Industrial Support of University Research in Biotechnology

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A 1984 study of biotechnology companies reveals that nearly one-half of all such firms fund research in universities. Industry may support as much as one-quarter of all biotechnology research in institutions of higher education. These investments seem to be yielding substantial benefits to involved firms. Per dollar invested, university research is generating more patent applications than is other company research. Research relationships do pose some risks to traditional university values such as openness of communication among scholars. These risks may be greater in relationships involving small firms. The data also reveal that government is now, and seems likely to remain, the principal source of support for university research in biotechnology.

INDUSTRIAL SUPPORT OF UNIVERSITY RESEARCH IN BIOTECHnology has been the subject of lively discussion in universities (*1, 2*), government (*3, 4*), academic journals (*5*), and the popular press (*6, 7*). The potential commercial and scientific benefits of such research relationships have been widely acclaimed (*8*), and the potential risks to academic and scientific values and practices widely deplored (*9, 10*).

The growth of university-industry research relationships (UIRR's) in biotechnology has also raised important generic issues regarding industrial support of university research. Universities face questions concerning whether and how to structure and monitor research relationships to avoid potential conflicts of interest among faculty and threats to traditional university values (*11*). Companies must assess whether university research is yielding commercial benefits sufficient to justify their investment. For its part, government must decide whether the level and type of industrial support is sufficient to justify reductions in federal support of biotechnology research in universities. Commenting on this last issue, the *New York Times* recently editorialized: "There are also times when a field of research no longer needs the Government as nursemaid: The rich flow of venture capital into biotechnology means the Government need no longer support that element of biomedical research so heavily" (*12*).

Despite much speculation and the anecdotal reporting of large-scale support by a few companies such as Hoechst and Monsanto, relatively little systematic information exists concerning the prevalence of university-industry research relationships in biotechnology, the characteristics of such relationships, or their consequences for industries, universities, or society at large. Such information is vital to informing emerging policy debates. To help develop that information, we recently surveyed 106 randomly selected companies that conduct biotechnology research, asking them about their support of such research in universities.

We found that nearly half of all biotechnology firms support research in universities, that firms see promise of important commercial returns from that investment (measured by a surprising number of patent applications), and that universities seem to be benefiting as well. However, we also found evidence that UIRR's pose risks to traditional university values and practices. Most importantly, we found that government continues to fund the great bulk of biotechnology research on the nation's campuses and that industry shows no signs of supplanting government support of research in this field.

Study Design

This industry survey is part of a series of surveys and case studies that constitute the Harvard Project on University-Industry Relationships in Biotechnology. The project is designed to investigate the extent and consequences of university-industry relationships that involve what the Office of Technology Assessment has called the "new biotechnologies" (*13*). For our purposes, the new biotechnologies include recombinant DNA technology, monoclonal antibody technology, gene synthesis, gene sequencing, cell or tissue culture techniques, fermentation technologies, large-scale purification, and enzymology.

This article reports the results of a survey of companies that support or conduct biotechnology research. To construct a list representing the universe of such firms, two techniques were used. First, we obtained existing lists published in trade journals or available from other sources. To ensure completeness, executives of several major firms on the list were contacted and asked to name new firms or other firms that might not be well known. Second, names of the 1984 *Fortune* magazine listing of the 500 largest companies in four industrial sectors (pharmaceuticals, petroleum-related products, chemicals, and agriculture) were added, even if these companies were not on the original lists. It was assumed that some of the larger firms might be supporting small amounts of biotechnology research without the knowledge of trade journals or other involved companies.

These procedures yielded 115 Fortune 500 (F5) companies and 435 non–Fortune 500 (NF5) firms. To ensure adequate representation of large firms, a stratified random sample of 76 F5 and 129 NF5 firms was selected.

