The Global Biomedical Industry: Preserving U.S. Leadership

Executive Summary & Research Findings

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Executive Summary

Biomedical innovation is an intricate process that begins in the lab and spans years of effort to transform scientific discoveries into vaccines, diagnostics, devices, and therapies that improve patients' lives. Over the past few decades, the United States has created and refined a remarkably productive framework for developing new biomedical innovations and bringing them to the marketplace—in fact, it's one of the most dramatic success stories written by any American industry in the past century. Whether measured by international or domestic market share, revenue, jobs, number of regulatory approvals, patents, R&D expenditures, or publications in the biomedical field, the U.S. holds a commanding position.

Biomedical innovation is one of the most dramatic success stories written by any American industry in the past century.

Prior to 1980, European firms defined the industry, both in terms of market presence and in their ability to create and produce innovative new products. Historical advantages and an enviable concentration of resources fueled the success of firms in Germany, France, the U.K., and Switzerland. Japan had a presence in the industry as well.

But beginning in the 1980s, the United States surged to the forefront of biomedical innovation. This sudden and remarkable shift was no accident: It was the result of strong policy positions taken by the federal government. The absence of price controls, the clarity of regulatory approvals, a thoughtful intellectual property system, and the ability to attract foreign scientific talent to outstanding research universities put the U.S. on top.

The resulting ecosystem—defined by university-business collaborations, industry clusters, private equity finance, and entrepreneurship—far surpassed the prevailing model in Europe. The innovative leaps made in biopharmaceutical research, medical devices, and diagnostics gave the U.S. a major advantage that it continues to hold today.

Based on the most recent data from the Bureau of Labor Statistics, private-sector employment in the U.S. biomedical industry in 2009 was 1,219,200. Breaking this total down into its three major components, there were 283,700 jobs in the biopharmaceutical industry; 409,200 in medical devices (including diagnostics); and 526,300 in related R&D, testing, and labs. Wages and output stemming directly from the industry comprised $96 billion and $213.2 billion, respectively. The average job in the U.S. biomedical industry paid $78,600, more than 70 percent higher than the nation's average job. Once all the ripple effects of the biomedical supply chain are taken into consideration, the industry accounts for 5.3 million jobs, or 4 percent of non-farm jobs in the United States. Every job in the biomedical sector supports another 3.3 jobs elsewhere.

Size of biomedical industry: 2009

Industry	Employment	Wages, US$B	Output, US$B
Biopharmaceuticals	283,700	$29.0	$82.4
Medical devices and equipment	409,200	$26.5	$59.4
Research, testing and medical labs	526,300	$40.3	$64.5
Total Biomedical	1,219,200	$95.9	$213.2

Sources: Bureau of Labor Statistics, Moody's Analytics, Milken Institute.

But U.S. industry leadership, so carefully cultivated over the past 30 years, is eroding. Europe and Japan are working to close the gap, while China, India, and Singapore have made impressive strides. In addition to improving the quantity and quality of their scientific research, competing nations are developing mechanisms to support entrepreneurs and strengthen commercialization. They are also instituting regulatory reforms and a range of public policies to improve incentives for innovation. These efforts are part of larger economic development plans that increasingly focus on cultivating biomedical innovation for its economic contributions and high-wage jobs.

Multiple factors leave the U.S. vulnerable to falling behind: increasing complexity, rigidity, and uncertainties in the Food and Drug Administration's regulatory approval process; funding cuts at the National Institutes of Health and at the state level; a corporate tax rate and R&D tax credit that are not globally competitive; unfavorable coverage and payment policies that limit access to new medical advances; and public policies that hamper the nation's ability to develop and retain human capital.

The dominance enjoyed by the U.S. biomedical industry does not come with a long-term guarantee. The U.S. assumed the mantle of leadership by being the first to commercialize recombinant DNA research—and that achievement was made possible only because it had built an environment and infrastructure that allowed innovation to flourish. But if another nation duplicates or improves upon this formula by building a similar ecosystem and subsequently makes a pivotal scientific breakthrough in nanotechnology, personalized medicine, embryonic stem cell research, or some other cutting-edge field, it could tip the scales in the other direction. That scenario is a real possibility: While the U.S. led with 29.7 percent of nanotech-related patents granted between 1996 and 2008 (as measured by resident country of first-name inventor), China was a close second, with 24.3 percent of these patents.

Many countries are actively building the infrastructure for biomedical research and courting the private-sector operations associated with it in an effort to create high-wage, high-value-added jobs. They also realize that biomedical advances enable their citizens to live longer and more productive lives.

