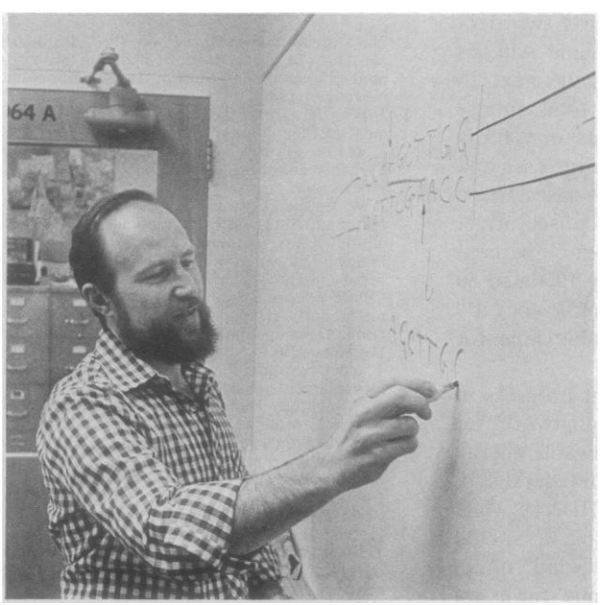
The Hoechst Department at Mass General

A corporate investment of $70 million is the financial cornerstone of what may become a major center for molecular biology

In October 1980, biochemist Howard M. Goodman approached officials of Hoechst AG, the giant West German chemical company, with a powerful idea. Goodman wanted to create a new center for molecular biology where a concentrated corps of talented researchers could work on the field's most challenging basic questions without having to worry constantly about money. He envisioned a fairly large enterprise—ultimately some 100 persons strong—whose security could be assured for at least a decade. Goodman suggested that Hoechst put up the money.

The Academic-Industrial Complex

This is the second in a series of occasional articles about the emerging relationships between industry and universities.



Howard M. Goodman

Initiated the Hoechst agreement

Just 8 months later, Goodman's idea became reality when Hoechst signed an agreement with the Massachusetts General Hospital (MGH), committing $70 million over 10 years to completely equip and support a brand new Department of Molecular Biology. Goodman is its director.

Even in the rapidly expanding drama of the academic-industrial complex, where corporations are parceling out millions for university research, the MGH-Hoechst deal is a showstopper. No matter how you look at it, $70 million for a single department is a lot of money and the contract, which its signers describe as a "model" for university-industry agreements, is the object of intense interest.

Howard Goodman, 43, is one of the principal figures in molecular biology, whose early research contributed to the purification of restriction endonucleases—the enzymes that make recombinant-DNA technology possible. In 1977 at the University of California at San Francisco (UCSF), Goodman, collaborating with William J. Rutter, was the first to announce the cloning of insulin genes. Subsequent achievements to Goodman's credit include successful cloning experiments with growth hormone and Australia antigen, a protein on the hepatitis B virus. It was the insulin work that first brought Goodman to the attention of Hoechst scientists, with whom he then began to consult. He says there is no doubt that his relationship with the company played a role in Hoechst's decision to back his proposal. "Their knowing me, the mutual trust we'd developed, plus my reputation as a scientist," all contributed, he said in an interview with *Science*. (Goodman has no stock or other personal financial interest in the company.)

In addition, Goodman approached the company at a propitious moment. Hoechst had been thinking about expanding its pharmaceutical operations for some time, he noted. "Now, the time was ripe." Developments in fundamental science made commercial prospects for new drugs and vaccines attractive. And Hoechst scientists saw the 1980's as a decade to "focus on biology." Thus, Goodman persuaded them they would be getting a valuable education. William H. Griesar, the New York attorney who negotiated the contract for Hoechst, told *Science*, "Others think it's disingenuous when we say this, but the Hoechst people really didn't go into this looking just for patentable inventions. Hoechst really wanted a 'window on science.' The knowledge happens to be in the university at the moment, so industry is going back to school." Hoechst may, at any one time, have four company scientists in training in Goodman's department, working on problems Goodman (not Hoechst) chooses. The expectation, Griesar says, is that many of these individuals will return to Germany to head the company's research laboratories.

Goodman initially intended to establish his new department at UCSF, where he had been on the faculty for years, but the constraints involved in dealing with the vast University of California bureaucracy seemed formidable. Goodman and Hoechst wished to complete their deal with dispatch. Said Goodman, "Because of the way public institutions have to make decisions, the time problems looked insurmountable." Provisions in the contract called for new or renovated laboratories, the creation of tenured faculty positions, and the admission of Hoechst scientists to the laboratory as trainees. At UCSF, these and other matters had to be cleared by the medical school dean, the university faculty senate, the president, and the board of regents. Although negotiations between Hoechst representatives and UCSF offi-

0036-8075/82/0611-1200$01.00/0

cials were begun, they never got far.

While discussions were taking place in California, Goodman was being courted by MGH, which quite independently had decided to establish a department of molecular biology. The MGH offer included a tenured post in the new genetics department at the Harvard Medical School, with which the hospital is affiliated. Harvard had recruited Goodman's friend Philip Leder away from the National Institutes of Health (NIH) to head the genetics department. "Phil Leder was a very positive attraction," Goodman stated, explaining his decision to leave UCSF and move to Boston. There were other attractive features about the MGH offer as well.

The Massachusetts General Hospital is an independent entity, run by its own director and board of trustees. Although affiliated with Harvard Medical School, it is in no way financially obligated to the university; nor is it governed by Harvard rules. In short, MGH was a place Goodman could bring the Hoechst contract where negotiations would not have to go through bureaucratic layers. "At MGH you deal directly with the trustees and the head of the hospital," Goodman notes. And that is precisely what he and Hoechst did.

The full measure of MGH's independence is evident in a statement made by Harvard president Derek C. Bok in response to a question from *Science* about the contract. "I prefer not to comment on it," Bok said. "It was signed without our participation. They [MGH] did the negotiating and we heard about it after it was substantially completed."

According to those who participated, the challenge in the negotiations was to accommodate Hoechst's interest in deriving substantial and, to the largest extent possible, exclusive benefit from its investment while also satisfying MGH's interest in preserving academic freedom. And, as former MGH director Charles A. Sanders (now executive vice president of E. R. Squibb & Sons, Inc.) recently observed, "There was worry within MGH about what would happen to the ecology of the hospital with a large and potentially unaccountable department" added on.

How the new department will eventually affect the hospital is anyone's guess, but there are provisions in the contract asserting MGH's control of decisions relating to selection of research projects and other academic matters. A sticky point in negotiating this and other university-industry contracts has been industry's natural inclination to exert as much control of research as it can. According to Hoechst attorney Griesar, it worked out satisfactorily at MGH but could, in general, be a problem in cases in which "more developmental research work were contemplated."

In this case, as the contract notes, the emphasis will be on those basic research areas that are hottest right now—"eukaryotic cell gene regulation, somatic cell genetics, microbial genetics, virolo-

The MGH-Hoechst Agreement

The $70 million agreement between the Massachusetts General Hospital (MGH) and Hoechst AG provides support for MGH's new Department of Molecular Biology for 10 years. Hoechst has the right to licenses to any commercially useful research results and to train at least 40 company scientists at its MGH laboratory. Among the provisions of the contract, which became effective on 14 May 1981, are these:

Exclusive Funding Rights. First, Hoechst "shall have the right to fund all research" in the department and to pay costs of laboratory space and equipment. Second, MGH "agrees to do nothing" when renovating old labs or equipping a new one that will "allow any third party, including the United States Government, to acquire any rights or equity in any work solely accomplished in the Department. . . ."

Personnel. Scientists in the department "shall be regular members of the staff at MGH, nominated for membership in the faculty of the Harvard Medical School. . . ."

Faculty Duties. The scientists "will devote their time primarily to research for the Department. . . ." They "may also devote a reasonable amount of time to faculty duties other than research and to consulting for non-profit-making entities so long as such activities do not interfere materially with their research activities under this Agreement."

Scientific Programs and Reports to the Company. Once a year, the department will hold a 2- or 3-day symposium to which Hoechst can send employees. In addition, department head Howard Goodman will report on research progress to Hoechst representatives at least three times a year.