To be eligible for inclusion in the survey, firms had to conduct or support research involving one or more of the biotechnologies listed above. Sample screening was conducted over the telephone by

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trained, professional interviewers at the Center for Survey Research, University of Massachusetts, Boston. Respondents were vice presidents for research and development or chief executive officers. Screening revealed that slightly over one-third of the companies were ineligible. The final sample consisted of 39 F5 firms and 88 NF5 firms. Eighty-four percent of eligible firms agreed to participate. Interviews were completed with 35 F5 firms and 71 NF5 companies. The majority of refusals occurred because of time constraints or company policies that prevented disclosure of proprietary information of the type that was being requested. Interviews were initiated in March 1984 and were completed in May 1984.

Weighted means and proportions were calculated to reflect the sampling of F5 and NF5 companies at different rates. Without the weights, estimates would not accurately reflect the universe from which the sample was drawn. In addition, in several analyses the sample was divided into F5 and smaller firms to compare their behavior.

In 1984 firm sales averaged $8.4 billion among the 35 F5 companies and $326 million among the 71 NF5 firms (Table 1). An examination of firm age reveals that this is a very young industry and that firm age and size are highly correlated. Seventy-one percent of NF5 companies were incorporated in 1972 or later, although all the F5 companies were founded before that time.

The most common products developed by these firms are chemicals or enzymes (80 percent of the F5 companies and 61 percent of the NF5 companies) and pharmaceuticals or diagnostics (66 percent of the F5 firms and 68 percent of the NF5 firms). Agricultural products (46 percent of the F5 firms and 42 percent of the NF5 firms) and medical devices (43 percent of the F5 firms and 39 percent of the NF5 firms) rank third and fourth, respectively. Other areas of development include food processes or products and petrochemicals.

Frequency of Support of Biotechnology Research in Universities

Our estimates suggest that 46 percent of all firms in the biotechnology industry support biotechnology research in universities. However, F5 companies are significantly ($P < 0.05$, t-test) more likely to support university research in biotechnology than NF5 firms (Table 2). Multivariate analysis controlling for a number of other firm characteristics tends to confirm this relationship between firm size and propensity to support university research (*14*).

There are several possible explanations for the significant association between firm size and the frequency of support of university research. One is that larger firms are simply more diversified in their investment strategies. Because of their greater size and resources, they undertake a broader array of research projects, some of which are most effectively pursued in universities. A second possible explanation is that their greater financial security may permit larger firms the luxury of supporting fundamental investigation, which is usually perceived to have less certain or immediate payoffs. Universities are usually considered to be superior to industry as a setting for basic research (*15*).

Magnitude and Duration of Industrial Support

As might be expected, larger firms give more money to universities than smaller ones and also tend to give larger amounts per grant. During 1984, the average F5 company involved in biotechnology planned to spend $1.1 million on such research in universities, while the average NF5 company planned to spend $106,000 (Table 2).

Another measure of the relative magnitude of private investment in university research is the proportion of a firm's biotechnology research & development (R&D) budget spent in universities. The data reveal that a significant minority of companies is heavily dependent on universities in conducting biotechnology research. Thirty-one percent of the firms in the biotechnology industry that support university research invest more than 10 percent of their biotechnology R&D expenditures in UIRR's. Twenty-one percent of involved companies invest more than 20 percent of their R&D funds in universities.

Table 3 shows the typical duration of biotechnology research projects supported in universities. UIRR's are often very short: 51 percent of firms report that projects last 1 year or less, and only 28 percent report UIRR's lasting more than 2 years. Although F5 companies are more likely than smaller firms to enter projects of longer duration, the difference is not statistically significant.

Our sample data also allow us to make the first reliable estimate of

Table 1. Characteristics of biotechnology firms sampled. Values are millions of dollars.

Type of firm	Sales	Total R&D expenditures	Biotechnology R&D expenditures	Proportion on biotechnology*
F5 (n = 35)				
Mean	8,357	188	19	0.17
Range	4,200 to 50,000	5 to >1,000	0.05 to 200	
NF5 (n = 71)				
Mean	326	18.2	5.1	0.79
Range	0 to 5,000	0.035 to 400	0.05 to 93.7	

*Mean proportion of R&D funds spent on biotechnology by sample firms.

