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Technology Commercialization at the Massachusetts General Hospital

To provide the highest quality care to individuals and to the local and distant communities we serve, to advance care through excellence in biomedical research, and to educate future academic and practice leaders of the health care professions.

—MGH Mission Statement

After a busy day, Frances Toneguzzo was finally able to relax in her office at the Massachusetts General Hospital (MGH) research building, located in Boston's Charlestown Navy Yard. She wanted time to consider her upcoming meeting with the Chairman of the Executive Committee on Research at the Massachusetts General Hospital. Toneguzzo had been Director of the hospital's Corporate Sponsored Research & Licensing office for more than three hectic years, and it was now time to take stock and plan for the future. The upcoming meeting would be important.

Like many not-for-profit medical research establishments, her hospital's commercial activities had expanded enormously in recent years, and the demands on her office had grown commensurately. In 2003, with a staff of only 22, her group had negotiated more than 100 technology license agreements, up from 32 the previous year, facilitated the creation of seven new companies, received $33 million in sponsored research income and $46 million in license and royalty income, and put together dozens of agreements governing consulting arrangements, confidentiality, and the transfer of research materials.

But all this activity was now creating tensions. How exactly did commercialization of hospital innovations fit with the hospital's broader aims, and what roles was her group expected to play? Did the hospital's conflict-of-interest rules inhibit innovation? Should—indeed *could*—they be changed? Should her group's overarching aim be simply to raise as much money as possible for research, or perhaps to speed innovations to market for the benefit of patients, or to help researchers? Were all these aims in harmony with one another, and if not, which should dominate? She hoped the upcoming meeting would address these issues, but what should she herself propose?

Professor Jonathan West and Research Associate Mona Ashiya prepared this case. HBS cases are developed solely as the basis for class discussion. Cases are not intended to serve as endorsements, sources of primary data, or illustrations of effective or ineffective management.

Background: The Hospital's History and Mission

Government funding for MGH research in the life sciences had more than tripled since 1990 but the hospital's endowment, many believed, needed to be enlarged to help stabilize the institution's precarious dependence on external grants. As revenues from licenses and royalties had increased, Toneguzzo saw that some within the MGH community looked to her office as an additional revenue source, albeit one that could not be counted on.

Established as a corporation in 1811, the Massachusetts General Hospital was the largest and oldest hospital in New England. Its stated missions were to improve patient care, teach medicine, and understand disease. By 2004, it had grown to become the largest non-governmental employer in Boston, employing more than 16,000 people. It employed 2900 nursing staff, and 3700 member medical staff, including physicians, dentists, psychologists, residents, and fellows.

In March 1994, the MGH had joined with the Brigham and Women's Hospital (BWH), another prominent hospital in Boston, to form the Partners HealthCare System, which aimed to deliver integrated health-care to eastern Massachusetts. Between 1994 and 2004, in addition to the two founding institutions, the Partners system grew to include several other specialty and community hospitals in the greater Boston area.

Patient care

Since its inception, the MGH had been a world leader in patient-care innovation. The beginnings of anesthesia could be traced to MGH, where the first use of ether took place in 1846. An MGH physician made the first X-ray in the US in 1896, 30 days after the technique was first demonstrated in Europe. And in 1905 the MGH was the first hospital to create a social service department to help patients with non-medical issues arising from illness or injury.

By 2004, the MGH was a world-renowned medical center that offered sophisticated diagnostic and therapeutic care in most medical and surgical specialties and sub-specialties. Each year, approximately 42,000 inpatients were admitted to the 868-bed medical center, and the hospital handled more than 1.2 million outpatient visits at its main campus and its four health centers in the greater Boston area.[1] *US News and World Report* repeatedly ranked the MGH one the country's best hospitals, counting it among the top four nation-wide for five consecutive years.

Education

The MGH was also the oldest and largest teaching hospital of the Harvard Medical School. Most of the hospital's active staff physicians held faculty appointments at Harvard. In 2004, Partners Healthcare, through Brigham and Women's and MGH, offered residency and fellowship programs in adult and pediatric advanced specialties and sub-specialties. The MGH was also affiliated with other teaching hospitals in the greater Boston area and some affiliates provided training for health care specialists in nursing, physical therapy, and medical imaging. Continuing medical education for physicians was available through accredited courses offered in conjunction with the Harvard Medical School Department of Continuing Education. Most investigators at MGH, however, were not paid for their teaching duties.

[1] In the Back Bay, Charlestown, Chelsea, and Revere.

Research

The MGH was also one of the first hospitals in the US to conduct research. Its cancer research program, for example, began in 1925, when the institution opened the first hospital tumor clinic. By 2004, it operated the largest hospital-based research program in the world, with more than $400 million in research revenues. Its parent organization, the Partners Healthcare system booked $559 million in direct research revenue for 2003, a 15.5% increase over 2002. See **Exhibit 1** for financial statements for the Partners Healthcare System.

One measure of research activity at the hospital was growth in the amount of laboratory space dedicated to researchers. Following construction of the Wellman Research Building on the hospital's main campus and a 400,000 square-foot research facility at the nearby Charlestown Navy Yard in 1988, research space had grown to nearly 800,000 square feet by 2002. In 2004, the hospital was constructing another new research building on its main campus which would house four multi-disciplinary initiatives in bioengineering and regenerative medicine, integrative and computational biology, physiologic genomics, and human genetics. See **Exhibit 2** for growth of research space at MGH.

In 2004, approximately 400 principal investigators in five major research centers[2] and hospital departments undertook basic biomedical research. Full-time employees included 653 research fellows and more than 4000 additional part-time or full-time professional or technical staff were affiliated with the nationally renowned institution.

Growing demand for funding

Between 1990 and 2003, direct and indirect research spending at MGH grew 271%. The hospital received more funds from the National Institutes of Health (NIH) than any other independent US hospital, and like its sister institution, the Brigham and Women's, enjoyed NIH grant approval rates well above the national average. As biomedical research was becoming increasingly expensive, the hospital's research activities were not able fully to cover their expense; additional funds were needed from other sources each year. In the past, funds from clinical operations contributed to the stability of research operations. Such support was made possible because research outlays had been comparatively small and margins on clinical activities were healthy. In 1993, for instance, an estimated $20 million of clinical revenues were used to cover research costs.[3] Through the 1990s, however, margins from clinical activities shrank as pharmaceutical companies shifted clinical trials to less costly institutions, at the same time as the demand for research funding mushroomed. See **Exhibit 3** for MGH and Partners research expenditure.

Moreover, unlike universities, MGH ran entirely on "soft money". That is, most investigators at MGH were entirely dependent for their salary and research support on grants from external sources. Research grants paid for partial laboratory overhead costs, the cost of equipment, as well as the salaries of researchers and laboratory technicians.

John Potts, former Chief of Medicine at the MGH, explained, "Big, powerful clinical departments were the guarantors of the rainy day needs of research groups. Now, they have no endowment and are struggling to make ends meet. They can't take money from nursing budgets to protect scientists."

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[2] These were the Cardiovascular Research Center, the Neuroscience Center, the Cancer Center, the Cutaneous Biology Research Center, the Transplantation Biology Research Center, and the Wellman Laboratory of Photomedicine. Additional research was carried out at the NMR Center, and the Center for Imaging and Pharmaceutical Research.

[3] Partners HealthCare System, Inc. (A) Harvard Business School. 9-696-062

Richard Bringhurst, Senior VP of Medical Services at MGH, added, "Now, if a grant doesn't come through for a group, they cannot meet their payroll needs for six to nine months, and the group may be broken up. That can be tragic."

Thus, as its research activities had grown, the MGH had become increasingly vulnerable to fluctuations in NIH funding levels. Bringhurst lamented, "The amount of money we have to cover lapses in grant support is less than 1% of our annual funding. There's no safety net." Although some 'bridge-funding' could be offered to help investigators who lost grant support, such funds were modest and typically insufficient to support staff that had been hired on grant money.

The lack of funds also had an impact on the hospital's recruiting activities. While it could draw on the excellence of its clinical studies to recruit the best clinicians, it was harder to recruit faculty in basic scientific research since MGH did not have a tenure system that guaranteed salaries and did not provide start-up funds[4] as universities typically did. A recently completed Partners five-year strategic plan on research recognized the problem, noting the need to provide basic science researchers with greater infrastructure and start-up funds in the future. Such efforts, it was envisioned, would enable MGH to compete more effectively with universities for top-notch candidates.

To finance all these efforts, individual departments at MGH looked to technology transfer, along with philanthropy and industrial relationships, as sources of funds.[5]

Evolution of MGH-industry relations

Prior to 1977, MGH had had little interaction with industry. In 1977, however, the MGH recruited a staff lawyer who had also been a patent attorney, Marvin Guthrie, to draft a patent policy. Guthrie soon also became responsible for the hospital's nascent technology transfer program.[6]

In 1979, MGH formalized its technology transfer program by creating the Office of Technology Affairs (OTA). Although the hospital had cooperated with companies such as Centocor and Du Pont, which sought access to MGH faculty and their research, most of these agreements were small. During these early years, Guthrie also crafted the institution's policy on consulting agreements and, with his staff of two, assisted investigators in filing patents and negotiating agreements with the private sector.

The hospital's first large agreement, approximately $1 million in research funding per year from Johnson & Johnson, was initiated in 1979.[7] It immediately generated concern within the hospital's

[4] New faculty recruits were typically offered start-up funds that could be used over two to three years to set up research laboratories.

