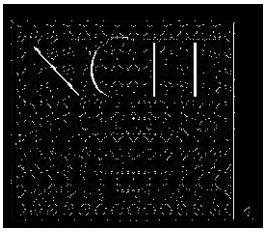

Biotechnology Industry Trends[1]

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The biotechnology industry is not defined by its products, but by the technologies employed in making them. Those technologies involve the use of biological processes to solve problems or to make useful products. Biotechnologies are primarily employed in the medical and pharmaceutical industries, but they are also used to increase crop yields, clean up hazardous waste, and increase the efficiency of industrial processes. Biotech firms span more than 60 industrial classifications, giving the industry influence far beyond the firms narrowly defined as "biotech," which vary greatly in size and scope, ranging from small, mainly R&D operations to large, diversified companies with established production and distribution systems.

In 2004, the latest year for which figures are available, there were 1,444 US firms narrowly defined as engaged in biotechnology, employing close to 200,000 people. Other estimates, using a broader definition of "biotech," put employment as high as 885,000.[2] Biotech jobs pay roughly $26,600 more than the overall national average private sector wage. Biotech firms are very research-intensive, spending roughly a third of their budgets on R&D, compared to the US corporate average of around 4 percent.[3]

Currently, 40 states are targeting biotech for development. Twelve states -- California, Illinois, Indiana, Iowa, Massachusetts, Minnesota, New Jersey, North Carolina, Pennsylvania, South Carolina, Tennessee and Virginia -- have a significant number of people employed in biotech. The heaviest concentrations of biotech firms are clustered around Boston, Massachusetts, the Bay Area in California, and Research Triangle Park in North Carolina.

This report describes the market dynamics that are shaping the biotechnology industry, how firms are responding to them, what impact that is having on employment, and where the industry may be headed.

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[1] This report was prepared for the New Commission on the Skills of the American Workforce, which issued its report *Tough Choices or Tough Times* in December 2006. Information about the commission and copies of other industry studies can be found at www.skillscommission.org.

[2] Biotechnology Industry Organization (BIO) website; Battelle Technology Partnership Practice and SSTI, "Laboratories of Innovation: State Bioscience Initiatives 2004," Report Prepared for the Biotechnology Industry Organization, June 2004.

[3] "A Survey of the Use of Biotechnology in U.S. Industry," U.S. Department of Commerce, Technology Administration, Bureau of Industry and Security, October 2003.

Market Dynamics

The manipulation of biological processes has been going on for thousands of years, from the fermenting of grains and fruits to create alcoholic beverages up through the discovery of penicillin in the 1920s. The latest wave of discovery, the biotech revolution that began in the 1980s, is marked by advances in molecular biology, genomics, and computing power that have made it possible to sequence the human genome, develop more targeted medicines, grow high-yield/high-nutrition crops, and grow artificial organs and tissues for transplant surgery. These developments attracted public attention and fueled growth in the industry throughout the 1990s.

When the dot.com bubble burst in the late 1990s, the spotlight shifted to biotech as the next hot investment prospect. Many fund managers shifted their money into biotech stocks because they believed that the health care industry was recession-proof. Excitement over the mapping of the human genome bid up biotech stocks to record highs, as investors concluded that this scientific breakthrough heralded a new era in medicine. The boom peaked in 2000 with 68 initial public offerings, and record levels of venture capital.

However, a string of high-profile product failures and the securities scandal at ImClone Systems undermined the industry's credibility. Investors also began to realize that it would be years, if ever, before these companies would bring products to market. Biotech financing fell 76 percent from 2000 to 2001.[4] Stock prices for such high-fliers as Human Genome Sciences, Celera Genomics, and InforMax fell by as much as 95 percent, making it hard for them to raise money. Venture capital, a key source of funding for biotech firms, also fell dramatically after 2000, although funding has increased somewhat in the past couple of years.

Biotech firms depend heavily on capital markets to fund the long-term investments needed to bring products to market. Very few firms generate enough revenue to fund their own research. On average, it takes $802 million and over 14 years to develop and bring a new drug to market in the US.[5] Few investors are patient enough to wait that long to see if their investments will pay off. Venture capitalists in the US now tend to fund only the late stages of drug development – at the time when data are available indicating the safety and efficacy of a product, when regulatory approval of the product can be gauged, and when marketing of the product appears feasible.