Table 2. Frequency and magnitude of support for biotechnology R&D among firms sampled and estimated for the industry.

Type of firm	Firms supporting university research*	Mean 1984 expenditures on university research ($ thousand)	Mean expenditure per project, 1984 ($ thousand)
F5 (n = 35)	29 (0.83)	1052	108
NF5 (n = 71)	27 (0.38)	106	19
Biotechnology industry estimate† (n = 293)	135 (0.46)	418	67

*Figures in parentheses are proportions of each type of firm that supports university research. Proportions of F5 and NF5 companies supporting UIRR's are significantly different ($P < 0.05$). †Weighted to correct for oversampling of F5 firms.

Table 3. Distribution of firms by typical duration of UIRR's in biotechnology. The durations of support reported by F5 and NF5 companies were not significantly different.

Type of firm	Duration of UIRR (years)			
	<1	1	2	>2
F5 (n = 28)	0	9	7	12
NF5 (n = 27)	1	15	5	6
Industry estimate* (n = 134)	3 (0.02)	65 (0.49)	28 (0.21)	38 (0.28)

*Weighted to correct for oversampling of F5 firms. Figures in parentheses represent estimated proportions of firms reporting typical duration as noted.

Table 4. Biotechnology patent applications among firms with UIRR's, by site of research and size of firm.

Type of firm	Number of firms reporting patent applications	Patent applications by site*		
		Total	Nonuniversity	University†
F5	22	400	334	66 (0.17)
NF5	21	266	195	71 (0.26)
Industry estimate‡	103	1493	1156	337 (0.23)

*All figures for patent applications represent totals for samples over the previous 5-year period. Firms were asked to report only those resulting from biotechnology R&D. †Figures in parentheses represent proportions of all patent applications resulting from university research. Proportion significantly greater for NF5 companies ($P < 0.05$). ‡Weighted to correct for oversampling of F5 firms.

Table 5. Productivity of biotechnology research investments among firms with UIRR's, by site of investment and size of firm.

Type of firm	Patent applications per $10 million invested*	
	Nonuniversity	University
F5	13.1	22.6
NF5	20.5	100.3
Industry estimate†	18.2	76.1

*Total of all patent applications over the past 5 years from biotechnology R&D divided by total dollars invested by all companies in each research site. †Weighted to correct for oversampling of F5 firms.

the total amount of money industry supplies to universities for biotechnology research. To make a realistic calculation, it is necessary to decide how the firms that refused to participate in the study would behave. The extreme assumption that none of the refusing companies support university research leads to a lower bound estimate of about $81.1 million invested in UIRR's in biotechnology. Assuming that all refusals support UIRR's in amounts comparable to respondents yields an upper bound estimate of about $135.7 million. Finally, if one assumes that refusals support UIRR's with the same frequency and with amounts comparable to respondents, one obtains an estimate of $120.7 million. Since we have no evidence that refusals differ markedly from participating companies, we believe that this last figure constitutes the best guess concerning total industry support of UIRR's in biotechnology during 1984.

These estimates indicate that universities benefit financially from their research grants and contracts with industry. How important is this industry support to academia? The National Science Foundation has estimated that federal support for biotechnology research totaled $560 million to $600 million in fiscal year 1983 (*16*). By making certain assumptions, this estimate of federal support can be combined with our estimates of total industry support to calculate the proportion of all university research in biotechnology supported by industry in 1984.

We assumed first that one-half of all federal support for biotechnology research is spent in universities, a figure typical of health R&D generally (*17*). Second, it is assumed arbitrarily that federal support for biotechnology research increased by 10 percent between 1983 and 1984 in current dollars. Third, we assumed that, as a percentage of federal funding, state, local, and nonprofit support of biotechnology research in universities is the same as their support of health research and development generally. This last assumption permits an estimate of nonprofit and nonfederal governmental support of biotechnology research using available data from the National Institutes of Health (NIH) (*16*). On the basis of these stipulations and taking into account our high and low figures for actual industry support, we estimate that UIRR's in biotechnology accounted for 16 to 24 percent of all funds for biotechnology R&D available to institutions of higher education in 1984.