[5] Only a few departments currently enjoyed a satisfactory level of stability; the Department of Molecular Biology, for instance, had a $90 million endowment built through its relationship with Hoechst, a prominent German chemical and pharmaceutical company.

[6] The development of the MGH patent policy was also enabled, in part, by Harvard's change of its IP policy for inventions made in medical and life sciences. Inventions could now belong to Harvard, where they had previously been dedicated to the public. Indeed, a research agreement between Harvard University and Monsanto, which stipulated the protection of any intellectual property, instigated changes in Harvard IP policy. Harvard's earlier policy prevented the university from taking any patents on technology developed in its environs.

[7] Protracted negotiations relating to the company's desire to have a secure facility that ensured confidentiality had initially resulted in a compromise, in which scientists were required to sign in and out of the company's sponsored research facility at MGH. This arrangement was ultimately scrapped.

staff over the appropriate form and level of relations with for-profit industry. Concern exploded into outright controversy, however, with the hospital's landmark 1981 agreement with Hoechst. Hoechst offered more than $70 million over 10 years to finance a new Department of Molecular Biology, in return for exclusive rights to any patents that emerged from the sponsored research.[8] For Hoechst, the agreement provided a window into cutting-edge research and access to a first-class molecular biology department, where its own scientists could be trained. The company also anticipated that inventions resulting from the agreement would translate into products. At MGH, the creation of the department reflected a commitment to basic scientific research. Although the agreement had been carefully vetted within MGH to ensure that academic prerogatives, including rights to publish, were not compromised, and had been reviewed by the NIH before it was signed, cries of protest erupted when the agreement was made public. Some scientists denounced the agreement outright, and subsequent congressional hearings voiced concern about a foreign company benefiting from US government-funded research. An NIH review eventually found the agreement to be acceptable.

While the initial terms of the agreement stipulated that Hoechst (later, Aventis) would be the sole funding source for the department, over time other external funding sources were accepted. Later, the company's support evolved further, as it chose to sponsor research programs in specific laboratories, on an ad hoc basis.[9] Throughout, the OTA worked closely with the company whenever a potentially commercial discovery was reported, and Hoechst was then free to decide if it wanted to file a patent.

At MGH, the Hoechst funding enabled key discoveries by Brian Seed, an investigator in the molecular biology department, that were important to the development of Enbrel, a best-selling drug for rheumatoid arthritis and other related diseases. Seed recalled:

> The Hoechst funding was particularly beneficial for scientists here because it provided a stream of unrestricted funds, which effectively meant that we didn't have to apply for grants. That's a huge advantage. It was especially beneficial for me. A lot of my work, in particular in its early phases, involved technology development, which is not looked upon with favor by the study sections of the grant review panels of the NIH. So I would have had a much, much harder time had I not had industrial funding.

The agreement with Hoechst/Aventis ended in 2000. While some within the company regarded the agreement as a failure, Seed, who had also trained Hoechst scientists, was adamant that MGH had met all requirements of the agreement. Hoechst-funded research at MGH had resulted in products and Seed maintained that the royalties alone that the company had received from Enbrel had more than compensated for the funds Hoechst contributed to MGH.[10]

Later, the Hoechst agreement served as a blueprint for subsequent agreements, including a 1989 agreement with Japanese cosmetics company Shiseido. This multi-year, multi-million dollar agreement initiated by dermatology department chair John Parrish funded the creation of the Cutaneous Biology Research Center at MGH. Shiseido's formal influence over research directions

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[8] Under the initial terms of the agreement, Hoechst would pay for all equipment and other expenses in the Department of Molecular biology.

[9] Hoechst would have the option of exclusive rights to any IP resulting from the sponsored research but MGH would control the disposition of any IP that Hoechst did not want.

[10] While new products (such as the bacterial strain for the insulin production process) had emerged as a result of the agreement, differing expectations and perceptions of success, as well as management changes at Hoechst contributed to growing discomfort between the two parties. At MGH, some investigators in the molecular biology department were enthusiastic about the Hoechst agreement but most were not; at Hoechst, tensions arose as some company scientists resented that Hoechst was funding research in Boston rather than the company's projects in Germany.

was limited to an advisory role, and a scientific board would oversee the new center. In return, Shiseido would enjoy first rights to any patents resulting from the sponsored research. As well as providing research funding at a time when federal support was being reduced, the agreement added 35 new research positions at MGH. Slated to end in March 2006, the agreement had brought in $150 million in research support and had yielded several significant products for Shiseido.

By the late 1980s, industry-sponsored research had grown from 3% in 1976 to more than 30% of total MGH research funding. By the mid-1990s, the MGH possessed four of the six largest industrial sponsorships of academic biomedical research in the US[11] but the 1990s also saw a shift in emphasis towards licensing and start-ups. Large industry sponsored agreements were becoming scarce. Academic researchers were now more willing to work for pharmaceutical and biotechnology companies, and for large companies, sponsoring specific research projects at academic institutions made more sense than long-term broad-based agreements.

By the mid-to-late 1990s, the MGH itself held patents on several products, but royalties were small. Guthrie recalled:

> Some people believed we were doing something wrong [and] perhaps not marketing our discoveries aggressively enough. People began to feel like they weren't getting enough return on their research investment dollar. And because we led the pack in NIH funding, they thought that if we held equity and had more startups based on our research, we should be getting more money from industry.

Others felt the institution suffered from hubris. "People here saw Berkeley and Columbia making money from licenses and there was a question as to why we weren't making $50 million a year", noted one senior administrator. He recalled, "[There was] a dichotomy between expectations of faculty regarding what the OTA could and should do, and what they were actually capable of [given resource constraints]."

Through the 1990s, there was also a growing awareness among junior investigators of the commercial applications of their research, and an interest in start-ups and technology licensing. Guthrie recalled, "Many came after doing postdocs and PhDs in labs where patents were filed, equity taken, and their experience was different." The result was a more aggressive emphasis on licensing and start-ups at MGH.

Corporate Sponsored Research and Licensing

In 2001, Frances Toneguzzo was recruited to head the department of Corporate Sponsored Research & Licensing (CSRL) at MGH. Following 12 years in industry, Toneguzzo had worked in Harvard's technology transfer office, before founding a similar department at Tufts University. Her office at MGH would serve as the primary interface between the hospital and the private sector. In addition to its technology transfer efforts, CSRL was responsible for negotiating and executing agreements to access materials, funding, and resources at MGH. See **Exhibit 4** for the new group's organizational structure.

CSRL's responsibilities were broad. CSRL tailored each agreement, for funding and materials as well as licensing agreements, to the specific needs of the MGH researchers and the company involved, but ensured all adhered to MGH policies; agreements could not infringe on the academic

[11] www.mghra.partners.org/overview.html accessed March 3, 2004.

freedom of researchers.[12] Case managers were responsible for guarding against potential liabilities to MGH, and ensuring that the hospital's IP and tangible assets were protected. CSRL also reviewed all consulting agreements by MGH staff. More generally, CSRL served as an in-house resource on all facets of relations with industry, and helped educate investigators and researchers on technology transfer issues. Toneguzzo and the associate directors were also involved in complex litigation issues. See **Exhibit 5** for trends in CSRL activities.

As government funding for the life sciences grew at an unprecedented rate during the 1980s and 1990s (see **Exhibit 6** for federal R&D expenditures, by discipline; **Exhibit 7** for NIH financing), pressure on Toneguzzo's office intensified. At MGH alone, NIH research expenditures increased four-fold in the decade to 2003, to more than $200 million. Over the same period, research conducted by academic scientists was seen to be increasingly relevant to the emerging biotech sector, as well as to pharmaceutical companies. More recently, the need for increased interactions with academic scientists had prompted major pharmaceutical companies such as Novartis and Merck to relocate substantial segments of their research operations to the Boston area. At US academic institutions, the passage of the landmark Bayh-Dole Act[13] in 1980 also accelerated the filing of invention disclosures which grew from 6,337 in FY 1991 to 15,573 in FY 2002.[14]

The process of bringing an MGH discovery to market traversed several well-defined steps. First, inventions with commercial potential were identified, through invention-disclosure forms that investigators submitted to CSRL. A case manager assigned to each new disclosure would then work with each investigator to assess the discovery's commercial potential. Case managers oversaw the decision-making process leading to patent applications, which were filed by patent attorneys hired by CSRL.

Once promising technologies were identified and patents filed, Toneguzzo and her staff worked in cooperation with researchers to develop a commercialization strategy for the invention. Case managers might conduct market research to identify potential industrial licensees. In other instances, investigators had already identified potential licensees. Exclusive licenses might be granted where technology development was unlikely to proceed without one, as with therapeutics, for instance.

As the 1990s drew to a close, MGH's commercialization activities began to bear fruit. Royalties from Enbrel, a therapeutic protein for the treatment of rheumatoid arthritis and other related diseases, began to contribute to MGH's income stream in 1999. Marketed by Amgen, Enbrel was one of the hospital's first major therapeutic products and was based, in part, on key technology developed by Seed (through Hoechst funding). Other key revenue-generating technologies included cross-linked polyethylene for artificial joints and inhaled nitric oxide. These three inventions, all a decade or more in the making, accounted for more than 75% of the $46 million MGH earned as license income in 2003. Indeed, over the past two years, the top 10 inventions accounted for more than 97% of all license income. See **Exhibit 8** for trends in total license income at CSRL, **Exhibit 9** for the volume of invention disclosures leading to licenses generating income, and **Exhibit 10** for the relative contribution of top 10 products to royalty income.

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[12] All agreements between MGH and industry had to protect the researchers' freedom to choose subjects and directions of research; to publish, communicate, and discuss research results; and to collaborate with other investigators.