The lack of funding available for research and development has led many biotech firms to seek partners willing to provide financing for the long product development cycle. Many are turning to the big pharmaceutical companies. Currently, nearly two-thirds of the funding for biotech research and development comes from the pharmaceutical industry, while over one-quarter comes from government sources, and less than 4 percent comes from universities.[6] However, the pharmaceutical companies are reluctant to get involved until late in Phase II, so biotech firms still have few sources of funding to help them cross the "valley of death" from the early work in the lab to Phase II trials of the product.

[4] Terence Chea, "Biotech Industry Digs In," *Washington Post*, June 26, 2002, p. E01.
[5] Bryan Bergeron and Paul Chan, *Biotech Industry* (Hoboken, NJ: John Wiley & Sons, Inc. 2004), p 71.
[6] National Science Foundation.

Many pharmaceutical companies see biotechnologies as a solution for their own problems. For the past decade, drug companies have been able to ride a wave of multi-million dollar blockbuster drugs such as Prozac, Lipitor, and Viagra. These blockbuster drugs drove worldwide sales growth from $22 billion in 1980 to $149 billion in 2000. Drug industry earnings rose an average of 15 percent a year throughout the 1990s.[7] But between 2002 and 2006, patents have expired on 35 drugs with aggregate sales of more than $73 billion a year, while only 14 potential blockbuster drugs are in the pipeline to be launched through 2006.[8]

At the same time, the pharmaceutical industry is coming under increasing pressure to reduce drug costs. Managed care organizations are stepping up their efforts to negotiate more favorable prices, and there is growing political pressure on drug companies to lower prices. One approach to containing the high cost of drug development has been to reduce delays in the FDA's approval process. Over the past couple years under a new administrator, the FDA has streamlined the drug approval process, cutting a year or two off the 10-15 year development process. A shorter approval process is worth several billion dollars, but there are limits to the amount of time that clinical trials can be shortened. Patients must still be followed for many months or years to determine the safety and efficacy of drugs and other regulated products.

The biotech industry offers pharmaceutical companies an alternative to blockbuster drugs, focusing instead on targeted drugs aimed at a relatively small number of patients with a specific form of a disease. So the market for a particular drug tends to be limited. However, because the drugs are targeted and often customized to a particular patient, they can produce dramatic results. In the history of the pharmaceutical industry, only about 500 disease-causing functions in cells or viruses have been found. But with the growing understanding of how DNA works, the number of potential new targets could grow into the thousands.[9]

The costs associated with a targeted approach to drug development are much lower than with blockbuster drugs. For one thing, there's no need for massive advertising campaigns, or for a standing army of sales representatives to cover the universe of doctors' offices. Trying to wring more sales out of a dwindling number of patented blockbuster drugs, the pharmaceutical industry currently spends more than $3 billion a year on ads aimed directly at consumers.

Pharmaceutical companies are starting to cash in on the potential of offering more drugs at lower cost by partnering with biotech firms. The biotech firms provide a "farm system" for the big drug companies, doing the early research and development, while the big drug companies invest in promising late-stage development and provide the capacity to market and distribute the drug once it has been approved. In 2004, biotech firms produced two-thirds of the drugs in clinical trials, but spent only 3 percent of the total $40 billion that drug companies spent on R&D,[10] because much of their late stage financing came from the big drug companies.

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[7] Brian O'Reilly, "There's Still Gold in Them Thar Pills," *Fortune*, July 9, 2001.
[8] David Stipp, "How Genentech Got It," *Fortune*, May 27, 2003.
[9] O'Reilly, "There's Still Gold in Them Thar Pills."
[10] Arlene Weintraub, John Carey, Kerry Capell, and Michael Arndt, "Biotech, Finally," *Business Week*, June 13, 2005.

The big drug companies aren't likely to abandon their reliance on blockbuster drugs any time soon, especially since they still account for half of the market growth, and there are still a number of potential blockbusters in the pipeline.[11] Biotech products still only represent about 10 percent of the pharmaceutical market. But, the growing number of partnerships with biotech firms to develop targeted drugs suggests a new business model that could become dominant in the pharmaceutical industry over time.

