

REGIONAL DEVELOPMENT

Minnesota's biotechnology portfolio

A well-diversified biotechnology portfolio, strong financial community, and excellence in technology transfer position Minnesota for continued expansion.

Todd R. Nelson and Andrea H. Lauber

Minnesota is recognized as a leading provider of innovative, quality medical care through its world renowned academic healthcare centers, the Mayo Clinic and the University of Minnesota. An expertly experienced healthcare-oriented financial community, a relatively low cost of living, and excellent educational systems with which to attract business professionals and biomedical research scientists, have facilitated the expansion of the medical device and managed care organizations. Not surprisingly, these same driving forces have been instrumental in the recent surge of biotechnology and biopharmaceutical activity within the state.

The biotechnology portfolio

Minnesota is home to a rapidly expanding, well diversified biotechnology community. When extracted from the medical device arena, the contributions to the states economy remain substantial. A recent survey of the biotechnology community revealed that this market sector employs more than 6,000 people and contributes in excess of \$2.1 billion in sales revenues annually to the states economy. More than 200 biotechnology companies, categorized as biomedical, bio-agricultural, environmental, or suppliers for these market sectors have been identified (see Fig. 1). The biomedical portion of the industry's portfolio contains such notable companies as 3M's pharmaceutical division (St. Paul, MN), R & D Systems (Minneapo-



lis, MN), Sanofi Diagnostics (Chaska, MN), IncStar (Stillwater, MN; recently acquired by American Standard's Life Sciences Division for US\$120 million), Cellex Biosciences (Minneapolis, MN), Galagen (Arden Hills, MN), ALZA (Blaine, MN), and Protein Design Labs PDL (Plymouth, MN).

The state's recent biotechnology sector activity has also been facilitated by big pharma investment in the region. In the past year, numerous corporate expansions have been targeted at Minnesota. Protein Design Labs (Palo Alto, CA) has recently expanded their manufacturing facilities to Plymouth, Minnesota. ALZA has initiated plans to build a 60,000 square foot biotechnology research manufacturing facility on 140 acres of land in Blaine, Minnesota. Novartis Seeds (Basel, Switzerland) generates significant revenues in the area of plant biotechnology is currently located in Stanton, Minnesota.

Continued expansion of this industry is likely to be augmented by the close association of the University of Minnesota's Academic Health Center (AHC) and the Mayo Clinic with the biotechnology community. As outstanding academic and health care organizations, these institutions have devoted human and financial resources to biomedical research that has resulted in core

competencies of innovation, basic and applied research, and productivity, as well as a strong commitment to ensuring the economic growth of this market sector.

Concomitant with the growth of this industry comes the opportunity to benefit from the resources developed inside these biomedical research engines. As such, effective technology transfer brings together academic and industrial resources building, synergistically, a newly formed machine. It is in part through the efforts of the technology transfer offices at two of the countries leading biomedical research institutions that Minnesota capitalizes further on the growth potential of the biotechnology industry.

Biotechnology transfer

"Technology transfer" refers to the transfer of novel inventions from the private or academic sector into the hands of industry that can further develop and bring the invention to market. The purpose of an individual or office devoted to technology transfer is to protect and commercialize discoveries developed within the institution.

The major steps involved in the technology transfer process include: First, disclosure of innovations; second, protecting the technology; and third, licensing the rights to the innovations and or processes to biomedical and related industries for commercial development. Depending upon the novelty, industrial interest/support and budget, the

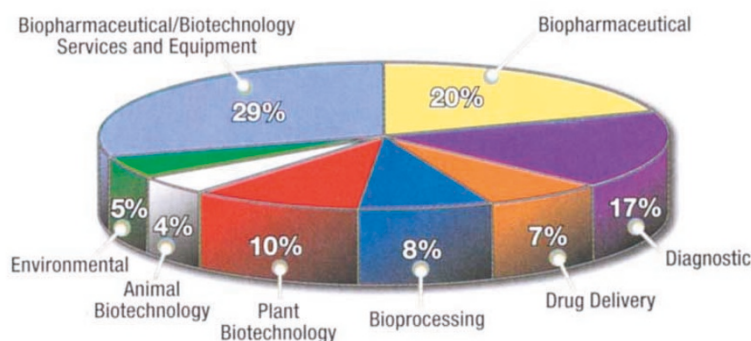


Figure 1. Minnesota's biotechnology market sectors. Source: Minnesota Biotechnology Association (www.holoweb.com).

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technology may be the subject of a patent application. Applications may be filed if it is determined that patent protection would enhance the commercial value of the invention. In all cases, however, technologies are protected under nondisclosure agreements before attempts are made to license the rights to the inventions to biotechnology and pharmaceutical companies.

The process of technology transfer and protection of intellectual property is a relatively recent development. Before 1980 fewer than 250 patents were issued to US universities each year, and discoveries often were not available for commercialization by industry participants^{1,2}. The 1980 Bayh-Dole Act³ allowed universities, nonprofit research institutions, and small businesses to own patent rights to inventions developed using federal funding.

This legislation has had a dramatic impact on the way that academic organizations view discoveries developed under their auspices. The Bayh-Dole legislation, coupled with a bipartisan effort that continues to reduce government-sponsored research, has pointed to technology transfer as a means of generating significant revenues for nonprofit institutions. In fact, monies obtained from industrial sources support the research programs and goals of the investigators and the institution.

Furthermore, these activities can help to move the technology along the value path, enabling the company to keep costs down in bringing to market inventions while conferring to the public the efficient transfer of relevant and timely discoveries. Both the Mayo Clinic/Medical Foundation (Rochester, MN) and the University of Minnesota (Minneapolis, MN) have well-established technology transfer divisions whose functions are to protect and commercialize technologies developed within the respective institutions.

Mayo clinic

Located in the southeastern corner of Minnesota, within the city of Rochester, is the Mayo Clinic. Known well beyond the confines of the state, and outside the US boundaries, Mayo ranks as a top healthcare organization. Lesser known, however, is the role that basic and applied biotechnology has begun to play within the institution and how Mayo is using proprietary technologies to further its mandate to advance patient care.

Mayo Medical Ventures (MMV) was conceived 11 years ago, in part to address the transfer of the institution's technology to the public sector. The areas of MMV

most connected with biotechnology are aspects within the new ventures division and the division of technology and services, which houses the office of technology transfer. MMV is guided by the executive director, Rick Colvin, and the executive medical

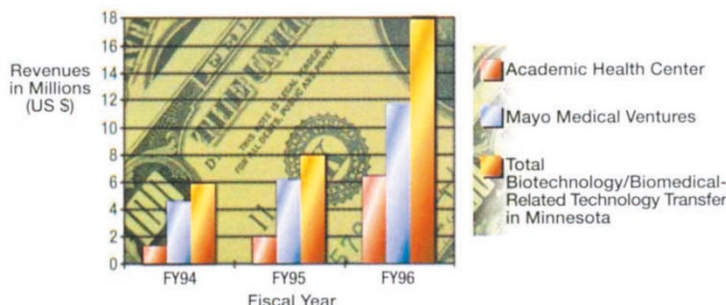


Figure 2. Biomedical technology transfer revenues.

director, Richard Brubaker. Since its inception in 1986, MMV has sustained an average annualized rate of growth of 27% and, in 1996, reported revenues in excess of US\$50 million. In 1994, 1995, and 1996, biomedical-related technology transfer accounted for a gross incomes of US\$4,565,000, US\$5,995,000, and US\$11,575,777, respectively (see Fig. 2).

From inception through to 1996, MMV has collected 1,091 disclosures, 274 licenses, and 69 patents. In 1994, 1995, and 1996, of all license agreements executed, biotechnology licenses accounted for 36%, 46%, and 45%, respectively. In the years 1995 and 1996, of all patents issued to the institution, biotechnologies accounted for 33% and 43%, respectively. Mayo ranked 18th out of 154 US universities and medical centers for royalties received from technology transfer ventures³. Although biotechnology disclosures, licensures and patents constitute only approximately 30% of MMV's technology portfolio, they provide significant revenues, and the amounts are growing annually.

MMV's Rick Colvin attributes the growing success of the portfolio to the integration of several business models into the infrastructure of the organization, allowing MMV to function as a business-like unit that renders a didactic approach to biotechnology transfer in Minnesota. Although MMV started with typical licensing arrangements for intellectual properties, over time they have developed several strategies, including: First, formation of strategic alliances with the biotechnology and pharmaceutical industry through forward marketing; second, equity participation; third, in-licensing of externally developed biotechnology; and fourth, formation of venture capital alliances that facilitate the establishment of biotechnology companies around ideas generated or enhanced at the institution.

Chief financial officer Ann Hovland suggests the recent successful growth in the portfolio is due in part to MMV's ability to participate in equity offerings and venture capital investments as part of a defined technology transfer paradigm. MMV not only serves to

enhance the process of invention through collaboration, but has turned this very fascinating and rapidly expanding field into a business that generates significant revenues.

Unique to MMV's approach is the ability to in-license and improve upon, or integrate, processes at the institution such that the end result is the presentation of a "product" to industry

and not just an "idea." This is accomplished by using a modeled approach to business development that vertically integrates the institution's clinical and basic science resources. MMV plans to invest further in this strategy by forming a distinct initiative dedicated to the genesis of biomedical- and biotechnology-related activities. Mayo Technology Based Ventures will serve as a platform from which enabling technologies can be launched. Using a proactive approach to such new ventures, these investments will involve technologies available either from within, or outside of Mayo, and as such this division will serve a much-needed function within the process of biotechnology and biomedical commercial development.

The most prevalent activity to date related to technology transfer, however, involves licensing proprietary biotechnologies to industry. As within other academic and medically based institutions, biotechnologies disclosed by Mayo inventors are often in the very early stages of development. This situation renders questions related to the commercial potential of the technology difficult to address, as "good science" does not necessarily equal "commercializable technology". Thus, this is the time in the technology life-cycle that engenders the greatest financial risk, but also represents the greatest potential value for the investor.

Biotechnology-related disclosures are submitted in nearly equal proportions by clinicians and basic researchers spanning institutional departments to MMV. The technologies take a myriad forms: Antibodies, cell lines, transgenic mice useful for models of disease (including asthma and inflammation), recombinant proteins, novel targets for vaccine development, the use of PCR-based technologies to detect blood-borne parasites, unique bioassays,

identified sites of genomic instability in cancer cells, novel autologous methods for wound healing and platelet replenishment, new uses for old drugs.

In all areas, Mayo's business attitude toward industrial relations affords investigators and companies the ability to establish relations that can take on any number of configurations, depending upon the requirements of the specific project and the desires of the parties involved. Strategic alliances, contract research, sponsored research with attached options, licensing of technologies and know-how, and various forms of industry-supported collaborative projects are all encouraged. The vast areas of accomplishment within biotechnology, combined with a flexible, integrated, and business-like approach to industrial partnerships, has led to fruitful endeavors for all parties.

The University of Minnesota

The University of Minnesota, located in the twin cities of Minneapolis and St. Paul, has a long-standing relationship with the medical and research communities. In 1995, the University's Academic Health Center received US\$180 million in funding, of which US\$58 million (or 33%) was generated from biotechnology-related industry financing. In 1994, the University of Minnesota's Office of Patents and Licensing undertook a significant strategic planning process to look at ways to improve its service to faculty and to enhance its ability to generate revenues from licenses and patents. The results of the analysis suggested that it was desirable for professionals to focus on more defined technical areas in order to gain expertise in the industries that are most directly associated with the inventions that may come from these areas. As such, in 1995, the division was named patents and technology marketing (PTM) to reflect an emphasis on proactive invention marketing. From this restructuring, a health technologies portfolio was formed that encompasses inventions stemming from the University AHC's 52 departments and divisions relating to biomedical and biotechnology research endeavors.

The University of Minnesota's School of Medicine contains 27 departments that account for 60% of the AHC-related activities, and it plays an integral role in facilitating the relationship between clinical and basic science researchers with PTM. Since its inception, the AHC portfolio has grown at 140% annually and reported 1996 fiscal year revenues of US\$6,334,717 (Fig. 2). Biotechnology licensing accounts for 85% of net revenues in the health technologies portfolio and are anticipated to grow at an accelerated rate for the next five years. For the period 1992 to 1996, the portfolio has presented 392 disclosures, filed 184 patents (of which 69 have been issued), and completed in excess of 70 licenses with the

biotechnology community. The increased patent and licensing-related revenues within the portfolio demonstrate that new discoveries are moving through the development pipeline more actively and efficiently. On a per patent and licensure basis, revenues resulting from biotechnology-related activity have increased by 1050% or US\$357,889 and 711% or US\$343,686, respectively.

Jim Severson, director of the university's health technologies portfolio attributes the rate of growth to the ability of the division to take a proactive posture relating to technol-

ogy development. Under the direction of Leo Furcht, vice provost of the AHC, the division is pursuing vertically integrated business strategies to bring the wealth of biomedical knowledge and research ability from the engine of the University of Minnesota's AHC to the industrial community.