[13] The 1980 Bayh-Dole Act passed by the US Congress aimed to promote innovation, economic development, and US competitiveness. The act focused on inventions created with federal funding and allowed universities and other non-profit institutions to retain rights to and profit from such inventions.

[14] AUTM licensing survey, FY 2002

By FY2003, royalty streams at MGH had increased sufficiently so that even after the annual cost of running the MGH CSRL office was subtracted from the hospital's 25% share of royalty and license income, more than $7 million remained.[15] Such funds were particularly valuable since they were not earmarked and, so, could be used to fund a broad range of activities at the hospital.

Debating CSRL's Mission

Within this context, debate had escalated within MGH over what role exactly it should play in delivering medical advances to the public, and what should be the primary focus of CSRL's efforts. Bringhurst highlighted the value of income derived from CSRL's technology transfer activities:

> It's fair to say that there is no articulated goal of the [CSRL] office which stipulates that financial success of a scientific idea is most important…. And while we're not in the business of making money, we have a mission that is not adequately supported. So there has been an institutional buy-in for MGH to reap at least some financial benefits in the form of royalties and licenses, and there has been a discussion of holding equity at the institutional level to keep the enterprise moving forward.
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> The hospital's research committee would very much like to be able to provide interim financial support for some projects, as well as support for core labs and special innovative projects that are high risk and which NIH would never approve. We would like to tap into the revenues from commercialization activities at MGH for the sake of the whole community.[16]

But if CSRL were to focus primarily on income generation, Toneguzzo believed it important to understand the impact that decision would have on the service her office could provide to investigators. She explained, "If I'm going to concentrate on maximizing revenue, then I'm going to focus on a subset of inventions. I may not be able to pick all the winners, but I should be able to pick some good ones. But we won't be able to support all inventions equally. We will be forced to relinquish some inventions, and tell some inventors, 'Sorry, we can't work on these.'"

In early 2003, following the release of CSRL's 2002 annual report, the hospital's General Executive Committee convened a taskforce to clarify CSRL's mission. Toneguzzo wanted guidance on what the specific aims and focus of her office should be. Where exactly should "income generation" fit within the overall goals and priorities of the hospital and Partners? CSRL might be judged by the good it accomplished for society (without consideration of the financial return to MGH), or it could be evaluated by the revenue it attracted. Alternatively, the success of her office might be gauged by the service it provided to MGH investigators. There were several instances where Toneguzzo believed CSRL was faced with choices between 'doing good for the public' versus maximizing revenue. See **Exhibit 11** for some of these examples.

However, some at MGH did not believe that revenue maximization as a goal necessarily was at odds with a focus on 'doing good'. Seed argued:

> If you naturally prioritize technology innovation by its impact on society, you will find almost invariably that discoveries with the biggest impact have the biggest return. If you get into

[15] However, when the cost of running the Partners CSRL office was subtracted from the Partners' share of license and royalty income (derived from the MGH and BWH), less than $3 million remained in contributions to the institution's non-operational earnings.

[16] Case writer interview with Richard Bringhurst.

> technologies for third-world hygiene or other similar kinds of advances [with low financial return], then I'd be all in favor of that. But [MGH's] metric should be maximum impact on society. And dollars can be a good proxy for [such] impact.

In the end, the taskforce concluded that, "income generation, while important and an expected outcome, is not the sole strategic goal of technology transfer—doing good is at least as important as doing well." Moreover, CSRL had to maintain an equal focus on research support and technology transfer activities. The conclusions of the taskforce, William Terry, VP of CSRL at Partners observed, meant that:

> Basically, CSRL [at MGH] has to do everything. But I would say that one place we're not egalitarian is in terms of looking at technologies and where to invest resources. We make some estimation of what the bang is going to be in terms of return [on investment] and that's where we put our efforts.

Toneguzzo interpreted the task force's ambiguous language to mean that financial considerations were not the sole aim of her office. Her office would not negotiate so severely as to maximize revenue; it was more important that the deal be closed on equitable terms and the technology be transferred for further development. In November 2003, the Executive Committee on Research voted to accept the taskforce's conclusions.

To increase revenues, Toneguzzo anticipated more deals in the future. "We can do more deals once we have the infrastructure in place and everything is working smoothly. We'll get a bit [of money] on each deal, but we'll have a lot of them and sooner or later something is going to hit". Some, however, believed that such efforts to market and license MGH technologies were misguided. One investigator declared:

> Industry ain't dumb. When they see great ideas, they buy them. To be honest, there are not that many great ideas here. There is a view around that many great ideas are dying here. But there's no evidence of that. Great ideas break through and move across. I don't think there are gems that are laying a-waste because no one will develop them. It's possible but it's a low probability [event].

Protecting patients and academic prerogatives: Policies on Conflicts of Interest

All faculty and staff at MGH were bound by the Harvard Medical School (HMS) Policy on conflict of interest or the Partners policy on conflict of interest, which was very similar to the HMS policy. Developed to avert the actual or perceived influence of financial interests on patient care and academic pursuits, the HMS policy was reconsidered from time to time by the dean of HMS. The dean was advised by a committee charged with reviewing the rules.[17] The policies, considered among the strictest in the US, prohibited investigators from participating in any clinical research (i.e. research involving human subjects) on a technology owned by a company in which the investigator possessed any financial interest. This included holding an equity stake or maintaining a consulting

[17] There had, thus far, been two attempts in the 1990s to review and modify the policy. In 2000, the HMS committee charged with reviewing the guidelines proposed that investigators holding an equity interest in a company also be able to receive sponsored research support from the same company for basic scientific research which did not involve human subjects. Those engaged in clinical research involving patients could receive greater financial interest than currently possible through consulting agreement, though they could not hold an equity interest in the company. However, a day after a gene therapy patient at the University of Pennsylvania died, the proposal was withdrawn and no changes were made to the policy. It was later revealed that the lead clinical researcher and the institution had financial ties to the company developing the therapy and potentially stood to profit from the research.

relationship with compensation above certain *de minimus* levels. In conducting research not involving human subjects—that is, basic research—an investigator was prohibited from receiving sponsored research support (in dollars or in kind) from a company in which the investigator held an equity interest. See **Exhibit 12** for the complete HMS policy.

If, for instance, an investigator held equity and received sponsored research support, Ronald Newbower, Senior VP for Research and Technology at Partners, explained, "The concern is that the equity of a company does not necessarily reflect substance, it may be hype, and it's the volatility that makes it disturbing. The market cap[italization] can increase a hundred fold based on one seemingly promising lab result which may or may not prove to be reproducible." The concern was that the investigator would then be in a position to bias research results in a manner where he or she could reap financial benefits. Still, financial gain was only of many factors that could lead to bias in research. As Seed observed:

> I've seen many examples of misbehavior among scientists for personal gain and rarely was money involved. I don't think money is the evil that's going to suddenly impel the Jekyll side of people. I see that people have an internal barometer that tells them what's ok and what's not ok. And whether money is involved, or whether it is fame, prestige, or advancement that are involved is really a bit immaterial. People will misbehave when there is something they really want.

Nonetheless, he, like others, conceded that the public's trust was particularly sensitive to perceived bias motivated by financial interests.

Protecting patients

Concerns relating to the influence of an investigator's financial interest were particularly acute in the clinical research arena. Warren M. Zapol, Chief of the Department of Anesthesia and Critical Care at MGH, believed that HMS was right to maintain its conservative COI policy. He elaborated:

> I worked on our technology (inhaled nitric oxide as a therapeutic agent to dilate pulmonary circulation) for ten years before we got FDA approval and we're now receiving royalties of $6 million a year. If you held stock and were taking care of a patient, you would never know when you made a decision to start or stop your investigational drug, if your decision was based on the patient's disease or what your [financial gain] would be. If you didn't report something, or if you said a side-effect was not important, we would never know if you made that decision because the stock price would go down…it requires leaving the money on the table and saying that I need the patient's respect and the respect of my colleagues and that I can't make decisions if I am polluted by stock ownership…One can't be too tough ensuring this necessary isolation. You cannot and should not do human trials if a person or institution holds equity.

While allowing that the potential for financial gain could influence a physician's decisions on a patient, others at MGH were more sympathetic to those investigators faced with the choice between equity ownership and sponsored research funding. Investigators with expertise in a particular clinical area, for instance, were often in the best position to develop a technology further but were proscribed from doing so if they wanted to reap financial benefit from their research. One investigator lamented, "From an intellectual and career standpoint that can be devastating. Great ideas come by rarely, and now these people are taken out of the equation."

Some believed there were ways to avert any potential betrayal of the public trust. For instance, one investigator suggested, a technology in development could be used at MGH even if a clinical investigator held an equity stake in the company developing the technology as long as the decision

on whether to use that technology on a patient would not be taken by those associated with or controlling development of the technology. For instance, co-principal investigators (who did not hold equity in the company) could be appointed to make the decision on use of the technology on a patient. Moreover, in such a scenario, patients would be informed that someone at the hospital had a financial stake.

Protecting academic prerogatives

Although some MGH researchers distrusted and did not favor industry-supported research at the hospital, the institution tolerated certain arrangements in which the hospital's research was aligned with corporate interests. Royalty-based arrangements were considered acceptable because they accrued following independent validation of the research. They also typically took many years to earn and, moreover, substantial royalties were earned only when product sales were high.

The conflict of interest policies, however, prohibited receipt of sponsored research support (in dollars or in kind) from a company if an investigator held an equity interest in the company because of the greater potential for bias (where a seemingly important lab result could potentially inflate the company's stock price in the near term).