Agricultural Biotech. The use of biotechnologies in agriculture has grown rapidly over the past decade in the US. The rate at which traditional crops have been replaced by genetically modified versions rose from 4 percent in 1996 to 45 percent in 2004 for corn. The rate for soybeans rose from 9 percent in 1996 to 85 percent in 2004. And the rate for cotton rose from 17 percent in 1996 to 76 percent in 2004.[12]

Proponents claim that the replacement of traditional crops with genetically modified versions has enhanced nutrition, increased resistance to pests, pesticides, and herbicides, and extended product shelf life. These benefits could have a significant impact on the economy, since only 24 plants supply nearly all of our food derived from plants, while eight plants supply more than 85 percent of our diet.[13]

Numerous studies have shown widespread improvements in profits and in management capacity from adopting biotech varieties of plants. For example, a study conducted by Louisiana State University and Auburn University found that farmers growing genetically modified cotton saved 2.4 million gallons of fuel, 93 million gallons of water, and 41,000 10-hour days by avoiding the need to spray pesticides on their crops.[14] Estimates vary by crop and area, but average profits rose by $15 per acre for soybeans, by $55 per acre for corn, and by several hundred dollars per acre for cotton.[15] Another study by the National Center for Food and Agricultural Policy found that biotech crops increase grower incomes in the US by $1.9 billion and crop yields by 5.3 billion pounds, while reducing pesticide use by 46.4 million pounds.[16]

Prior to the 1980s, most of the R&D in plant biotech was publicly funded, mainly through land grant universities, in part because it took 20-30 years for those investments to pay off. However, advances in molecular biology have made it possible to compress the time needed to enhance the characteristics of a plant from a few decades to a matter of years. Lured by a quicker return on investments, private R&D now significantly exceeds public investments. Although there are hundreds of companies invested in some aspect of plant biotech, six companies lead that sector – Syngenta, Bayer, Monsanto, DuPont/Pioneer Hi-Bred, Dow, and BASF.

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[11] John Simons, "Blockbusters to the Rescue," *Fortune*, January 23, 2006.
[12] C. Ford Runge and Barry Ryan, "The Economic Status and Performance of Plant Biotechnology in 2003: Adoption, Research, and Development in the United States," a study prepared for the Council for Biotechnology Information, Washington, DC, December 11, 2003; Biotechnology Industry Association, "James Greenwood Assumes BIO Presidency as Industry Has Banner Year," News Release, January 1, 2005.
[13] Bergeron and Chan, p.92.
[14] Bergeron and Chan, p. 97.
[15] Runge and Ryan.
[16] Biotechnology Industry Organization, News Release, January 1, 2005.

Global Competition

The US established an early lead in biotechnology research and commercialization and has maintained that lead. There are more biotech companies in the US than in any other country, about 35 percent of the world's total. US biotech firms have higher revenues than those in other countries, in part because of strategic alliances with drug companies in the US. Most of the financing for biotech companies in the US comes from the big pharmaceutical firms, including European firms, which have been very profitable and have been consistently increasing their global market share.

Canada is second to the US in number of biotech companies, with 10 percent of the world's total, although Canadian biotech firms tend to be smaller in size than those in the US. Canada ranks third in the world in revenue from its biotech sector. Many multinational pharmaceutical firms have built production and research facilities in Canada to take advantage of its low costs, low risks, and close proximity to the US market. Unlike the US, stem cell research is permitted in Canada, and is a national research priority. However, Canadian firms are hampered by a shortage of scientists and skilled support personnel coming out of their university system, as well as price caps negotiated through their single-payer health system.

Europe is the biggest biotech region after North America, with 40 percent of the total number of firms in the world. However, Europe has been losing ground to the US since the early 1990s, mainly due to the lack of innovation among the European pharmaceutical firms. In the late 1980s, European firms released nearly twice as many new drugs as firms in the US. By the end of the 1990s, however, US firms had taken the lead. In 2001, biotech companies in the US generated around $25 billion in revenue, compared to around $8 billion for European firms. [17]

