NIH Ponders Pitfalls of Industrial Support

Collaborative research on campus is sticky business for NIH advisory group; is "publish or perish" now "patent or perish"?

The German corporation Hoechst last month dazzled the scientific community when it gave Massachusetts General Hospital a 10-year grant of $50 million for research in genetic engineering. It was the most recent and spectacular example of the rush of industrial money into academic biomedical research, which in the past has relied mainly on dollars from the National Institutes of Health. This funneling of industrial money into university research—especially into genetic engineering—poses policy problems for NIH as well as for the universities. The problems were the subject of a wide-ranging discussion recently by the advisory committee to the director of NIH.

At a meeting held in Bethesda, Maryland, on 8 and 9 June, the committee asked whether the quality of basic research is compromised by industrial support, an issue that was addressed on Capitol Hill at the same time by a House committee (*Science*, 19 June, p. 1368). The group also questioned just what NIH's policy on patents should be now that industry is funding projects that also have federal support.

"We see ourselves as Dr. Faustus with all sorts of evil things surrounding us," said Walsh McDermott of the Robert Wood Johnson Foundation. The real question, he said, is, "How does one behave with money? We're not talking about things that are wrong. We need a code of etiquette."

An official from Massachusetts General contended that basic research is not imperiled by the Hoechst agreement. Director of research policy and administration Ronald Lamont-Havers noted that 30 years ago universities were fretting about the large amounts of government subsidy streaming into campus research. The same alarms are being raised now, he said, noting that academic research has not suffered at the hands of federal money.

NIH director Donald Fredrickson asked at one point, "Are we turning university labs into industrial labs?" Lamont-Havers said little to convince the committee that investigators would truly be free to pursue basic research. He said that, although Hoechst is expected to support most projects, proposals that the company refuses may then be submitted to NIH for funding. When asked by Fredrickson if Hoechst, in effect, was directing university research, Lamont-Havers replied that the company's foremost interest is not in inventions and patents, but rather in obtaining the latest information and having a place to train its own people. Under the agreement, Mass General has first option on patent rights and will grant Hoechst exclusive license.

Fredrickson asked if scientists funded by Hoechst could also accept support from other companies. Lamont-Havers hedged the question, saying that the hospital will have to decide on a case-by-case basis.

The NIH committee was also worried that industrial funding will discourage the free flow of information among scientists. Several individuals, including Stuart Bondurant, dean of the University of North Carolina School of Medicine, and Frederick Andrews, vice president of the Purdue Foundation, said that they have noticed that researchers are now more inhibited about sharing research information. Bondurant said, "The lure of the dollar makes people clam up." Doris Merritt, a special assistant to Fredrickson, warned, "Publish or perish doesn't need the corollary of patent or perish." In contrast, officials from the Hybritech company of California, which manufactures hybridomas, said they allow scientists to send out cell lines to other investigators, a privilege that not all genetic engineering companies grant.

The committee spent much of its time discussing NIH's present patent policy. Federal patent policy has differed from agency to agency, but a new set of draft regulations that will provide uniformity to the code is expected to be published any day now by the Office of Management and Budget (OMB). The proposed regulations are not expected to change NIH's present system significantly. Despite the new code, government patent policy remains "confusing at best," said Peter Hutt, an attorney for the Washington firm of Covington and Burling and former general counsel for the Food and Drug Administration.

One aspect of patent policy that is likely to generate problems is a requirement that a scientist report to NIH every potentially patentable invention developed with institute money. As industry contributes more dollars toward academic research, the committee is uncertain whether NIH can insist that researchers follow the reporting rule because, for example, it becomes much more difficult to sort out the sponsor of the project—namely, government or industry.

The reporting rule has caused problems already with researchers receiving only government money. Investigators in genetic engineering must report every new hybridoma to their institution. But some scientists have mistaken the rule to mean that every invention needs a patent. Matthew D. Scharff, chairman of cell biology department at Albert Einstein College of Medicine, said that patent policy can often be mystifying to bench scientists because they do not understand the details of the requirements. In one extreme case, a young scientist paid out $28,000 of his government grant to patent every new hybridoma he developed, said Charles Lowe, acting associate director for medical application of NIH research.

The reporting rule is impractical in and of itself, Scharff said. Some laboratories are producing 100 different monoclonal antibodies a week and only a handful may prove useful. "How can you report all of it?" he asked. The draft regulations will require strict reporting of inventions, although attorneys from the Department of Health and Human Services, who represent NIH, contested the rule set down by OMB.

Cosponsored research has also prompted the committee to think about its role in monitoring the development of patents. In the past, NIH has automatically given patent rights to major universities when the government has been the only outside source of funding. The arrangement is known as an institutional patent agreement and, under the proposed regulations, will apply to all other universities and nonprofit institutions not now covered, and to small businesses as well.