The U.S. could retain and bolster its leadership in biomedical innovation by taking the following actions to respond to a new era of heightened global competition:

- Increase R&D tax incentives and make them permanent
- Cut corporate tax rates to match the OECD average
- Extend support for emerging biomedical research fields
- Provide adequate resources for the FDA and the NIH to expedite regulatory reviews and clinical trials
- Leverage existing strengths in medical devices
- Build human capital for biomedical innovation
- Promote and expand the role of universities by adopting best practices in technology transfer and commercialization

The U.S. Ascent to Dominance

Pharmaceuticals and medical devices have a long history of innovation that can be traced back to 19th-century European apothecaries and the continent's early chemical industry. Merck, for example, began as a humble apothecary shop in Germany in 1668 and began producing wholesale drugs in the 1840s. German and Swiss firms were the world's first pharmaceutical manufacturers.

Europe established and refined the tradition of a research-based industry. Thanks to this strong foundation, its pharmaceutical and device companies were able to recover after World War II and continue to lead the industry for a number of years. European firms introduced innovative drugs and discoveries created through well-established research and distribution pipelines. But the lack of a unified European market, groundbreaking discoveries that fell outside the traditional reach of European firms, and significant changes to the U.S. regulatory system and its patent laws paved the way for a change in leadership.

The molecular biology revolution that began in the 1970s altered the landscape of drug discovery and development. Recombinant DNA technology allowed an upstart American company to pioneer the birth of a new industry. In 1976, Genentech, headquartered in San Francisco, was founded to take advantage of advances in large molecule drug development. Europe had actually been ahead of the U.S. in scientific advancements in this promising research area—but given the significant regulatory differences between the U.S. and Europe, the size of the U.S. market, and Europe's difficulties in commercializing research by smaller firms and universities, the United States positioned itself to seize momentum.

U.S. Public Policies and Regulatory Framework

The Bayh-Dole Act of 1980, subsequently amended in 1986, allowed universities and businesses operating under federal research contracts to have exclusive rights to the intellectual property they produced for further development and commercialization. Industry was now willing to collaborate more closely with universities since the results were easier to patent and bring to the market in a profitable manner. The biotech revolution was greatly aided by the Bayh-Dole Act, and clusters of small firms soon sprung up around universities in Boston, Greater San Francisco, San Diego, Raleigh-Durham, Greater Washington, D.C., Seattle, and elsewhere.

The Bayh-Dole Act proved to be one of the most important pieces of legislation to come out of Congress since World War II. It made possible the birth of an industry that the United States subsequently came to dominate. It allowed universities with outstanding biomedical science capabilities to partner with entrepreneurs and large firms, and to gain access to venture capital.

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Another landmark piece of legislation was the Drug Price Competition and Patent Term Restoration Act of 1984 (referred to as the Hatch-Waxman Act). Because drug discovery is a long, arduous, and costly process (now running in excess of $1 billion to bring a new therapeutic to the market), the financial risks are immense. A run of losing bets can even bring a large multinational firm to the brink of insolvency. Hatch-Waxman helped restore some of the patent terms lost during the lengthy development, clinical testing, and approval process. While the legislation was intended to balance the desire for the speedy introduction of lower-cost generic drugs with the need to

maintain adequate incentives for biopharmaceutical R&D investment, that balance no longer holds, with more than 70 percent of prescriptions being filled with generics and an effective patent life of less than 12 years for innovative medicines.

The passage of the Prescription Drug User Fee Act (PDUFA) was another critical regulatory policy change. Implemented in 1992, the act allowed the FDA to collect fees from the industry to provide resources for expediting the drug review process. Before this legislation passed, the number and complexity of new medication submissions had been escalating due to advances in scientific discovery, and the FDA found itself ill-equipped to handle their review in a timely manner, undermining firms' ability to bring treatments and cures to the marketplace. PDUFA cut the average review time for new innovative drugs from 30.2 months in 1991 to 16.9 months in 2003.

These legislative and regulatory changes provided a competitive advantage for U.S. firms—and an incentive for more European-headquartered firms to perform drug discovery in the United States. For example, Switzerland-based Novartis AG established its main research hub in Cambridge, Mass., in the early 2000s; another Swiss firm, Roche, acquired a majority stake in Genentech in 1990 and bought out full ownership in 2009. Sanofi, which is headquartered in France, announced a deal in February 2011 to acquire Cambridge-based biotechnology firm Genzyme. These moves are a positive reflection on the strengths of U.S. assets.

Another significant development in the rise of the U.S. biomedical industry occurred in the field of medical devices. In 1976, the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act became law. These amendments allowed the FDA to establish procedures and safeguards governing the introduction and usage of a broad class of products called medical devices. (Before the law, some diagnostic technologies made use of antibiotic drugs and were considered drugs for regulatory purposes, and the overall scope of the industry was limited.)