In contrast, industry provides only 3 to 4 percent of all research funds expended in institutions of higher education (*17*) and about 3 percent of these institutions' funds for health R&D (*18*). Industry, therefore, provides a much larger proportion of the funds available for university research in biotechnology than in most other fields.

Benefits and Risks of UIRR's for Involved Firms

Our survey offers evidence that supporting biotechnology research in universities has both benefits and risks for involved companies but that on balance it is likely to repay the investment.

Patent applications and trade secrets. To assess the benefits of UIRR's, respondents were asked about patent applications that have resulted from biotechnology research they have supported in universities. The numbers of patents generated is a standard measure of the commercial benefits of R&D expenditures (*19*). However, for very young industries such as this, applications for patents may be a better indicator of the flow of commercially useful research results because there is often a lag of several years from the time of application until patents are granted. Since many patent applications do not result in patents or licenses and thus do not produce income (*20*), the number of patent applications may overstate the commercial benefits of research. Nevertheless, this measure is useful for comparing groups within our sample.

Table 4 shows the total number of patent applications over the past 5 years that have resulted from biotechnology research supported by sample firms involved in UIRR's. Firms were asked to indicate how many applications resulted from work supported in universities and how many from other company-sponsored research. During this period, university research accounted for 23 percent of all biotechnology patent applications resulting from the work of involved firms. Among F5 companies, university research accounted for 17 percent of all patent applications. Among smaller companies, it accounted for 27 percent, a significantly higher proportion ($P < 0.05$).

Respondents were also asked whether their support of university research has resulted in any trade secrets—another measure of commercial benefits from UIRR's. Trade secrets consist of information the proprietary value of which is protected through systematic attempts to prevent disclosure, including prohibiting publication of research results. Some companies prefer trade secrets to patents as a way of protecting intellectual property; to obtain patents, companies must disclose the patentable finding, and infringement of patent rights is often difficult to detect and costly to prosecute. We estimate that 41 percent of biotechnology firms involved in UIRR's have derived at least one trade secret from the biotechnology work they support in universities. The proportion of NF5 companies reporting such commercial benefits (50 percent) is significantly higher ($P < 0.05$) than the proportion of F5 firms (28 percent).

The commercial productivity of UIRR's is further detailed in Table 5. Pooling data from all involved companies in our sample, we calculated the number of patent applications resulting from UIRR's and from other company research over the past 5 years. We then divided each figure by the total investment of sample firms in UIRR's and in other research during fiscal year 1984. Finally, weighted averages of the F5 and NF5 figures were calculated to arrive at productivity measures for the whole biotechnology industry. If we assume that the relative investments of companies in

UIRR's and nonuniversity research have not changed over the past 5 years, then the figures provide an indication of the relative productivity of these two research sectors.

The results indicate that UIRR's have been dramatically more productive than other research. Per current dollar invested, university laboratories over the past 5 years have generated 4.2 times as many patent applications as company laboratories. NF5 companies seem to do particularly well investing in university research.

For several reasons, our figures should be interpreted with caution. First, if companies have increased the proportion of their biotechnology R&D conducted in their own laboratories, our calculations might overestimate the relative productivity of UIRR's. Second, even if UIRR's were more productive of patent applications during the early years of the industry, this apparent efficiency may reflect universities' near-monopoly on knowledge of these new techniques at the time the industry began, rather than a general ability to outperform industrial laboratories in doing commercially relevant research.

Other benefits. Firms may also derive benefits that cannot be readily captured through figures on patents or trade secrets. Respondents with UIRR's were asked to judge the extent to which their firms had realized eight specific benefits. Table 6 presents the results weighted to reflect the entire biotechnology industry.

The benefits that firms realize most often are that UIRR's help keep the firm current with important research, that they reduce the cost of mounting R&D programs in new fields, that they provide training and staff development for company scientists, and that they enhance the firm's public image.