Training. "The Company shall have the right to send up to four individuals to work and be trained at the Department at any one time. These individuals shall have qualifications acceptable to the Department."

Collaborative Work. The contract states that "Each scientist at the Department shall be free to collaborate with others . . ." and provides that "Research collaborations funded in part by the Company and in part by others shall take into account the interest of the Company in obtaining exclusive, world-wide licenses." If Hoechst cannot get an exclusive license, it must at the least be assured a "nonexclusive license."

Right to Publish. This provision offers something for MGH and something for Hoechst. "The right of individual scientists . . . to publish research results in accordance with the educational and scientific purposes and policies of MGH shall not be infringed," it states. Then, it says, "MGH will submit to the Company early drafts of all manuscripts [from Hoechst-sponsored research] not less than 30 days prior to the submission of the manuscript for publication." This provision is to give Hoechst officials time to review the paper with an eye to patentable results. "At the end of such thirty-day period, the scientist shall have the right, at his sole discretion, to submit such manuscripts for publication."

Patents, Licenses, and Royalties. Under the terms of the agreement, MGH will be the one to hold any patents that may arise out of Hoechst-sponsored research. The hospital, in turn, will grant Hoechst a license for commercial exploitation, and Hoechst will pay MGH royalties at rates that give "due consideration" to the fact that Hoechst paid for the research in the first place. Should some particularly valuable product come out of this, MGH could end up with money from royalties that would be used for the general support of the hospital rather than the Department of Molecular Biology alone. However, no one expects that the Hoechst agreement will turn out to be a source of substantial funds for the hospital in general.—B.J.C.

0036-8075/82/0611-1201$01.00/0

gy, immunology, and plant molecular biology." Goodman is adamant on the subject of control of research. "Hoechst has no influence on the direction of research," he states. Contractual "legalese" aside, "as far as I'm concerned, this is a grant. This [department] is not an industrial extension."

The department is, nonetheless, perceived as very much a creature of Hoechst, which has promised to spend $3.6 million in 1982 and 1983 to support research and $6 million a year from 1984 through 1990. In addition, Hoechst has a contractual right of first refusal for the support of any research in the department above the guaranteed minimum. This will help ensure Hoechst's position with respect to exclusive, worldwide licenses for marketing any commercially useful inventions. (For a more detailed discussion of the contract provisions, see box on p. 1201.) On the basis of the Hoechst agreement alone, 100 new staff members will join MGH within the next couple of years; Goodman says he expects that all the "academic people" will receive Harvard faculty positions, as is the case at MGH now. Although the contract provides for renewal in 5-year increments after 1990, there is no guarantee that Hoechst will decide to renew, raising the obvious question—What happens then?

Another consequence of Hoechst's exclusive funding of the molecular biology department is that it generally precludes scientists from seeking NIH grants, thereby taking them out of the peer review process. "You would think," Griesar said recently, "that researchers would be glad to be free of the requirement of constantly writing grant applications. But at the same time, it takes him from the peer review process and the discipline it imposes and feedback it provides." To solve the problem, the department will report to a scientific advisory committee of at least six members—two from MGH, two from Hoechst, and two from elsewhere. "An advisory committee for peer review is a critical component," says Goodman, who hopes to increase the number of outsiders on that panel.

Perhaps the most serious concern the Hoechst agreement raises is its effect on scientific collaboration and the much touted tradition of "open communication" with one's colleagues. The issue, of course, is not unique to the present case—indeed, it comes up in virtually all situations in which corporate funding brings the corporate profit motive into the picture. But the MGH-Hoechst contract, because of its sheer size and exclusivity, raises the question most starkly. The contract places substantial emphasis on Hoechst's right to fund the department exclusively and to obtain exclusive license or "the most favorable license obtainable," in every case. It goes to great length to guarantee that the department will be physically separate (it will occupy its own two floors) and provides

Goodman insists that traditions of open communication and scientific collaboration will be upheld.

that equipment and furniture will be purchased with Hoechst money. As Griesar notes, referring to Hoechst's decision to fund the entire department, right down to the last test tube, "The mere fact that we have everything under one roof made exclusivity more possible."