Lack of private sector financing remains a serious problem for European biotech firms. Unlike the US, the pharmaceutical industry finances only around 20 percent of biotech research and development in Europe. Moreover, European pharmaceutical firms have been transferring much of their research and development activity to the US. In 1990, they spent 73 percent of their research and development funds in Europe. By 1999, this figure had dropped to 59 percent. Private companies attribute this trend to the increasing regulation of the biotech industry and the difficulty in getting decisions made in a timely way by the European Commission's bureaucratic structures.[18]

The European Union has adopted the same kind of restrictions on federally funded stem cell research as the US, although it does allow financing for some new embryonic stem cell lines. But, the policies in the European countries vary widely. For example, Britain is actively encouraging stem cell research, while Germany and Italy have criminalized the extraction of stem cells from embryos.[19]

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[17] Bergeron and Chan, Chapter 7.
[18] Robert L. Paarlberg, "The Great Stem Cell Race," *Foreign Policy*, May/June 2005.
[19] Michael Woods, "U.S. Relatively Hospitable to Stem-Cell Research," *Pittsburgh Post-Gazette*, June 5, 2005.

Even in Britain's favorable environment for innovation, progress is slowed by heavy reliance on public funding sources with slow-moving budget cycles, and by bureaucratic delays. In addition, there is less experience or capacity in Europe, relative to the US, in mobilizing resources through partnerships between universities, companies, and venture capitalists.

As a result, the European biotech industry remains in a slump, while other regions are experiencing a resurgence. In 2003, while the market cap of US biotech firms gained 60 percent and Canadian firms gained 56 percent, the market cap of European firms gained only 17 percent. In Europe, 43 percent of the publicly traded biotech companies have less than two years of cash on hand, compared to 31 percent of publicly traded firms in the US.[20]

In Asia, several governments are making it a strategic national priority to grow their biotech industries. Japan, concerned about its maturing semiconductor and electronics industries, has set a goal of tripling its number of biotech firms by 2010. Singapore has a goal of doubling the value of its biomedical production to $12 billion by 2010. And China, already a world leader in agricultural biotech, is targeting the global pharmaceutical biotech market.

Japan got a slow start in biotech. Its efforts in the 1980s to commercially exploit recombinant DNA were hampered by weak intellectual property laws. That problem was not addressed until 2003. However, with its ageing population, Japan is the second largest pharmaceutical market in the world, giving it a strong incentive to develop its biotech industry. The five-year plan developed by the Ministry of Health, Labor, and Welfare sets a goal of becoming a significant supplier of pharmaceuticals worldwide, while becoming self-reliant at home.[21] Japan is also a leader in agricultural biotech research.

There is strong government support for biotech research and development in Japan. The stability of that funding has reduced the risk for other investors and attracted significant industry support and venture capital. Japan has also formed a strategic alliance with Korea, Taiwan, and Singapore to conduct research and development, spreading the risk and pooling investment capital.

Singapore has been actively courting the biotech industry for the past decade. Since 1994, it has attracted more than $1.6 billion in factory investments from Schering-Plough, Merck, Wyeth, and Pfizer.[22] Manufacturing costs are 30-40 percent lower in Singapore than in the US. But the government is also pushing hard to attract research and development, luring leading scientists from the US and Europe with high salaries, state-of-the-art laboratory equipment, few restrictions on stem cell research, ample funds for research, a highly educated workforce, and a legal environment that respects international patents. Many of the major pharmaceutical companies have established research and development centers in Singapore, such as Pfizer, GlaxoSmithKline, Merck & Co., Aventis, Roche, Novartis, Eli Lilly and Wyeth

[20] Ernst & Young, "Ernst & Young Global Biotechnology Reports Track Dramatic Industry Rebound," News Release, May 12, 2004.
[21] Japan Bioindustry Association.
[22] Jim Hopkins, "Drugmakers Shift More Production Outside USA," *USA Today*, October 19, 2004.

Pharmaceuticals. They are actively engaged in drug development and clinical trials, hoping to gain entry into the larger Asian economy.

China's biotech industry dates back to the mid-1980s, when Chinese Premier Deng Xiaoping identified genetic engineering as one of seven technologies critical to economic growth. The emphasis has been mainly on agricultural biotech to feed an expanding population and to improve the competitiveness of small farms. Most of the funding has come from the government, which has aggressively funded research and development. The most recent five-year plan (2001-2005) called for a 400 percent increase in government biotech funding over the previous plan.[23] China ranks second in the world in biotech research funding behind the US, accounting for as much as one-third of global spending on agricultural biotech.[24]

China's pharmaceutical production is also expanding, although most of it is for internal consumption. China is currently the world's largest producer of antibiotics, accounting for about one half of the world's production.

However, China faces a number of obstacles in expanding its biotech industry. The biggest obstacle is funding. Although there is growing government support for research and development, Chinese biotech firms have little access to private investment capital. The stock markets in China are designed for state-owned enterprises that have been privatized. Although China has removed some of the barriers to foreign investment, there is still a high level of risk involved. There's no clear exit strategy for venture capitalists to use to sell out their stake and get a return on their investment. One solution has been to spin off new technologies to a Hong Kong or US-based company, making it possible for the company to go public through an IPO, but this practice is not widespread.[25]

Another obstacle is the shortage of trained scientists and managers. Most Chinese researchers and scientists who study abroad choose to remain abroad to work. China is addressing this problem by giving researchers joint appointments that allow them to spend half their time in China and half their time abroad. China is also offering stock options, profit sharing, bonuses, and protected research budgets. These incentives are starting to make a difference. Many Chinese are starting to return home, expanding the talent pool for biotech firms.

A final obstacle is the weakness of intellectual property rights. Although China has been taking steps to strengthen protections since it became a member of the World Trade Organization, concern about intellectual property rights remains one of the biggest obstacles to biotech investments in China.[26] Full compliance with WTO obligations may take a decade or more.

A final country worth mentioning is India, although mainly for the absence of a viable biotech industry there. Many of the multinational pharmaceutical companies have sales offices in India,

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[23] "Biotech Outsourcing Lures Chinese Firms," *China Daily*, July 29, 2004.
[24] Randi Fabi, "Half of China Crops May be Biotech by 2014," *Reuters*, September 12, 2004; Valerie Karplus, "Global Anti-GM Sentiment Slows China's Biotech Agenda," *YaleGlobal*, September 26, 2003.
[25] Fred Greguras, "Will China Become a Global Power in Biotech?" Fenwick and West LLP, December 5, 2003.
[26] Matthew Chervenak, "An Emerging Biotech Giant?" *China Business Review*, May/June 2005.

but they generally avoid locating research and development functions there, because India's patent law only recognizes processes, not products. As a result, Indian scientists can transform drugs patented elsewhere into their generic equivalents without any legal consequences. The government funds some research, and there are pockets of expertise. The tightening of intellectual property protections in 2005 may lead to increased foreign investment.[27]

Outlook

Employment in the biotech industry has been growing at around 10 percent a year, and the Bureau of Labor Statistics expects the industry to continue to grow rapidly during the next decade, outpacing the average for overall employment by 13 percent.[28] However, it's important to remember that increases in biotech employment are starting from a relatively small base. For instance, the state of California estimates that the Bay Area saw a 40 percent increase in biotech jobs from 1993 to 2003. But that added up to just 13,640 new jobs, nowhere near the 200,000 high-tech jobs lost in Silicon Valley when the dot.com bubble burst.[29]

Even the largest biotech companies are comparatively small. Genentech, the second-largest biotech company in the world, which is located in the Bay Area, has approximately 9,500 employees. Most biotech companies have fewer than 100 employees. So, it will take a lot of new biotech companies to make up for the jobs lost in other industries such as high tech.

There are some promising signs for the biotech industry. A decade ago, 14 biotech firms in the US marketed a total of 22 products. In 2003, 66 companies marketed 187 products, including 12 blockbusters that reap over a billion dollars a year. Today, there are 230 medicines on the market developed using biotech techniques. An estimated 50 more in late-stage clinical trials are expected to win FDA approval, and another 400 products are in the pipeline going through Phase III trials.[30] Four out of five drugs currently in development are founded on biotech discoveries or employ biotech tools.[31] A particular area of focus is cancer. Over 400 cancer drugs are currently being tested in humans, almost all of which are targeted biotech medicines, which have minimal side effects, compared to the highly toxic chemotherapies common in many cancer treatments.[32]

Investment in private biotech firms, mainly by venture capitalists, hit a record of $5 billion in 2004. In addition, the new federal BioShield law provides $5.6 billion over the next 10 years to develop products critical to defending against bioterrorism. In California, voters passed an initiative to fund $3 billion in stem cell research over the next 10 years, and Connecticut