In the 1980s, the medical device industry saw rapid growth as a number of innovative U.S.-derived products were introduced into the health-care field, led by high-resolution imaging (notably radiographic and fluoroscopic units). By 2008, 12 out of the top 20 medical device companies by sales revenue were headquartered in the U.S.

The FDA's seal of approval has long been considered the world's gold standard for determining the safety and efficacy of new drugs and devices—a factor that has given the United States a major market advantage. Having a relatively streamlined, consistent, and well-defined approval process provides companies with a clear road map for commercializing their discoveries. Given the importance of this framework, recent increases in review times and a lack of transparency at the FDA raise concerns about our future competitiveness.

Innovation Measures: R&D, New Chemical Entities, and Drug Approvals

Examining the number of new chemical entities (NCEs) being produced is a good gauge of the innovative capacity of various countries. The accompanying table illustrates the dramatic changes from European to U.S. dominance over the past four decades. During the 1970s, the four largest European countries were responsible for 55 percent of NCEs produced by major nations, while the U.S. held a 31 percent share. But over the decade from 2001 to 2010, the U.S. share jumped to 57 percent, while France, Germany, Switzerland, and the U.K. saw their share of NCEs plummet to 33 percent in a complete reversal of fortunes.

During the 1970s, the four largest European countries were responsible for 55 percent of NCEs produced by major nations, while the U.S. held a 31 percent share. But over the decade from 2001 to 2010, the U.S. share jumped to 57 percent.

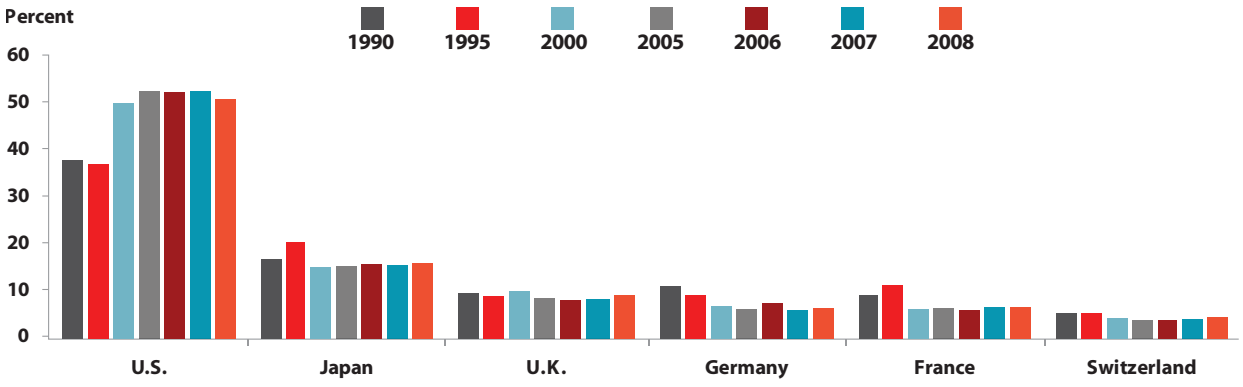
New chemical entities By headquarter country of inventing firm								
	1971-1980		1981-1990		1991-2000		2001-2010	
Country	NCEs	% total	NCEs	% total	NCEs	% total	NCEs	% total
U.S.	157	31	145	32	75	42	111	57
France	98	19	37	8	10	6	11	6
Germany	96	20	67	15	24	13	12	6
Japan	75	15	130	29	16	9	18	9
Switzerland	53	10	48	11	26	14	26	13
U.K.	29	6	29	6	29	16	16	8
Total NCEs	508		456		180		194	

Sources: Arthur Daemmrich, "Where Is the Pharmacy to the World? International Variation and Pharmaceutical Industry Location," Harvard Business School Working Paper, 2009; Milken Institute.

Because of the legal and regulatory framework discussed above and the subsequent formation of a superior ecosystem of biomedical innovation, U.S. firms were able to reinvest more of their profits back into R&D—and their European counterparts began to shift more of their R&D operations to the U.S. The research productivity of the United States tops all other nations as measured by the ratio of world-first patents filed for marketed new molecular entities relative to R&D spending by biopharmaceutical firms. Additionally, the U.S. captured 68.3 percent of total venture capital investment in the life sciences among OECD nations in 2007.

The ability of a nation to maintain high levels of R&D expenditures is another reliable measure of its innovation capacity. In 1990, as the graph below illustrates, the United States accounted for 38 percent of the total biopharmaceutical R&D spending of leading nations. However, by 2004, the U.S. share was 55 percent of biopharmaceutical R&D spending. Somewhat troubling is the decline experienced since then, as the U.S. slipped to 51 percent in 2008. Nevertheless, even in the aftermath of the Great Recession, U.S. biopharmaceutical companies invested a record $67 billion in 2010 to develop new life-changing and life-saving treatments—an increase of more than $1.5 billion from 2009.