Risks of UIRR's. UIRR's may also pose some risks for investing firms. Respondents supporting university research were asked to judge the extent to which UIRR's pose five possible risks. Table 6 presents the weighted results. Firms most often reported that UIRR's risk a poor payoff in marketable products and that they risk a loss of proprietary information. (Interestingly, sample firms without UIRR's perceived both benefits and risks to be significantly greater than did firms with UIRR's.)

In sum, traditional measures of innovation and commercial productivity indicate substantial short-term benefits but do not address the ultimate dollar value of UIRR's in biotechnology. Companies tend to agree that, like all investment decisions, UIRR's pose the risk of poor payoff. Their uncertainties will be resolved only over time and through future research. On the basis of available data, however, it seems likely that industry has benefited substantially from its investment in UIRR's during the past 5 years.

Table 6. Perceived benefits and risks reported by firms with UIRR's.

To what extent does sponsoring university research	Percent answering: to a great or some extent*
Benefits	
Help your company to keep current with important research?	83
Reduce the costs of mounting R&D programs in a new field?	60
Result in licenses for products or processes?	53
Enhance your firm's public image?	52
Provide training and staff development for company scientists?	52
Aid in recruiting faculty to work in the company?	41
Make your company more attractive to investors?	31
Provide tax benefits to the company?	19
Risks	
Risk a poor payoff in marketable products?	62
Risk a loss of proprietary information?	58
Take too much effort to monitor and control?	42
Run the risk that universities may choose to withdraw from relationship before the firm receives anticipated benefits?	21
Adversely affect the morale of company scientists?	19

*Weighted to correct for oversampling of F5 firms. Remaining firms reported the benefit occurring only a little or not at all.

Implications of UIRR's for Universities

Universities may also be affected in major ways by UIRR's in biotechnology. We are completing separate surveys of university administrators, faculty, and students to explore more fully the implications of UIRR's for academia, including prevalence and types of university and faculty involvement in UIRR's, the effects of such involvement on faculty attitudes, publication rates, teaching behavior, commercial productivity, and other matters of concern to the university community. Some important insights for universities emerge from this study of industry involvement in UIRR's in biotechnology.

As we have indicated, UIRR's constitute a substantial source of support for biotechnology research on the nation's campuses. This support must be counted among their benefits to universities. UIRR's may also provide financial benefits to universities in the future in the form of income from licenses sold to industry on discoveries patented by the university. In the past, patents in biology and other fields have rarely produced significant income for universities (*21*), but it is possible that the new biotechnologies will result in patents that are more profitable.

Against these and other proven or potential benefits, universities must balance the potential risks of UIRR's in biotechnology. To explore the extent of such risks, we questioned companies about circumstances that might create conflicts of interest among faculty or threaten traditional university values, such as openness of communication among scholars.

We asked each company involved in biotechnology UIRR's whether they fund the university research of any faculty members who hold "significant" equity in the firm. Some have expressed concern that this situation would create strong incentives for faculty to design their research to serve the narrow commercial interests of the firm rather than the broader goals of basic science (*11*). We found that 21 percent of NF5 companies, but none of the F5 firms, reported funding faculty holding significant equity. The fact that all positive responses came from smaller firms is not surprising. Equity in virtually all F5 companies is publicly traded, making it unlikely that any single faculty member would hold enough equity for the firm's management to be aware of that scientist's investment.

Companies were also asked whether they directly support, through grants or scholarships, the university training of graduate students or postdoctoral fellows in the life sciences. Thirty-two percent of all firms provide such support. Of these, one-third stipulate that students must work on problems or projects defined by the company, work for the firm during the summer, or work for the company after completing their training. Some universities may be concerned that such obligations place undesirable constraints on young scientists at a vulnerable and potentially very creative time in their careers.

The frequency with which companies report that trade secrets result from their UIRR's may also be of concern to some universities (*22*). Research results treated as trade secrets cannot be published and cannot be freely discussed with colleagues or students. As previously noted, small firms are significantly more likely to report the occurrence of trade secrets than are large firms.

Finally, the typically short duration of UIRR's in biotechnology raises questions about whether some of these relationships shift the focus of university research toward applied work. As previously noted, about one-half of all respondents and a full 60 percent of NF5 companies reported that their UIRR's typically last 1 year or less. It is possible that UIRR's will be renewed for longer periods, but so far, at least, projects have been of short duration and thus seem likely to be applied in nature.

Conclusions

A number of policy implications emerge from our data. It is apparent that the biotechnology industry has reason to be pleased with its investment in university research to date. UIRR's seem to have produced a plentiful stream of patent applications. Indeed, over the past 5 years, UIRR's appear to have produced more than four times as many patent applications per industry dollar invested than has other company research. UIRR's have also resulted in trade secrets and other benefits that are more difficult to quantify.

While they seem to be deriving important financial benefits from UIRR's, universities have reason to be concerned about the risks created by these relationships. A significant minority of firms report the existence of arrangements and behaviors that may threaten traditional university values, such as openness of communication and the unhampered pursuit of knowledge.

In general, UIRR's with small firms seem to constitute the greatest gamble for universities. On the one hand, the financial benefits of these relationships could be very large, since these UIRR's seem to produce many more patent applications per dollar invested than do relationships with large firms (Table 5). On the other hand, it is far from certain that applications for patents held by universities will ever produce profitable licenses. Moreover, the amounts of research support provided by these relationships is small compared to UIRR's with larger firms, and the potential threats to university values seem greater. Compared with large companies in our study, small firms are more likely to support faculty with significant equity in their companies, are more likely to report the occurrence of trade secrets, and tend to fund projects of very short duration.

Small firms may be playing a more important role in UIRR's in biotechnology than they have recently played in other fields, such as the chemical and petroleum industries. Universities should be cautious, therefore, in concluding from the experience of the physical, chemical, and engineering sciences that the development of UIRR's in biotechnology will be trouble-free. University administrators, therefore, may want to devote more of their limited resources to monitoring relationships with smaller companies than with large ones.

Our data also have policy implications for government and for society at large. Industry has a strong interest in biotechnology research in universities. The new biotechnologies were created in universities. Their commercial potential has been widely acclaimed (*23, 24*). Many firms in this new industry still lack the internal resources to exploit these techniques fully. For all these reasons, it comes as no surprise that industry supports a larger proportion of university research in biotechnology than it supports in the average scientific field.

Perhaps more striking, however, is the finding that industry funding remains small compared to government support of biotechnology research on the nation's campuses. This suggests that, even in research areas offering the possibility of great, short-term commercial application, government funding remains the cornerstone of academic research. It follows that any substantial reduction in federal support is likely to reduce the total amount of biotechnology research conducted in institutions of higher education. For example, if the federal government reduced its funding of biotechnology research by roughly 10 percent ($60 million), and if we assume that one-half of those funds would have gone to universities, as it usually has, industry would have to increase its support by roughly 25 percent to make up the difference. This seems unlikely, at least in the near future (*25*).

Even if industry increased its support to compensate fully for federal cutbacks, society might not be completely satisfied with the result. Industry support seems different from government support of university research. Industry projects tend to be shorter in duration. In 1982, 92 percent of NIH's extramural awards were for 3 years or longer (*26*). In contrast, 72 percent of companies in our sample reported that the typical duration of their UIRR's is 2 years or less. Since short-term projects are usually associated with applied research, an increase in the proportion of university research supported by industry is likely to result in a shift toward more applied investigations. Whether such a shift is desirable remains unclear. Industry sponsorship also carries risks to openness of communication among scientists and to faculty independence that have not been encountered with government support of biotechnology research up to this point (*27*).

A final lesson of our study is that UIRR's in biotechnology seem to be playing a critical role in the birth of a new industry. The commercial consequences of UIRR's to date provide tangible evidence of the practical value of government support of fundamental research in universities.

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