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[27] Kerry Dolan, "The Drug Research War," *Forbes*, May 28, 2004.
[28] U.S. Department of Labor, "Industry Output and Employment Projections to 2012," February 2004; Battelle Technology Partnership Practice and SSTI, "Laboratories of Innovation: State Bioscience Initiatives 2004," Report Prepared for the Biotechnology Industry Organization, June 2004.
[29] Paul Jacobs, "Biotech Companies Growing, but They're Not a Panacea," *San Jose Mercury News,* August 15, 2004.
[30] Mike Hildreth, "Resurgence Reported in U.S. Biotech Sector," Ernst & Young Video Transcript; Cynthia Webb, "Biotech: Mainstream or Pipe Dream?" *The Washington Post*, June 7, 2004.
[31] Arthur D. Levinson, "Beyond Borders: The Global Biotechnology Report 2005," Ernst & Young, June 21, 2005.
[32] Arlene Weintraub, John Carey, Kerry Capell, and Michael Arndt, "Biotech, Finally," *Business Week*, June 13, 2005.

followed suit with a similar $1 billion initiative. These public funds will spur research that is likely to spin off many new commercial applications.

A growing number of states are targeting biotech as an economic development opportunity. In 2001, 14 states had strategies to grow their biotech industries. That number has now grown to 40. These states are making significant investments in their universities and research institutions, looking for ways to promote more academic-industry interaction, and finding ways to help companies commercialize the products of their research. The states are also experimenting with ways to help fund the development of these new technologies through tax credits and equity investments, funded in some cases by state pension funds. Finally, state higher education systems are reaching out to biotech companies to better understand their needs, and responding with new curricula at colleges and universities.[33]

There is some concern that biotech jobs will be outsourced to other countries as the industry grows and matures. With the cost of doing early drug development work like toxicology studies in countries like China or Singapore as low as 10-40 percent of the US cost, there's strong incentive for companies to move this work overseas. Indeed, there's evidence that the pharmaceutical industry is conducting a growing number of clinical trials outside the US to lower costs and expedite approval. Since 2000, the number of principal investigators leading clinical trials in the US fell by 11 percent, while the number of principal investigators working on FDA-approved trials abroad increased by 8 percent. [34]

Clinical trials constitute 50-60 percent of a new drug's development costs. By conducting clinical trials overseas, drug companies can not only achieve cost savings, but also improve productivity. Currently, more than 70 percent of clinical trials miss their deadlines because they can't recruit patients quickly enough. With a broader base of physicians and patients in developing countries, drug companies can speed up recruitment by 20-30 percent. Cutting six months off the time it takes to get a drug to market could mean an extra $250 million in profits[35].

However, there are some limits to the ability of companies to do all of their drug development work offshore. First, the early research and development phase requires collaboration across disciplines and tends to flourish when linked to world-class universities. The leading university centers are currently located in the US, particularly in Boston and in the Bay Area. In fact, these centers are magnets for foreign researchers and scientists, and for foreign investment, which is flowing into the US much faster than work is being sent overseas. Most of private venture capital firms are also concentrated in the Bay Area.

A second reason, mentioned earlier, is concern about intellectual property rights. Unless there are legal protections and consistent enforcement against infringing intellectual property rights,

[33] Battelle Technology Partnership Practice and SSTI.
[34] Marc Kaufman, "Clinical Trials of Drugs Fewer, Study Says," *Washington Post*, May 4, 2005; Schmit, "US Drug Companies Conducting More Clinical Trials Overseas to Reduce Costs, Speed Approval," *USA Today*, May 18, 2005.
[35] Michael Bloch, Ajay Dhankar, and Shankar Narayanan, "Pharma Leaps Offshore," *The McKinsey Quarterly*, July 2006.

companies may continue to be wary of shipping their research operations overseas. Currently, the US has the strongest legal framework protecting biotech research.

Therefore, US biotech companies are likely to continue outsourcing clinical trials to other countries, but they are likely to keep their research and development operations close to home. That suggests that the clusters that have sprung up in certain regions of the US will continue to flourish, and new clusters are likely to appear.