Share of total pharmaceutical R&D spending of key countries, 1990-2008



Sources: National trade associations; U.K. Ministerial Industry Strategy Group/Association of the British Pharmaceutical Industry report (2009).

In the field of biotechnology, patenting activity provides a measure of innovation performance. The 2008 OECD Compendium of Patent Statistics shows that the U.S. accounted for 40.6 percent of world patents, while the European Union and Japan, at 25.1 and 17 percent, respectively, were second and third.

The U.S. is also a leader in R&D investment in medical devices. R&D spending among medical technology firms in the U.S. was twice the average of all industries. U.S. R&D expenditures equaled nearly 13 percent of medical device sales, compared to the EU and Japan, where they were approximately 8 percent. As a measure of their commercial success, U.S. firms receive nearly half of their revenue from abroad.

The sheer size of its consumer market is another advantage for the U.S., but its well-established infrastructure for clinical trials is even more critical to U.S. biomedical prowess. Clinical trials are not only an important step toward commercialization, but also indicative of a region's depth of biomedical R&D and innovation. As of May 2011, the U.S. was far and away the leader in hosting clinical trials, with 54,063 under way. Europe had 27,240 active trials, while Japan had 1,840. Even after normalizing for population, the U.S. held a clear advantage with 174 clinical trials per million residents (Europe had 37 and Japan 15 per million people). In fact, 50.9 percent of all clinical trials in the world as of this date were being held in the U.S. Furthermore, the U.S. accounted for almost 54 percent of the 75 leading global medicines (new active substances as measured by worldwide sales).

By virtually any credible measure of biomedical innovation outcomes, only one conclusion can be reached: The U.S. not only leads but dominates this sector. But history shows that hegemony is not the divine right of any continent or nation. When competitive advantages are taken for granted, they can be lost.

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The Changing Landscape

Other nations are actively working to close the gap with the U.S. They are focusing on increasing scientific capacity and infrastructure at their academic and research institutes as well as developing entrepreneurial support mechanisms to improve commercialization (including access to early-stage financing). They are also implementing regulatory reforms and public policies to improve incentives for innovation. The mix of strategies being deployed varies depending on whether the nation in question has a long legacy of excellence in biomedical research or whether it is a relative newcomer to the industry with rapidly improving capabilities.

Increased Research and Entrepreneurial Support Around the World

Europe

Across Europe, governments are injecting financial support in a concerted effort to regain leadership in biomedical research and development, recognizing that it produces high-paying jobs, positive economic impact, and the potential for advances in treatments for disease. The European Union introduced the Innovative Medicines Initiative (IMI), a public-private partnership founded to boost the continent's competitiveness in biopharmaceutical research. IMI, with a budget of US$2.66 billion, seeks to address bottlenecks in the drug development process and will focus on university and private institute startups.

Universities in the U.K. are among the world's elite in biomedical research. The 2010 QS World University Rankings place the University of Cambridge and the University of Oxford second and third in the life sciences, respectively, and three other U.K. institutions are in the top 20. Building on this strength, the British government has invested in Engineering and Physical Sciences Research Councils at three university research centers to mobilize a collaborative effort between researchers and industry to commercialize academic R&D, mostly in regenerative medicine and medical devices. Further, the U.K. launched the Innovation Investment Fund in 2009 to support promising technology-based businesses, especially in the life sciences and clean tech. The government hopes to attract capital from the private sector and eventually create the largest technology fund in Europe, which could be worth up to £1 billion over its 12- to 15-year life.

Germany, a pioneer in pharmaceuticals, medical devices, and biological products, has taken steps to regain its former prominence. These efforts began with implementation of the 1993 Genetic Engineering Act, which reduced some regulatory hurdles, and continued with the launch of the BioRegion competition in 1995 and finally passage of Germany's version of the Bayh-Dole Act in 1999. These moves have promoted commercialization of university biotech research and the formation of several clusters. Looking forward, Germany's High-Tech Strategy 2020 seeks to facilitate closer ties between academia and industry, thereby enhancing the biopharmaceutical sector's competitiveness.

France initiated its Fonds Stratégique d'Investissements in 2008 in an effort to support the industry as part of the government's fiscal stimulus package. The fund has allocated US$8.7 billion to invest in high-growth firms, and much of that capital will find its way into the biomedical area, potentially addressing long-standing complaints from French university startups and spinoff firms that it is difficult to secure financing. Switzerland, Italy, and other European countries have similar initiatives under way.

Asia

Multiple Asian countries are making aggressive moves to bolster biomedical research and commercialization as a means of advancing their knowledge-based economic development strategies.

Japan, for example, is building on the excellence of its universities to achieve these ends. The University of Tokyo and Kyoto University rank among the world's premier biomedical research institutions, in addition to several that are in the next tier down. