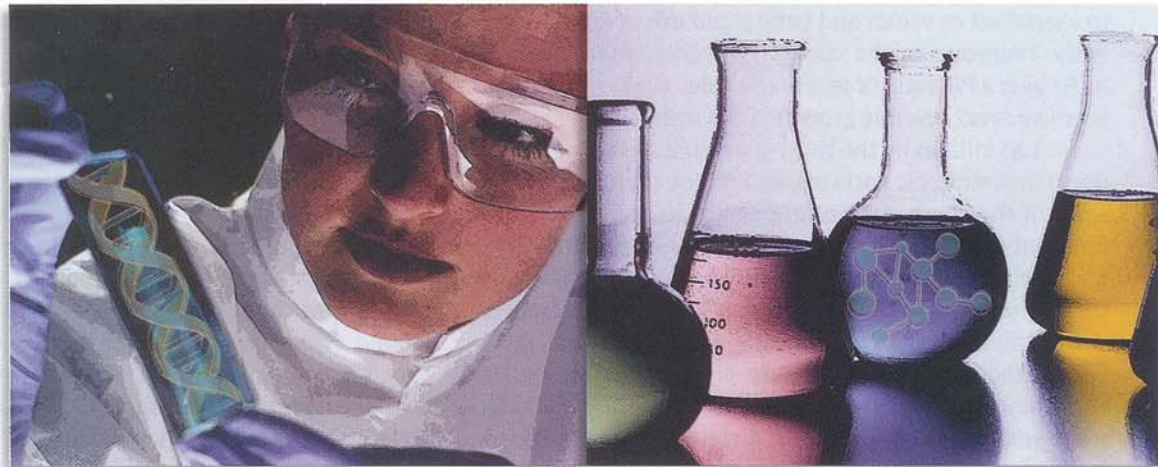


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BIOTECHNOLOGY



LEADS THE WAY

by April W. Klimley

Biotechnology has transformed the health care industry and has changed the way people are treated for disease. In three short decades, the industry has reached a new level of maturity. Now it is expanding into other fields—leading the way in sectors such as national defense and industrial development.

Signs of this expansion are everywhere, from the explosion in biotechnology hubs from Scotland to Singapore to a resurgence in VC financing and biotech IPOs. In the United States, state governments are actively vying for biotechnology investment, while the Department of Defense is exploring new ways to defend against bioterrorism using industry breakthroughs.

“Biotech is not just biotechnology and pharmaceuticals anymore,” explains Scott Morrison, a leader in Ernst & Young’s biotechnology sector. “There are a lot more uses for biotech, such as agricultural, industrial, and even nanotechnology. That is why so many countries are jumping into these initiatives.”

Transforming health care

Of course, biotechnology has had the greatest impact on health care. Advances such as high throughput screening, which makes it possible to better identify targets for treatment, and DNA sequencing machines, which speed up the process of mapping the human genome, have transformed the way medicine is practiced. This new genetic knowledge has resulted in the development of a growing number of drugs targeting very specific diseases. Called biologics, these medicines or therapies are produced through biological processes rather than by chemical synthesis, as in the case of the “small-molecule” drugs produced by the large pharmaceutical companies.

Today, there are more than 300 biotech drug products and vaccines on the market that take aim at more than 200 medical conditions, including macular degeneration, multiple sclerosis, AIDS, and Alzheimer's disease. In addition, hundreds of important medical diagnostic tests have been developed in the last few decades, from the home pregnancy test to DNA fingerprinting.

Biotechnology firms reached a milestone in 2003 when they received more approvals for new compounds from the Food and Drug Administration (FDA) than the large drug companies. These firms have continued to build strong pipelines and have received approval for a steady stream of new therapeutics since then. Last year's crop included two drugs from Amylin Pharmaceuticals: Byetta and Symlin, both treatments for diabetes; and one from Celgene: Revlimid, a treatment for transfusion-dependent anemia.

Breakthroughs such as these have transformed the standard medical discovery paradigm from a single-minded focus on blockbuster drugs that treat widespread disease to a focus on targeted therapeutics for medical conditions that affect smaller populations. Simultaneously, they have turned many hitherto fatal diseases into chronic conditions—which warrant a different type of treatment, medication, and support services than in the past.

Personalized medicine becomes a reality

Some of these new therapeutics only work successfully in conjunction with diagnostic testing. By identifying which patients will benefit from certain medicines, genetic testing has created an entire new field called “personalized medicine” or pharmacogenomics. Genentech's Herceptin was the first well-publicized drug in this category. Approved in 1998, Herceptin reduces cancer recurrences in patients who carry the HER2 gene, a gene that regulates cell growth. Through genetic makeup screening, the patients who produce too much HER2 can be identified and given the drug.

This past year saw another advancement in personalized medicine: The FDA approved BiDil, a drug produced by NitroMed that is specifically targeted to African Americans to lower the incidence of deaths in those who have had congestive heart failure. This result was discovered in clinical trials. BiDil is the first drug to be targeted exclusively to an ethnic population.