As part of this strategy, two divisions are being created. Internally, the research service organization will enhance the process of technology development with faculty of AHC and perform a diverse array of functions ranging from feasibility studies to contract execution

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for both basic and clinical applications. An integral part of this process is the placement of research process managers in each division as facilitators for commercial project development. In this way, the technology transfer department can participate in the value added process through their ability to identify promising technologies and discoveries early in the development stage. Teams of clinicians, scientists, and process managers can work together to advance the direction that will expedite the process of commercialization. Externally, the business development office will have responsibility for both the aggressive marketing of the AHC's technologies to industry, and the capturing of valuable opportunities outside of the institution for in-licensing and development at AHC.

The recent growth observed in the biotechnology portfolio of the AHC suggests that the region has responded to such efforts and that growth will likely continue as demand for transfer of valuable technologies and discoveries into the marketplace increases (Fig. 2). The ability to harness the discoveries that will result from the AHC should continue to enhance the region's attractiveness for development. Significant agreements continue to be made with the biomedical/biotechnology and

pharmaceutical companies, who benefit from the increased efficiency introduced into the system.

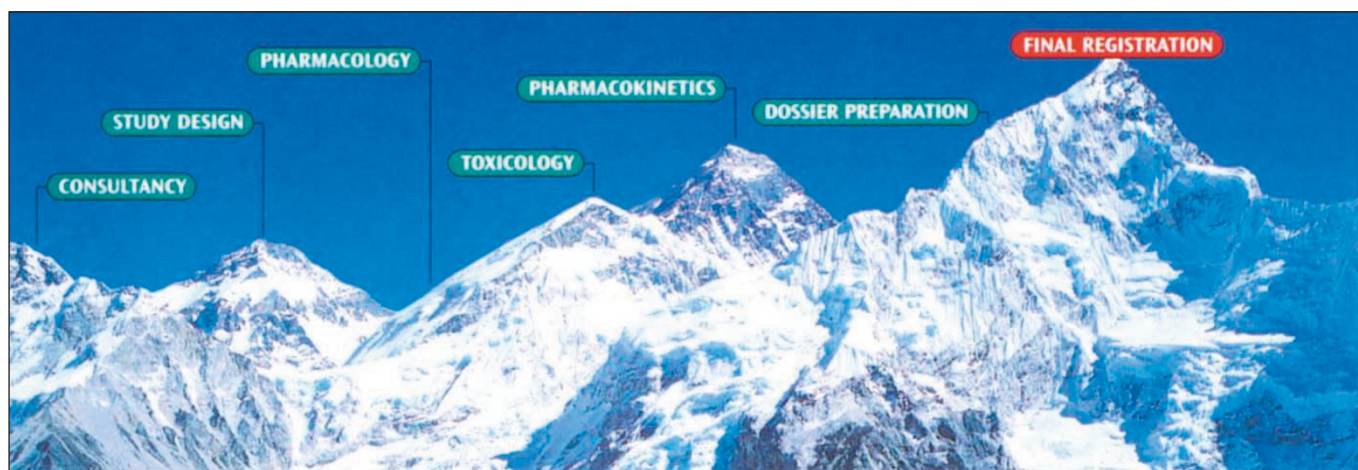
The accelerated licensing activity seen at MMV and the University of Minnesota's AHC illustrates a successful relationship with the industry. The increase in academia-biotechnology industry partnerships has created a very attractive environment for the biotechnology company⁴. World class biomedical and clinical facilities such as the Mayo Clinic and the University of Minnesota's Academic Health Center are able to attract significant research dollars to develop their technologies and gain access to the expertise of industrial physicians and scientists, while industry extends the scope of its research and development through funding and licensure. The flexible attitude of MMV and the University of Minnesota's AHC toward industrial relations affords investigators and companies the ability to establish relations that can take on any number of a wide array of guises, depending upon the desires of the parties involved.

Conclusions

The University of Minnesota and the Mayo Foundation create industrial resources that help to support basic and biomedical

research and patient care. In addition, the investigators, their research teams, and research programs continue to benefit greatly from commercial support. In return, the industrial partners receive great value in exchange for their investment dollars. The company receives technology and scientific support at a cost far below that required to bring the entire project in-house and with access to a vast array of dedicated expertise and "know-how." Together, Minnesota's biotechnology resources, whether in the form of a responsive industrial giant, world class research and medical institutions, or academic/industrial partnerships, make tremendous resources available to the biotechnology and pharmaceutical industries.

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3. Stevens, A.J. 1993. Testimony to US Department of Commerce Hearing on the Bayh-Dole Act, Washington, DC, October 1993.
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