Simultaneously, the contract declares that department scientists "shall be free to collaborate with others." According to Goodman, there will be joint collaboration with people at Harvard and elsewhere, funded by NIH and others. On that score, he insists, it will be business as usual. Will it work? As a practical matter, it has yet to be put to the test.

Goodman's appointment at Harvard is in the Department of Genetics. It is through that appointment that he will fulfill his obligations to teach, receive graduate students, and serve on faculty committees. He also intends to work closely with Leder, who has a 5-year, $6 million research agreement with DuPont. Were some formal collaboration to take place, under the terms of the Hoechst agreement, the company would have to give its permission—in writing.

It is not unlikely that Hoechst would give it. Nor is it a foregone conclusion that the company will resist collaborative projects in order to preserve its rights to exclusive licenses. It may well depend on the nature (and commercial potential) of the research involved. But it will not be easy to wade through the legal minefield of an agreement that recognizes free collaboration but also seems to favor keeping to oneself.

One of the issues that has assumed some importance in the debate over university-industry relations is that of releasing contracts for public inspection. It was, for instance, discussed without resolution at the recent meeting at Pajaro Dunes that was convened by the presidents of Stanford, Caltech, the Massachusetts Institute of Technology, and the University of California (*Science*, 9 April, p. 155).

Certainly when the MGH-Hoechst contract was signed, there was no plan to make it public. As Griesar notes, most such contracts have remained confidential, often for what are cited as "proprietary" reasons. But pressures for the release of this "model" contract were tremendous, coming from Harvard faculty who wanted to see how academic freedom had been protected, from other institutions and attorneys who were, themselves, negotiating with industry, and not least from Congress. Representative Albert Gore, Jr. (D–Tenn.), chairman of the subcommittee on investigation and oversight of the House Committee on Science and Technology, has taken a particular, and somewhat skeptical, interest in the academic-industrial complex. Specifically, Gore, who has populist leanings, asked the U.S. comptroller general for a legal analysis of the contract to be sure that Hoechst could not gain exclusive license to any research that was partly supported with funds from NIH. In October, Hoechst and MGH officials agreed to give Gore a copy of the agreement. In December, the agreement was made public, along with the comptroller general's analysis. In essence, it says that the MGH-Hoechst deal does not conflict with federal patent laws as long as the terms of the contract are adhered to rigidly. "Care must be taken . . . that no Federal funds directly or indirectly support the research leading to an invention if MGH is to claim that" certain research was supported exclusively by Hoechst. "This," says the comptroller general, "may very well mean that MGH must account separately for all expenses leading to an invention, including the cost of research itelf as well as indirect or overhead costs. . . ." MGH will do exactly that, it says.

Gore's second concern centered on the fact that Hoechst is a foreign company. "The consummation of relationships between American research institutions and foreign firms raises the specter of unwanted technology transfer among nations," Gore said in a speech. "I am neither particularly jingoistic nor chauvinistic," he said, but "I am concerned that we are again on the verge of being snookered by companies that are only too willing to take advantage of our basic research expertise, and convert that into foreign profits."

By and large, Gore's concerns have not met with much sympathy in academic circles, where international research

collaboration is common. The Goodman-Rutter team that achieved the first insulin cloning, for example, included at least foreign postdocs, one of them from Germany. Several months ago, in a statement released by the hospital, MGH trustee F. Sargent Cheever expressed the prevailing opinion when he said, "It has become difficult if not undesirable to set up artificial boundaries between nations," especially as far as biomedical research goes.

Nevertheless, Gore's view was echoed across the Atlantic. According to Goodman and others, scientists at German institutions were "angered" to learn that Hoechst was creating a major molecular biology center in Boston rather than Frankfurt or Berlin. Ironically, company officials and German banking leaders recently were startled and somewhat concerned to learn that the multinational Hoechst is even more multinational than they realized. Kuwaitis have acquired a nearly 25 percent interest in the Frankfurt-based chemical company.

As Hoechst attorney Griesar notes, relationships between industry and academe are nothing new, but the nature and magnitude of the MGH-Hoechst agreement set it apart. The contract is being scrutinized by lawyers for other corporations and universities, as well as by faculty, who want to see if it is a model they can adopt. Goodman, for his part, enthusiastically describes the whole thing as an "experiment." You can't argue with that.

—BARBARA J. CULLITON

NRC Must Weigh Psychic Costs

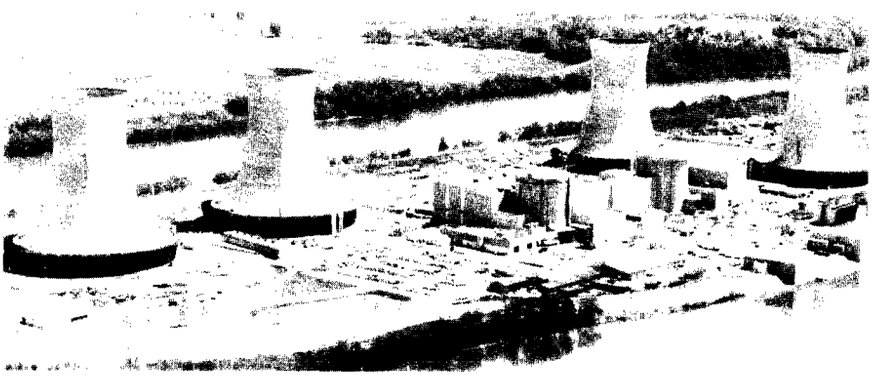
Environmental law protects mental health, an appeals court finds; federal attorneys see broad implications

An opinion released on 14 May by the U.S. Appeals Court for the District of Columbia may have a "revolutionary impact" on environmental law, according to officials at the Nuclear Regulatory Commission (NRC). The opinion says that the NRC must view psychological stress among Three Mile Island residents as a form of nuclear power pollution. This interpretation, Justice Department attorneys agree, could give legal headaches not just to the NRC, but to many other federal agencies.

The ruling is a reversal of an earlier NRC action. The court found that, contrary to what the NRC believed, the agency must recognize local residents' fears as one of the environmental impacts of starting up an idle reactor at Three Mile Island in Pennsylvania. This reactor, known as TMI-1, was closed for refueling and unaffected by the accident at its twin (TMI-2) in March 1979. Nevertheless, it has been kept out of service since 1979 by a series of mechanical and legal problems.

Not the least of its problems is a lawsuit brought by a group of citizens, People Against Nuclear Energy (PANE), in an attempt to stop the NRC from allowing TMI-1 to be turned on. Among other things, PANE said that restarting the reactor would injure public health by adding to the worries of people who had lived through the accident of 1979.

In deciding what to do about TMI-1, the NRC held some hearings in Pennsylvania and asked a licensing board to make a special review of the case. The board suggested that it would be wise to listen to PANE's complaints about psychological stress, but the NRC declined. The commissioners felt that neither the act that created the NRC nor the general environmental protection laws required the NRC to take note of such vaguely defined public fears. PANE's case was not based on an analysis of physical dangers, but on public perceptions of the dangers. PANE rejected the notion that expert estimates of risk should outweigh popular feelings.



Three Mile Island

Commissioner Joseph Hendrie (now retired) explained that, since the NRC was not going to take popular trepidations into account, it should not listen to testimony about them. To listen with no intention of heeding the testimony, he said, would be to patronize the witnesses. So the NRC turned PANE away and moved forward with plans for restarting TMI-1.

PANE's appeal made its way through the courts, and on 7 January, two of the three appeals court judges reviewing the case endorsed PANE's contention. They enjoined the NRC from acting on TMI-1 until it had considered the psychological problems raised by the lawsuit. In a revised judgment in April, the court lifted this injunction. The steam generator tubes at TMI-1 were found to be so corroded as to require months of repair work, temporarily mooting the argument over restarting the reactor. This did nothing to improve the credibility of the expert risk estimators. In any event, the court still demanded an assessment of the psychological impacts.

On 14 May, the court issued an opinion explaining its two judgments, followed by a strong dissent written by Judge Malcolm Wilkey. The majority statement was written by J. Skelly Wright, with Carl McGowan concurring.

According to the NRC and the Justice Department, the majority opinion confirmed the worst fears circulating in January (*Science*, 29 January, p. 481) about the broad application the case might have. Its breadth derives from two ele-

0036-8075/82/0611-1203$01.00/0