Drugs like BiDil, Byetta, and Revlimid have been

good for the biotech industry. Although these companies have yet to have blockbusters like the giant pharmas, the biotech industry as a whole now has at least three therapeutics in the top 10 list of prescription drugs sold in the United States.

Successes like these, coupled with a full pipeline, have brought the biotech industry steadily toward profitability. “The 2005 story of the day was therapeutic products,” observes Ernst & Young's Morrison. He says this is a new, positive development, and contrasts this situation with the early 2000s when many biotech firms concentrated on the creation of new technologies to create therapeutics. Now, with more products in the marketplace, he predicts that the industry may be profitable by 2010 or even earlier.

In the last few years, the capital markets have also been kinder to biotech firms—an industry that traditionally has needed substantial funding, since development time for most biologics, like small molecule drugs, takes years, and hundreds of thousands of dollars. In 2005, according to Nick Galakatos of Clarus Ventures, a VC specializing in biotech funding, total VC dollars invested in life sciences including biotechs came back up from a dip in 2003 to \$7 billion. In addition, he noted that “inflows and outflows” were balanced, suggesting that “the industry is very healthy.”

While most biotech companies remain very small and nimble, others have achieved so much success that the line between them and their larger pharmaceutical brothers is fading. Today at least three biotechs are in the top 15 pharmaceutical/biotechs in capitalization: Amgen, Genentech, and Gilead Sciences. Not only are these biotechs as big as some of the drug companies, they also have the integrated systems needed to take their compounds from discovery right through commercialization.

The large pharmaceutical firms, meanwhile, have tried to incorporate some of the nimbleness, speed and creativity of biotechs into their own product pipeline. They have done this a number of ways: by revamping their internal R&D discovery process; by forging alliances and in-licensing arrangements; and even by creating new research centers patterned after biotechnology firms.

The big drug companies adjust their pipelines

Biotechnology is changing how—and where—the big drugmakers do business. Swiss-based pharmaceutical giant

Novartis, for instance, recently built the Novartis Institute for Biomedical Research on MIT commercial property in Cambridge, MA, a hotbed of biotech research. The company said it was attracted by the strong pool of scientific talent in the area and it plans to center Novartis research activities there. In addition, this research center brings Novartis physically closer to some biotech alliance partners, such as Avalon Pharmaceuticals, based in Germantown, MD.

Alliances are another way in which the large drug companies have been able to take advantage of biotech inventions and discoveries. Roche is one of the leaders in this new world of alliances and in-licensing arrangements. It has one of the largest and best-managed biotech pipelines in the industry. "Our executives grasped the concept behind biotech in the early 1990s and had the courage to do something with it," says Dennis Burns, Roche's vice president, global head, global business development. Tamiflu, which Roche sells through a licensing arrangement with biotech Gilead Sciences, is one of Roche's most visible co-development successes. The company is highly regarded for its formal alliance process, as well as innovations such as its network of "global alliance directors."

Today, biotech firms are even forming alliances with one another—a true sign of maturity in the industry. In 2004, biotech-to-biotech alliances accounted for 57 percent of total industry partnerships. These arrangements enable biotech firms to maintain their independence longer and be less pressured to move from a licensing partner to being acquired by a much-larger pharmaceutical firm.

The "critical path" to FDA approval

While biotechnology has matured, the U.S. regulatory process has lagged behind the industry. In fact, over the past decade the FDA has seen its pipeline of compounds, drugs, and medical devices waiting for approval decline, not rise. This problem has been compounded by a number of negative incidents involving drug safety and production, most notably, the withdrawal of Merck's blockbuster drug Vioxx from the market in 2004.

These problems seem to have strengthened the FDA's resolve to find new tools and techniques to better

evaluate the new generation of therapeutics and drugs. In 2004, the FDA issued its Critical Path Initiative (CPI) report, which described the pressing need to modernize the product-development process, i.e., the Critical Path. This past March, the FDA issued another paper, a Critical Path Opportunities List and Report, which offered examples of how new discoveries could be applied to improve the accuracy of FDA tests and predict the safety and efficacy of investigational medical products. Earlier in the year, the FDA announced its partnership with a new, publicly funded organization, the Critical Path Institute (C-Path), to bring FDA scientists together with academe and industry to better address CPI goals.

Reinventing the Biotech Industry Organization (BIO)

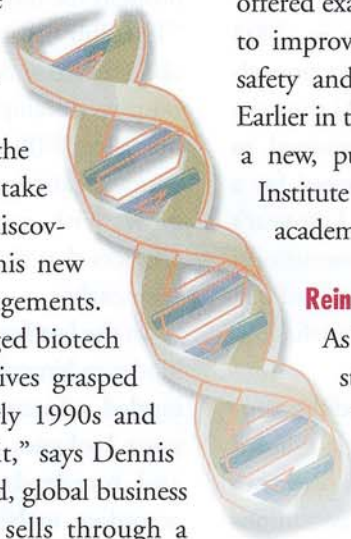
As biotechnology has grown, so has the need for a strong voice in Washington. The industry is faced with an increasing number of regulatory and legislative issues. That need may be answered by the Biotechnology Industry Organization (BIO), founded 16 years ago, but never considered an equal to the pharmaceutical industry's representation in Washington.

Under the leadership of Jim Greenwood, BIO's new CEO and a former Pennsylvania congressman, that may be changing. During his first year in office, Greenwood restructured BIO by bringing in a more dynamic, Washington-savvy staff including insiders such as Scott Whitaker, now COO, who previously served as chief of staff at the Department of Health and Human Services, and Amit Sachdey, a former top FDA official. He has also made sure BIO took a strong stand on major issues, such as guidelines for approval of generic versions of biotech medicines, and has strengthened BIO's role as a funding matchmaker for industry start-ups.

The global impact of biotechnology

Today, the United States remains the center of biotech innovation. About 80 percent of the world's publicly traded biotech companies, measured by market capitalization, are located there, according to Ernst & Young's 2005 Biotech Report. These companies remain largely bi-coastal, located primarily in California (the home of the largest firms) and along the Eastern seaboard.

But there has also been considerable activity in Canada and Europe, where governments have worked hard to



create “biotechnology hubs,” places where research and industry intersect. Ireland, for example, is gearing up to become a major hub. Ireland already benefits from the presence of a number of large pharmaceutical manufacturing facilities. It also has a motivated, well-trained, English-speaking workforce. These factors make it a very appealing location for biotech companies. And, according to Barry O’Leary, senior vice president, life sciences, at the Industrial Development Association of Ireland (IDA Ireland), the government is adding another attraction—construction of a \$75-million National Institute for Bioprocess Research and Training.

Asian countries are also creating their own biotechnology hubs. Both India and China are working hard to attract biotech firms. According to E&Y’s Morrison, there are already 700 biotech companies in Asia, approximately 100 of them publicly traded.

Recently, Malaysia launched a \$26-million biotech fund to support biotechnology research and development. To spearhead this initiative, the government created the Malaysian Biotechnology Corporation, headed by CEO Iskandar Mahmood. According to Mahmood, one thrust of the program will be to capitalize on the strengths of biodiversity in the country and to commercialize discoveries with good value propositions in biomedical, agricultural, and industrial biotechnology.

Industrial and environmental development

Outside of health care, two other biotech revolutions seem to be brewing. One is agricultural biotech, which is primarily genetically modified crops, and the other is industrial and environmental development. On the industrial side, enzymes have long been used to aid chemical processes. They are used in everything from the processing of waste materials to the creation of stonewashed jeans. This trend is continuing.

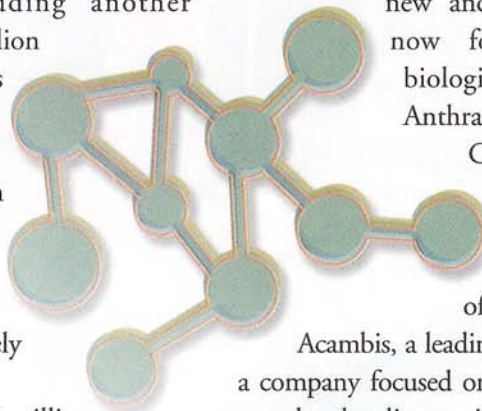
But a new emphasis has sprung up on biofuels and biodefense. In the United States, for instance, there is strong support for President Bush’s call for fuel alternatives, in particular cellulosic ethanol produced from plant products (like saw grass) to replace oil-derived products. Although the major chemical companies like Dow and

DuPont have been working on this for years and have not yet come up with realistic, low-cost replacements, there seems to be a resurgence of interest in finding solutions. The Energy Policy Act of 2005 provided for strong research programs at the Departments of Energy and Agriculture, and President Bush has proposed increasing the funding for this research to \$120 million for 2007.

Meanwhile, bioterrorism has been in the limelight ever since the Anthrax scare after 9/11. No wonder a number of new and existing biotech companies are now focusing on ways to counter biological threats from substances such as Anthrax, nerve gas and the Ebola virus.

Companies that have benefited from greater government spending on biodefense include Abenix, which focuses on the development of human therapeutic antibodies;

Acambis, a leading developer of vaccines; Gen-Probe, a company focused on nucleic acid testing; and Cepheid, a molecular diagnostics company.



A convergence of technologies

All this activity suggests that the biotechnology revolution is expanding. It is moving from the health care industry into other areas that will benefit large populations, tackling problems from feeding the world’s poor to cleaning up the environment. These broader benefits are one reason the industry is so appealing to developing countries. As Malaysia’s Mahmood puts it, “We see biotech as one of the key engines of growth in the future. But it is also a means to an end, a way to create economic activity and social well-being as well.”

In fact, biotechnology is part of a much broader revolution already under way. Jim Greenwood, CEO of BIO, explains: “There is a convergence of three technologies. Biotechnology, information technology, and nanotechnology are converging into a molecular revolution. This steep trajectory will transform our existence.”

April W. Klimley is an award-winning writer and editor whose work has appeared in many publications, including Fortune, Business Week, and Forbes. She also edits Visions, a quarterly magazine on “Insights into innovation”™ published by the Product Development & Management Association (PDMA). www.info@klimley.com