the potential benefits that accrue from university-industry research collaborations in biotechnology and the potential problems and risks associated with such relationships will depend on how the public and the policy-making community value the outcomes of these new partnerships. Two issues that must be balanced are:

- whether losses to science or to university values that result from increases in the level of secrecy in universities are offset by net additions to knowledge that result from the infusion of industry funds into university laboratories; and
- whether shifts in the direction of the university research agenda toward more applied and commercially relevant projects have benefits for human health and economic growth that far outweigh the risks to basic research.

University researchers are not the only ones concerned with the trade-offs. Others have said that it is truly in the national interest to develop new institutional arrangements that are potentially capable of reducing the time lag between advances made in the basic research laboratory and the application of those advances to human service (33). Advocates of active university-industry collaboration assert that the public interest is best served when the results of research are published and made available to the scientific community, and the academic work that is commercially valuable is patented and does in fact reach the marketplace faster through collaborations between the universities and the industrial community.

In the meantime, there are measures that can be taken to strengthen university-industry research relationships for all participants, and to maximize some of their potential benefits, while minimizing their problems and risks. Universities and the industrial firms involved could ease the introduction of academic-business partnerships on campus with extensive prior discussion in which all relevant parties including students, faculty, university administrators, and corporate executives participate.

Universities can negotiate collaborative agreements that are consistent with the values and missions of their institutions and can include as essential elements of any such agreement:

- the scope of the agreement (e.g., particular research area(s) supported; time commitments of faculty participants);
- control over the conduct of the research (e.g., who selects areas of research, specific projects, and methodologies; provisions for internal and/or external advice and review);
- sponsor's responsibilities (e.g., funding; staff support; equipment; materials contributed);
- treatment of proprietary information;
- publication requirements (e.g., pre-publication review delays); and
- patent rights and income (e.g., title retention; license agreements; term or life of the patent).

Once established, universities can monitor their collaborative research relationships with industry and rigorously enforce:

- disclosure rules;
- conflict of interest statutes;
- limitations on excessive outside consulting by faculty members; and
- sanctions against faculty that retain "full-time" status at the university and are simultaneously executives in their own companies with "full-time" management responsibilities.

It has been suggested that Federal law or regulation should dictate what is considered in and out of bounds for universities in their interactions with industry. A violation of the rules would mean a cut off of Federal funding for the university in question (18). While such an approach is extreme, the issue of private gain from public investment requires some degree of accountability.

Those who take a negative view of university-industry research relationships may be arguing for a return to a perceived simpler time, when academics were academics, and businessmen were businessmen. Times have clearly changed, and both the internal and external demands on the university are increasing and sometimes conflicting. Perhaps the most obvious example of those changes and conflicts is the ever-closing gap between business and academia in U.S. biotechnology.

Even though industrial support for university research in biotechnology has clearly changed the dynamics of that field at the individual and institutional levels, any funding source has the potential of influencing the research agenda and those that conduct the sponsored research.

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