An additional concern relating to the hospital's interactions with industry was that the pecuniary interests of a supervisor could potentially influence the training of students and post-doctoral fellows in an investigator's laboratory. Bringhurst elaborated, "A strong concern here is that we have lots of trainees who have important career goals of their own, which need to be nurtured. Some fear that the presence of corporate-sponsored support in a lab may in some way change the direction of the trainee's research away from what might be considered an ideal career trajectory."

Interpreting Conflict Of Interest policies

Over the years, the Partners Professional and Institutional Conduct Committee (PICC) had developed a substantial case log that defined the institution's conflict of interest policy in broad strokes. Made up of trustees from member institutions and some faculty, PICC typically met every six weeks to debate cases in which the COI policies were unclear. Many at Partners and at MGH firmly believed that decisions on the implementation of the institution's COI policy had to be made by disinterested people—not department heads—at a sufficiently high level so that the process was not politicized. As Newbower explained, "The [members of PICC] are not thinking about their own department or whether they're going to lose a faculty member. They take the long view."

Others held that the committee was excessively conservative and, "so ready to see problems that it was a struggle to move forward." These investigators and administrators believed that the current COI policy was, more often than not, interpreted too strictly. "They're [PICC] still of the philosophy that we shouldn't let anything bad happen, even at the interface where they can interpret the Harvard rules liberally", observed one senior investigator who advocated creation of a different committee that would vet such issues. For instance, if a company received money from the US government's Small Business Innovation Research program, and used the government funds to sub-contract research to an investigator, PICC viewed such funds as company money. The NIH, in contrast, had excluded this as a conflict. The situation had arisen more than once but investigators were bound by PICC's ruling.

In another instance, an MGH investigator was faced with an opportunity to receive substantial support for his research program from a particular company. The investigator was also a member of the board of directors of the parent company and retained an equity stake in the parent firm. However, although the investigator only had an indirect financial stake in the sponsoring company,

PICC viewed the proposed research support as equivalent to receiving research support from the parent company. So, the investigator had to choose between receiving the sponsored research grant and keeping his equity stake. He chose the latter and the sponsored research agreement went to another institution.

The HMS COI policy also considered the receipt of research reagents from a company as equivalent to sponsored research support (with the reagents seen as 'payment in kind') when an investigator held stock in the same company. Seed recalled the time he received two shipments of a particular reagent from a company in which he held stock. The receipt of these two "gift" shipments from the company posed no problem but after the submission of an Material Transfer Agreement (MTA) for the third shipment, CSRL contended that the reagent transfer was disallowed because the reagents were 'payment in kind' (even though the earlier shipments were still, Seed maintained, 'payment in kind'). He explained:

> If you create technology in academia and if you're in the Harvard system and you want to create a company, then as a lab [within the Harvard system] you have a difficult time working with that company. There is this wall and goods can't flow back and forth because of the [COI] rules. But the weird thing is that if you exchange materials as gifts, it's not a problem. That can continue indefinitely. If there's an MTA, then there's a problem—somehow the existence of an MTA makes it a payment in kind.

However, as Toneguzzo explained, the presence of an MTA, which defined the rights of the company relating to the materials and their use, had created a *quid pro quo* that did not exist when the materials were exchanged as gifts. While a one-time exception was made which allowed the reagent transfer to Seed, the policy remained unchanged. Later, faced with a similar situation, Seed simply chose to inform a company he co-founded (and in which he held stock) that his lab would infringe on the company's patents. Such policies, he maintained, were the *primary* reason he had chosen not to create a company based on technology being developed in his lab.

It was also unclear, until recently, how the returns of an institutional equity sale would be disbursed to investigators in certain cases. MGH, like other hospitals in the Partners system, owned its IP and held equity in start-up companies that were based on technology developed internally. See **Exhibit 13** for a list of MGH startups and equity holdings that the hospital retained. Importantly, MGH did not hold equity in any companies that sponsored clinical studies. Likewise, investigators could not perform clinical research on technologies owned by companies in which the hospital held equity. While no policy existed as yet for the conditions and circumstances under which institutional equity could be converted,[18] a key question was whether an investigator who had opted to receive sponsored research support over an individual equity stake could receive the 25% of the institution's equity interest when it was converted in the future. A recent clarification of the COI policy by PICC concluded that this scenario was little different than an investigator having a direct equity stake in the company. Toneguzzo disagreed with this interpretation, contending that control over the sale of an asset determined ownership—hence, the institution's equity was not equivalent to an individual's equity stake. Further, as Terry and others noted, the decision meant that, "there is a disincentive for a primary investigator to receive any sponsored research [support] because there is no upside for

[18] The trustees of the institution were charged with determining the conditions and circumstances under which equity could be converted but, as yet, there had been no set policy. As a result, MGH had by and large simply held onto its equity holdings and, as Terry observed, "the value is never realized....We do startups and [while] lots of people get nervous about equity, our only incentive to do a startup is to get equity and then optimize the value." In addition to liability issues, a major concern was that proceeds from an equity sale would flow either directly or indirectly back to the original science or affect the investigators advancement. However, many believed it was possible to design a process that averted such problems.

them." Indeed, when presented with the choice, investigators were increasingly opting to take an equity interest rather than sponsored research support.

Some proponents of liberalizing the COI guidelines pointed out that the conservative rules constraining an investigator's interactions with industry could also have an impact on faculty recruitment and retention. Investigators would be more inclined to consider other academic institutions in the US with more liberal policies. Most, however, did not see this as a real concern observing that there were few who had left for whom the stringent policies may have been a factor in their decision.

In 2003, a committee assembled to review the COI policy was convened again at HMS. Greater sensitivity to public perception and a zero-risk philosophy appeared to have been adopted and although the new set of rules had not yet been released most believed little would change. Instead, as one senior administrator remarked, "There is a trend for other institutions [in the US] to move closer to the HMS policy. It is seen as centrist."

Conclusion

In 2004, the greater Boston area was widely recognized as one of the pre-eminent centers of biomedical activity in the world. The area boasted several prominent universities including Harvard, MIT, Boston University, Brandeis, and Tufts, in addition to several world-class hospitals including the MGH, BWH, The Children's Hospital of Boston, the Dana-Farber Cancer Institute and many others. There were also numerous biotechnology companies, many of which were spawned by academic researchers from these institutions. And recognizing the vibrant nature of the local biomedical community and to be closer to MIT and Harvard and its affiliate hospitals, large pharmaceutical companies such as Merck and Novartis had recently decided to shift substantial segments of their research operations to the Boston area.

Shortly after taking office in 2001, Harvard President Larry Summers had noted, "We [at Harvard] have to think creatively and flexibly about how to work with the private sector, how to support entrepreneurship, and how to make sure research moves from the bench to the bedside."[19] Offices such as CSRL were centrally situated at the interface between academic researchers who were inventing new biomedical technologies and improving and optimizing others, and industry which could bring these advances to the public. Commercialization activities at the MGH, as at many academic research centers, had grown substantially in recent years but now, going forward, Toneguzzo wondered if technology transfer offices like CSRL should assume a different and perhaps more aggressive role—moving from 'transfer' of technology to the 'translation' of technology. Should CSRL, for instance, facilitate 'translational' research on early-stage technologies to bring these to the proof-of-concept stage where the risk was diminished sufficiently to elicit the interest of industry partners? These and related issues would have to be considered in determining the proper role of CSRL in the process described by Summers.

[19] Ibid.

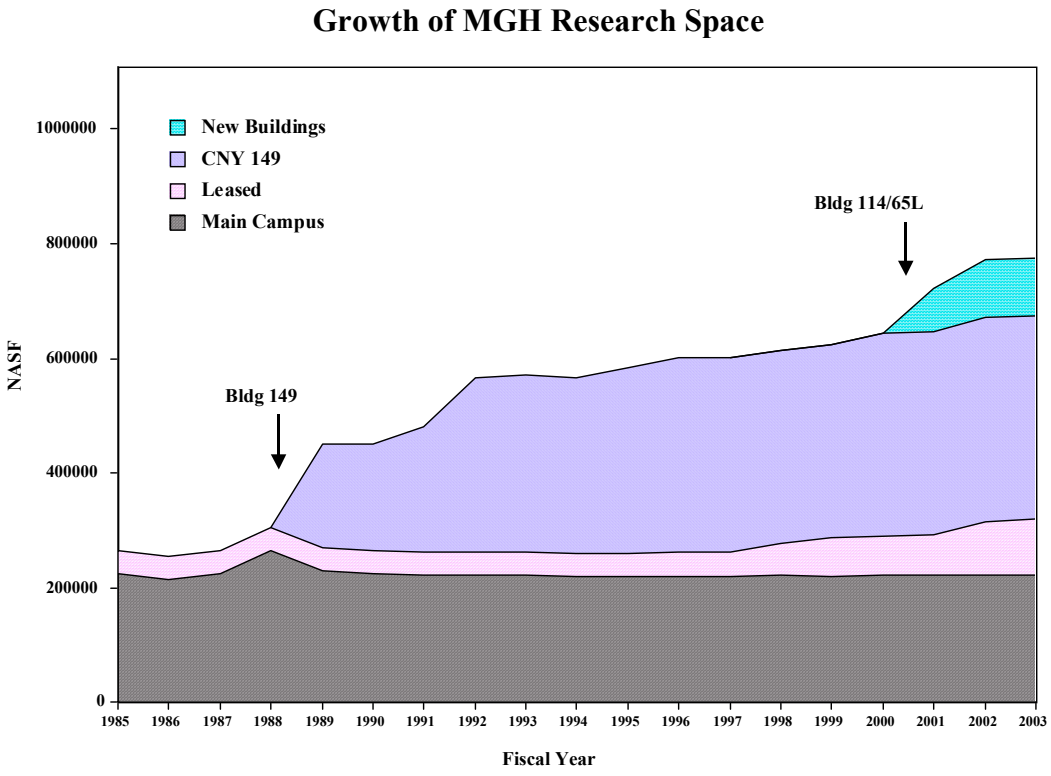
Exhibit 1 Partners Consolidated Statement of Operations (in thousands $ for FY ended Sep 30)