But even after relinquishing its rights to a patent, the government still has the final word on which party retains a patent on an invention it helped to fund. NIH may reclaim a patent from the university if it fails to develop an invention that the government deems important.

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NIH may choose to award title to another party or to license the invention itself. The committee wants a clearer definition of circumstances in which NIH might exercise this "march-in right," as it is called by patent attorneys.

Industry is apparently troubled by the provision because it has no certainty that a title to an invention it nursed through the research stage is protected if the patent remains undeveloped. Hutt said that industry needs assurances that its investment is secure. NIH has never used the march-in right, although it has brandished it on occasion to prompt action on a patent.

Setting aside the issue of patent policy, the advisory committee was worried about NIH's investment in academic research on yet another front and pondered how much the government should pay for indirect costs on research grants. The question is age-old, but, as NIH appropriations remain level, the agency wants to make sure that its money is being used for research rather than for university overhead costs or activities unrelated to research, such as curriculum development.

Fredrickson said that NIH may decide to pay a flat sum for total costs, rather than continuing with the current policy of placing a cap on indirect costs, and let researchers and campus administrators figure it out for themselves how to divide up expenses. Joseph Perpich, associate director of program planning and evaluation, predicts that there may now be some movement on the issue because of the new Administration's general belt tightening. One of the most vulnerable areas is departmental administration costs, which cover student and faculty recruitment, lecture series committees, and budget committees.

One proposal that the advisory committee is weighing that might enhance the quality of research is a grant system called a fixed obligation grant (FOG). Fredrickson said, "I'm beginning to glow about this. I think we may have something."

Such a grant would eliminate time-and-effort accounting by researchers, and the work would be graded on technical reports submitted periodically. The new system would also allow spillover of grant money from one year to the next to prevent the spending sprees with left-over federal money at the end of each fiscal year. The forecast is unclear if or when the FOG will roll into the nation's campuses.—MARJORIE SUN

Team Research: Responsibility at the Top

A debate develops over whether senior scientists should answer for the misconduct of junior colleagues

Few precepts of laboratory ethics seem more straightforward than the notion that a scientist should take responsibility for his research, accepting both praise and blame.

It is therefore noteworthy that a minor debate has emerged during the past year over whether a senior researcher should be held responsible for the work of junior members of a research team, especially for unethical work. So far, there seems to be anything but consensus.

In sharp contrast, the sharing of rewards is governed by long-standing tradition: it is common practice for a senior researcher to share coauthorship even when his specific contribution is more inspirational than substantial. An emerging debate over risk and reward for senior researchers may bode ill for collaborative research. Junior researchers joining the debate have voiced strong grievances.

The responsibility debate, overheard at various hearings called by presidential commissions and in Congress, was touched off by reports of misconduct and data falsification in collaborative research. Perhaps one of the more noted incidents centered on responsibilities of Yale senior researcher Philip Felig for the data falsification of a junior colleague (*Science*, 3 October 1980, p. 38). The dimensions of the debate at this point are quite broad: issues include how much responsibility a principal investigator should take for patient welfare in clinical studies, for the integrity of data in a multi-authored paper, for the integrity of data generated by research aides who may not have a stake in the publication process, and so on. Effects of the debate may be far reaching. The explosive growth of collaborative research in the postwar era has brought with it a variety of organizational tensions that are not as a rule examined in public. However, as federal officials and deliberative bodies make recommendations on how to avoid some of the ethical and administrative tangles that have recently emerged, what heretofore has been informal by way of dividing up various responsibilities in the lab might well be mandated by law.

The responsibility issue was most recently debated at a special meeting in Boston of the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research. The focus was the case of Marc J. Straus (*Science*, 19 June, p. 1367). In 1978 Straus was the principal investigator of a large research team at Boston University (BU) that submitted falsified data to a multi-institutional clinical study. Team members reported the misconduct to BU officials and said they falsified patient data on orders from Straus and because of "general anxiety" that there might be a shortage of statistically acceptable patients for their studies. Straus denied the charges and quit the school.

Publicly commenting on the case for the first time in 3 years, Straus at the hearing differentiated realms of responsibility. He said he took "full responsibility" for all aspects of patient care, but that paper work was a different story. "We had 40 full-time people, including eight nurses and data managers, and we had a series of very good checks and balances. . . . [But] there are certain types of studies that are almost beyond the ability for absolute surveillance. . . . You must rely on the integrity of people who are going to fill in those multiplicity of little boxes correctly. . . . There is a certain level of surveillance in any operation, medicine or otherwise, that requires the belief that the persons under you are acting properly."

Straus's attorney, Andrew Good of Boston, lamented the lack of uniform and clear federal guidelines on the responsibility issue. Good noted that the case is currently under investigation by the Food and Drug Administration and the National Institutes of Health, and

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