	2003	2002	2001	1993[a]
Operating revenue:				
Net patient revenue	3,368,373	3,137,260	2,819l726	529,311
Academic & research revenue	823,947	717,211	617,260	119,203
Other	368,870	363,143	335,508	91,115
Total operating revenue	4,561,190	4,217,614	3,772,494	739,629
Operating expenses:				
Compensation and expenses	2,396,483	2,159,288	1,903,353	345,754
Supplies and other expenses	1,147,464	1,061,553	996,242	192,170
Direct academic and research costs	613,777	534,305	455,662	119,203
Depreciation and amortization	223,206	223,755	210,559	46,886
Provision for bad debts	45,606	45,943	50,988	
Interest	45,606	45,943	50,988	15,360
Total operating expenses	4,529,325	4,147,537	3,724,524	732,637
Income from operations	**31,865**	**70,077**	**47,970**	**6,992**
Nonoperating gains (expenses):				
Income (loss) from investments	1,273	(66,442)	6,406	
Gifts and other	52,507	46,809	61,726	
Total nonoperating gains (expenses)	53,780	(19,633)		2,571
Excess of revenues over expenses	**85,645**	**50,444**	**83,544**	
Other changes in net assets:				
Change in net unrealized gains (losses) on investments	187,367	(26,949)	(87,950)	
Funds utilized for property and equipment and other	12,780	32,229	36,111	
Increase in unrestricted net assets	**285,792**	**55,724**	**31,705**	

Source: Partners

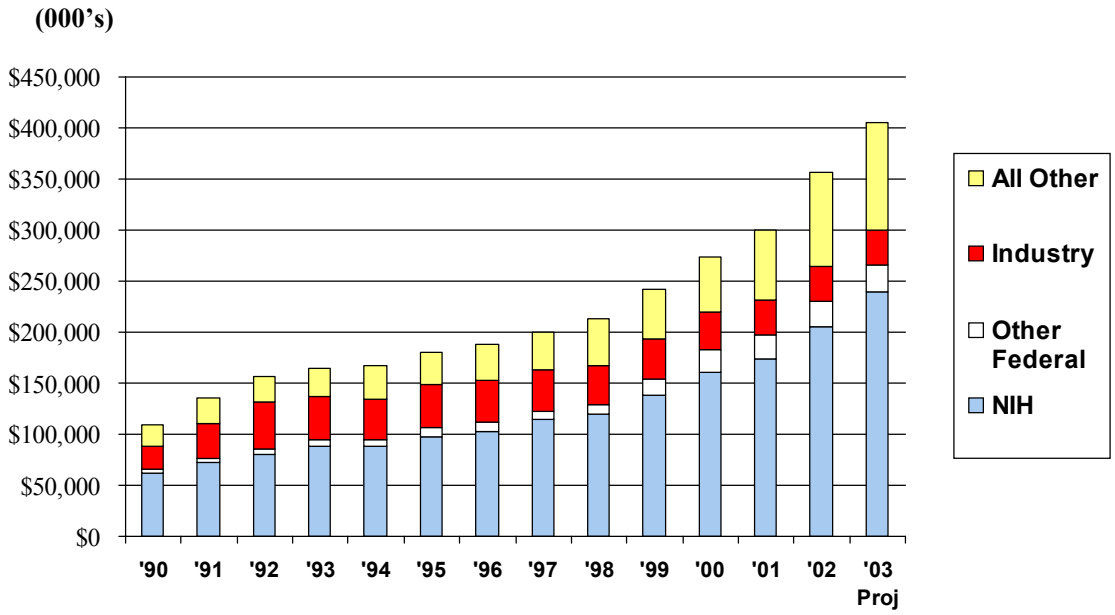
[a]Combined MGH and BWH Financials, Partners HealthCare System, Inc. (A) Harvard Business School. 9-696-062

Exhibit 2 Growth in research space at MGH



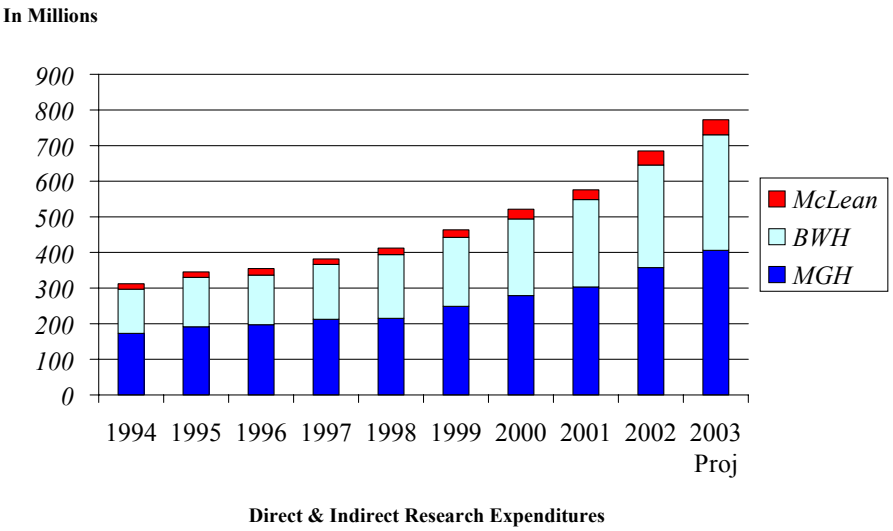
Source: Partners Healthcare Network

Exhibit 3 MGH research has grown 271% from 1990 to 2003 proj.



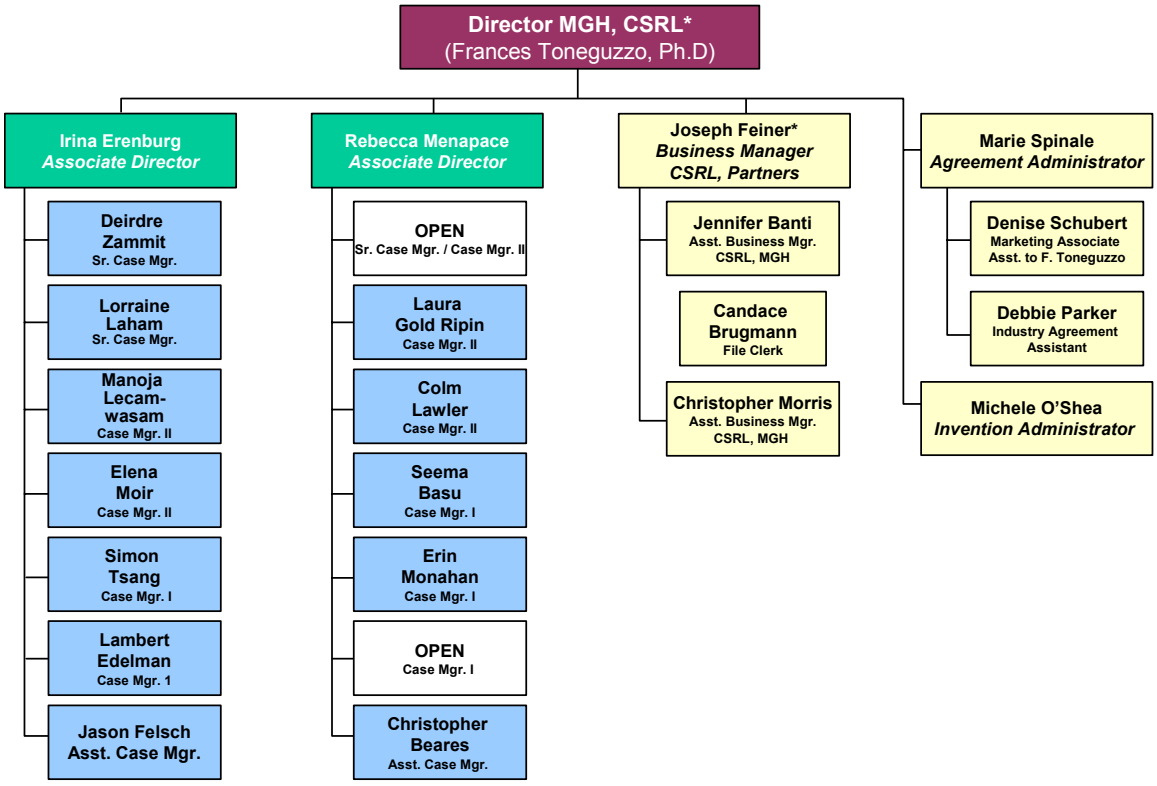
Direct & Indirect Research Expenditures

Partners combined research has grown by over $461 million from FY1994 to FY2003 Projected (compounded annual growth rate of 10.6%) to $773 million. The compounded growth rate has been 13.7% from FY99 to FY03.



Source: Partners Healthcare Network

Exhibit 4 Organization of CSRL



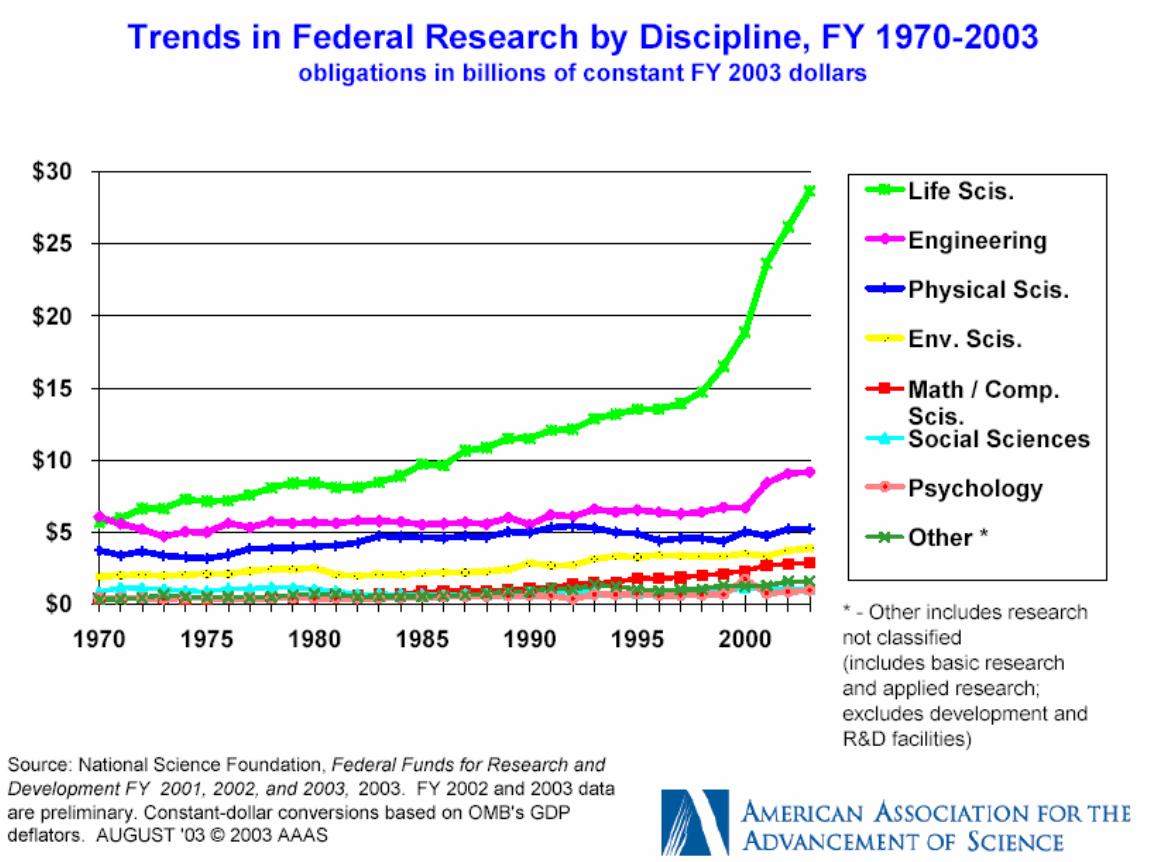
Source: MGH CSRL

Exhibit 5 CSRL Activity Volume, FY'96-FY'03

	FY'96	FY'97	FY'98	FY'99	FY'00	FY'01	FY'02	FY'03
Agreement Activity								
Material Transfer Agreements	399	223	200	233	268	206	249	295
Confidentiality Agreements	142	171	165	216	233	155	206	214
Consulting Agreements	89	126	131	134	156	94	80	100
Clinical Trial Agreements	148	136	176	163	142	123	136	206
Licenses	37	32	38	44	36	26	32	103
Sponsored Research	45	45	38	39	53	55	53	56
Misc.	26	37	54	55	49	25	48	55
Patent Activity								
Invention disclosures	146	123	145	174	150	197	213	199
Patents issued	37	42	57	85	62	72	49	85
Fiscal Activity								
License Income	$1.3m	$2.6m	$1.6m	$6.6m	$16.3m	$24m	$30m	$46m
Sponsored research income							$6m	$33m

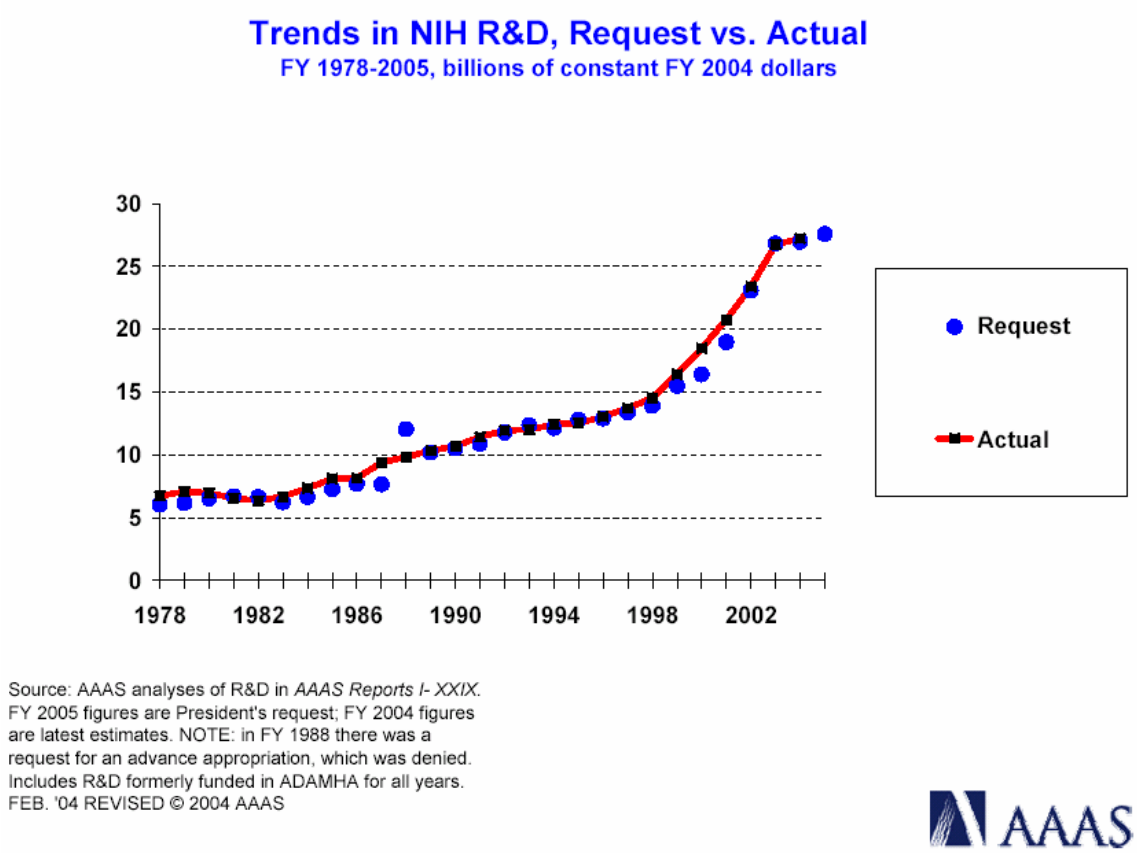
Source: MGH CSRL

Exhibit 6 Federally financed R&D expenditures, by field



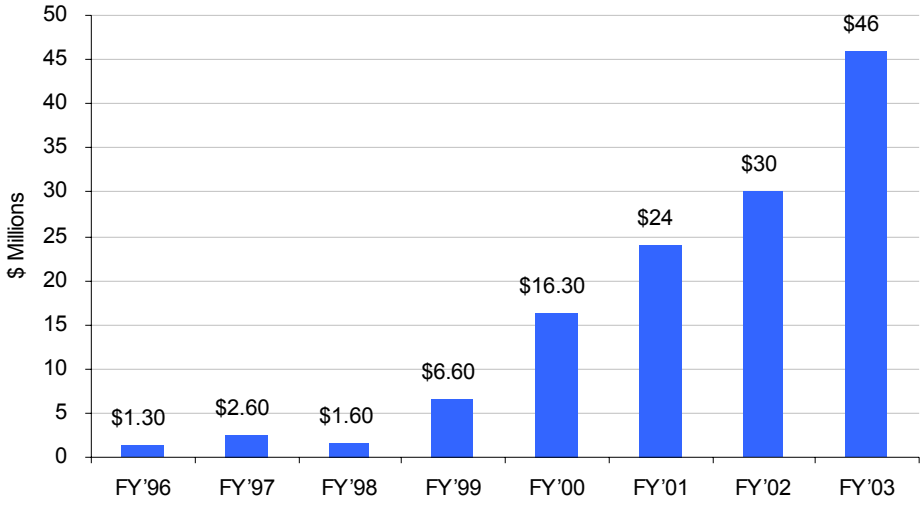
Source: AAAS

Exhibit 7 Trends in NIH financing



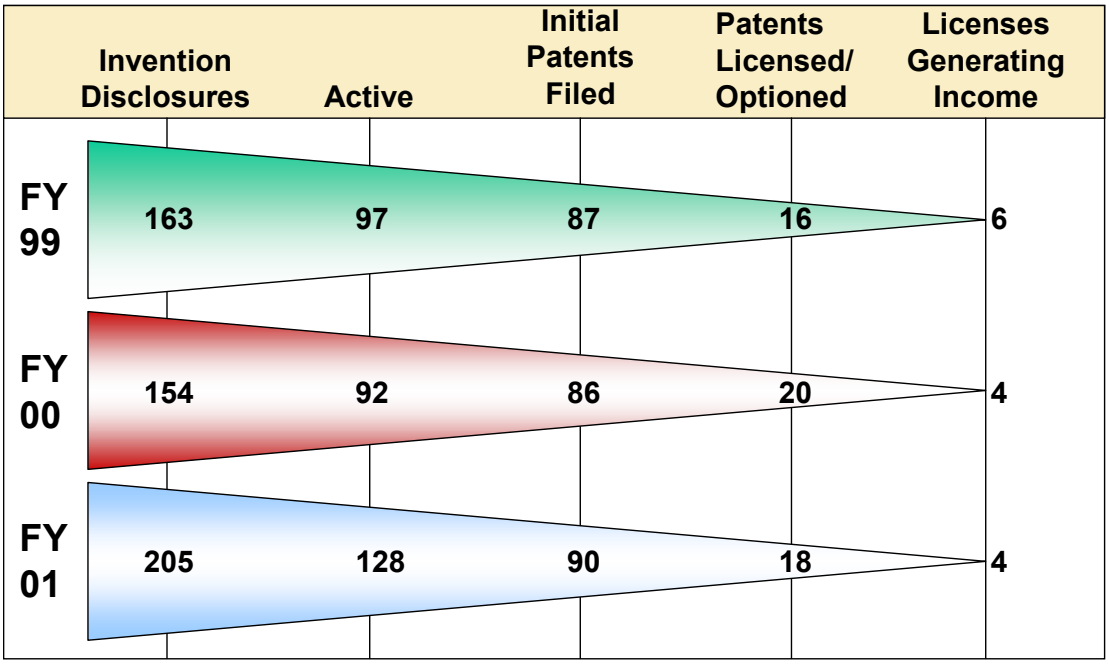
Source: AAAS

Exhibit 8 License Income History at CSRL



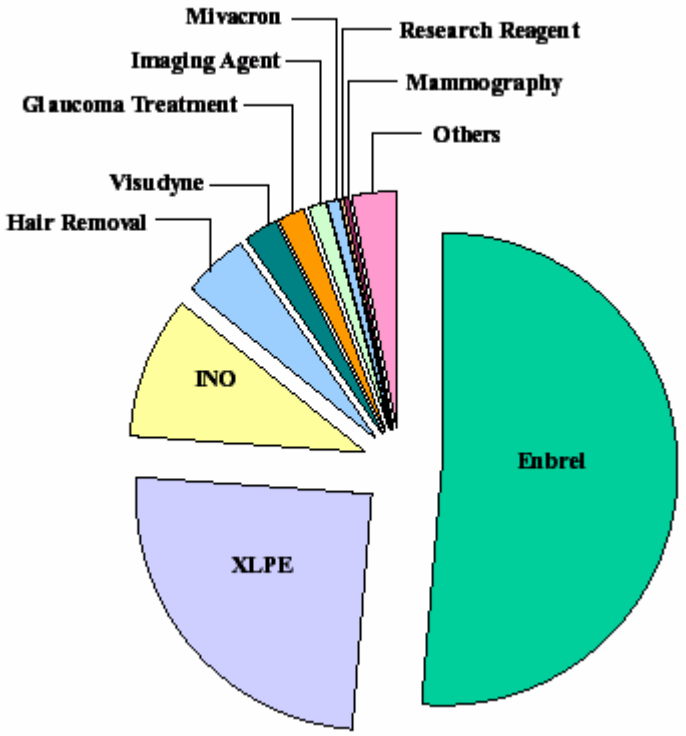
Source: MGH CSRL

Exhibit 9 High volume of invention disclosures leads to low number of license agreements generating income



Source: MGH CSRL

Exhibit 10 Top 10 license royalty income, by technology



Product	Licensee	Description
Enbrel	Immunex/Amgen	An anti-TNF fusion protein for the treatment of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis
Cross-linked polyethylene (XLPE)	Zimmer, Inc.	Cross-linked polyethylene is used in artificial joints, currently in hips and knees
Inhaled Nitric oxide (INO)	Linde AG	Inhaled nitric oxide is FDA-approved for vasodilation and hypoxemic respiratory failure in term or near-term infants
Hair removal and skin treatment devices	Palomar Medical Technologies	Laser-based hair removal systems and skin treatment systems
Visudyne	QLT	A method of treatment for age-related macular degeneration

Source: MGH CSRL

Exhibit 11 Cases that Toneguzzo believed posed mutually exclusive choices between maximizing revenue and public benefit.

1) Two clinicians approached Toneguzzo with a device to dispense pain medication that did not require patients to call on nurses. MGH patients typically self-administered intravenous pain medication using pumps with built-in controls to prevent over-dosing. When patients switched to oral pain medications, however, they had to call a nurse each time they needed the medication. The two clinicians had invented a box that would dispense pills, prevent over-dosing, and would keep a record of dispensed pills much like how the pump worked. The idea, Toneguzzo believed, was a good one but not one that CSRL could effectively protect; there were similar devices on the market and it was unclear what the market size for such a product would be. It was unlikely to be a financially lucrative investment but the clinicians asserted that using the device would help MGH operationally since nurses would now be free to do other things. Consequently, CSRL moved to protect the invention and began efforts to further development of the device.

2) CSRL had to decide how to move forward on a technology that had been in development for 20 years. Patents on the technology were beginning to expire but MGH had invested a few hundred thousand dollars on the patents and considerable effort on developing the technology as a potential ovarian cancer treatment. Research efforts on the technology were still ongoing but after having invested more than $400,000 on the project, would it be worth it? "If we are able to use the product as a therapeutic for ovarian cancer, that alone is sufficient for us to justify the expense. But from a financial perspective, it doesn't particularly make sense at this time when the patents are expiring", explained Toneguzzo. To her, the situation was reminiscent of the development of Taxol as a therapeutic for ovarian cancer; after an investment of close to $500 million on research and clinical trials related to Taxol, and with the patents expired, NIH provided Bristol-Myers Squibb with research results that allowed the company to complete development and bring the drug to market. In return, NIH received royalties totaling $35 million through 2002 for a drug that earned the company more than $9 billion between 1993 to 2002. For NIH, public health considerations had trumped financial ones in accepting the low royalty rate[20].

3) MGH held a large gene therapy portfolio. With some patents beginning to expire and the negative market sentiment surrounding gene therapy technologies, the portfolio held little financial value at the moment. If the aim of her office was to "do good", then Toneguzzo believed the portfolio held value but, "should we abandon these patents?

Source: MGH CSRL

[20] *NIH-Private Sector Partnership in the Development of Taxol*. US GAO Report to the Honorable Ron Wyden, US Senate, June 2003. GAO-03-829.

Exhibit 12 Harvard Medical School Conflict of Interest Policy

CATEGORY I **(a) and (b)** Activities are Generally Not Allowable. The only exceptions are conflicts that arise in extraordinary circumstances such as the recruitment of a new Faculty Member, where a conflict may be allowed to continue for a finite time period with disclosure and the approval of the Standing Committee, the Dean and the CEO.

Research Activities

(a) A Faculty Member Participating in Clinical Research on a Technology owned by or contractually obligated[(1)] to a Business[(2)] in which the Faculty Member, a member of his/her Family, or an Associated Entity has a consulting relationship, holds a stock or similar ownership interest, or has any other Financial Interest, other than receipt of University- or Hospital- supervised Sponsored Research support or royalties under institutional royalty-sharing policies.

(b) A Faculty Member receiving University- or Hospital-supervised Sponsored Research support (whether in dollars or in kind) for Clinical Research or research which does not involve human subjects, from a Business in which he/she, a member of his/her Family, or an Associated Entity holds a stock or similar ownership interest.

De Minimus Exception to Category I (a) and I (b) Conflicts

(a) A Faculty Member may continue to hold stock or similar ownership interest in a Business in a situation which would otherwise create an impermissible Category I (a) or I (b) conflict only if all of the following conditions are met:

The stock or similar ownership interest must be in a publicly held, widely traded Business.

The current value of the stock or similar ownership interest may not exceed $20,000 at any time.

There must be no relationship between acquisition of the stock or similar ownership interest and research to be conducted. Situations that satisfy this requirement include stock or similar ownership interest acquired in arms-length transactions or by family gift sufficiently prior to the beginning of the research to assure the lack of a relationship and stock or similar ownership interest acquired by inheritance. In any such situation there must be complete independence between a purchase decision or other acquisition and the research.

A Faculty Member who is a successful applicant for Public Health Service and/or National Science Foundation funding in a situation which would otherwise create an impermissible Category I(a) conflict can continue to hold stock or similar ownership interest in a publicly held, widely traded Business if the value of the ownership interest, when aggregated with that of spouse and dependent children, does not exceed $10,000 and the ownership interest was acquired in a manner unrelated to the research.

While meeting the above criteria excepts a Faculty Member from what would otherwise be an impermissible Category I (a) or I (b) conflict, it does not except a Faculty Member from other conflict categories such as Category I (h) which imposes an obligation to disclose a Financial Interest in the research in any publication or presentation.

(b) A Faculty Member may consult for a Business in a situation which would otherwise create an impermissible Category I (a) conflict only if all of the following conditions are met:

The amount of money received by the Faculty Member for consulting relationships or honoraria from a given Business should not exceed $10,000 a year. Consulting relationships include contractual relationships with a Business (or from an agent or other representative of such Business), service on advisory boards and any other relationship whereby the Faculty Member receives, or has the right or expectation to receive, income from a Business in exchange for services. Honoraria include commissioned papers and occasional lectures (no more than four lectures a year) for which money is received, either directly or indirectly, from a given Business (or from an agent or other representative of such Business).

While meeting the de minimis criteria above excepts a Faculty Member from what would otherwise be a Category I(a) conflict, it does not exempt the Faculty Member from other possible conflict categories such as Category I(h) which imposes an obligation to disclose a Financial Interest in the research in any publication or presentation.

CATEGORY I **(c) - (j)** Activites that May be Allowable Only after Disclosure, Review, and Approval by University or Affiliated Hospital with Advice from the Standing Committee When Requested:

Research Activities

(c) A Faculty Member conducting research externally that would ordinarily be conducted within the University or Hospitals.

Committee Participation

(d) A Faculty Member participating in the consideration by a committee of the FDA, other governmental agency, or private insurer of Clinical Research on a Technology which is owned by or contractually obligated to a Business in which that Faculty Member, a member of his/her Family, or an Associated Entity has a Financial Interest.

External Activities

(e) A full-time Faculty Member assuming an Executive Position in a for-profit Business engaged in commercial or research activities of a biomedical nature.

(f) A Faculty Member making clinical referrals to a Business in which such Faculty Member, a member of his/her Family, or an Associated Entity has a Financial Interest.

(g) A Faculty Member possessing a Financial Interest in a Business which competes with the services provided by the University or any Hospital with which the Faculty Member is affiliated.

Public Disclosure

(h) A Faculty Member publishing or formally presenting research results, or providing expert commentary on a subject, without simultaneously disclosing any Financial Interest in a Business which owns or has a contractual relationship to the Technology being reported or discussed or which sponsors the research being reported or discussed.

Administrative Responsibilities

(i) A Faculty Member taking administrative action within the University or any affiliated Hospital which is beneficial to a Business in which he/she has a Financial Interest.

Applicants for Public Health Service and/or National Science Foundation Non-Clinical Research Funding

(j) Under federal regulations[3] a Faculty Member who is an applicant for Public Health Service and/or National Science Foundation funding for non-Clinical Research has a potential conflict under the federal regulations, if the Faculty member, spouse and/or dependent children have a "significant financial interest", which could directly and significantly affect the design, conduct or reporting of the federally funded research. A Faculty Member who is an applicant for Public Health Service and/or National Science Foundation funding for Clinical Research is covered by Category I(a) above.

"Significant Financial Interest" **for Category I(j) Conflict**

For the purposes of a Category I(j) conflict, as defined above, a "significant financial interest" consists of "anything of monetary value" from the Business, including salary, consulting fees, honoraria, equity interests and intellectual property rights, with the exception of salaries, royalties and remuneration from University or an affiliated Hospital, honoraria for presentations sponsored by public or non-profit entities or income from service on advisory or review panels for public or non-profit entities. Also excepted for the purposes of a Category I(j)

conflict are salary, royalties or other payments that, when aggregated for the Faculty Member, spouse and/or dependent children, are not expected to exceed $10,000 over the subsequent twelve months and equity interests, that, when similarly aggregated, do not exceed $10,000 in value or, if the monetary value cannot be ascertained, 5% ownership interest in the business.

Resolution of Category I(j) Conflict

A Category I(j) conflict as defined above must be resolved by management, reduction or elimination, prior to the expenditure of funds from the Public Health Service and/or National Science Foundation. Possible resolution of Category I(j) conflicts may include, but is not limited to, public disclosure of the significant financial interest, monitoring of research by independent reviewers, modification of research plans, disqualification from participation in Public Health Service and/or National Science Foundation funded research, divestiture of the significant financial interest, and severance of relationships that create the Category I(j) conflict.

CATEGORY II Activities that are Ordinarily Allowable Following Disclosure and, Where Necessary, the Implementation of Oversight Procedures:

Research Activities

(a) A Faculty Member Participating in Clinical Research on a Technology developed by that Faculty Member or a member of his/her Family, unless the activity falls under the guidelines of Category I.

(b) A Faculty Member assigning students, post-doctoral fellows or other trainees to projects sponsored by a for-profit Business in which the Faculty Member, a member of his/her Family, or an Associated Entity has a Financial Interest, unless the activity falls under the guidelines of Category I.

Board Memberships

(c) A Faculty Member serving on the Board of Directors or Scientific Advisory Board of a Business from which that Faculty Member or a member of his/her Family receives University- or Hospital-supervised Sponsored Research support or with which the University has a substantial contractual relationship known to the Faculty Member, unless the activity falls under the guidelines of Category I.

External Activities

(d) A Faculty Member assuming an Executive Position in a not-for-profit Business engaged in commercial or research activities of a biomedical nature.

CATEGORY III Activities that are Routinely Allowable:

(a) A Faculty Member receiving royalties for published scholarly work and other writings.

(b) A Faculty Member receiving royalties under institutional royalty-sharing policies.

MENTORS' OBLIGATIONS TO STUDENTS AND TRAINEES IN INDUSTRIAL SPONSORED RESEARCH

(a) Trainees (medical students, graduate students and post doctoral fellows) must always be encouraged to conduct research in areas that optimize their training. Special care must be taken to assure that a trainee's research is not designed to (and does not apear to) enhance their mentor's Financial Interest, and is not adversely affected by that interest or by contractual aspects of the Sponsored Research agreement that inhibit scientific communication or that commit intellectual property rights to the industrial sponsor.

(b) Before embarking on a research project, a trainee must be provided by the mentor with a clear description of 1) any corporate support of the research to be undertaken, 2) any personal Financial Interest the mentor has in a sponsoring Business, and 3) any restrictions that might be imposed on the scientific communication of the data.

(c) Written approval must be obtained before a trainee can be assigned to conduct research which is sponsored by a Business or which involves a Technology to which the Business has license rights, and in which the mentor has any Financial Interest.

In the case of graduate students (Ph.D., M.D./Ph.D., M.P.H., and D.M.Sc. candidates), permission must be given by the chairperson (or desginated Faculty member or committee) for the graduate program and by the mentor's department chairperson.

In the case of medical and dental students (M.D., and D.M.D. degree candidates), permission must be given by the mentor's Medical School department chairperson. Additionally, for research in the Quadrangle departments, permission must be give by the Executive Dean for Academic Programs. For research in the Hospital, permission must be given by the appropriate Faculty Dean.

In the case of postdoctoral fellows, permission must be given by the mentor's Medical School department chairperson.

(d) A trainee may appeal his/her involvement in any industrially Sponsored Research or research which involves Technology to which a Business has license rights when the trainee believes that he or she is being adversely affected by any conflict of interest (real or apparent) resulting from the mentor's relations with the sponsoring Business or with any Business that may benefit from the trainee's research or from the Sponsored Research agreement. The appeal should be made as appropriate to the Executive Dean for Academic Programs, the Hospital's Faculty Dean, and or the School's or Hospital's Ombudsperson.

Footnotes:

[1]*By license or exercise of an option to license.*

[2]*The definition of 'Business' excludes the University, any affiliated hospital, any Private Medical Practice or any entity controlled by, controlling, or under common control with the University or affiliated hospital.*

[3]*Public Health Service Final Rule 42 CFR Part 50 and 45 CFR Part 94; National Science Foundation Rule 59 FR 3308 and 60 FR 35820.*

Exhibit 13 Companies started with MGH technology

Company	Year licensed	Equity?	Private/public
Dentigenix Inc.[a]	2003		Public
Descartes Therapeutics	2003		Private
Gamete Technology Inc.	2003		Private
Keel Pharmaceuticals Inc.	2003		Private
Neuroptix Corporation	2003 (MGH/BWH)		Private
Welgen	2003		Private
Mercury Therapeutics	2002 & 2003		Private
Living Microsystems	2002	Yes	Private
Aptanomics	2002	Yes	Private
Cytocure	2002	No	Private
MR Instruments	2002	Yes	Private
Viacell Endocrine Science	2002	No	Private
Nanopharma	2001	No	Private
Pharma-In	2001	No	Private
Prana Biotechnology	2001	No	Public
Transition Therapeutics (formerly Waratah Pharmaceuticals)	2001	No	Public
Viacell Neurosciences	2001	No	Private
Vis En	2001	No	Private
GI Company	2000	No	Private
Neurogenetics	2000	No	Private
Seacoast Technologies Inc.	2000	No	Private
Unbound Medicine	2000	Yes	Private
X-Ceptor Therapeutics (formerly Receptor)	2000	Yes	Private
Receptor	1999	Yes	Private
Freedom II	1999	Yes	Private
DevGen (warrants)	1999	Yes	Private
eNOS Pharmaceuticals	1999 (BWH)		Private
Coherent Diagnostics	1998	Yes	Private
Procyon (formerly Oncologic)	1998	No	Public
Biostream	1997	No	Private
Oxford Biomedica	1997	Yes	Public
Phylos (acquired by Compound Therapeutics)	1997	Yes	Private
Molecular Targeting Technology	1996	No	Private
Epix (formerly Metasyn)	1996		Public
Renaissance Pharmaceuticals*	1995	No	-
Bion*	1995	No	Private
Egenix (formerly Epigen)	1993	No	Private
RSTAR*	1992	No	-
Biotransplant Inc.*	1991	No	Public
TKT (sublicense of Hoechst)	1990	No	Public
Diacrin (sold to GenVec)	1989	Yes	Private
Centocor J&J	1980	No	Public

Source: MGH CSRL

[a]A wholly owned subsidiary of Ivoclar Vivadent, Inc.

*Out of business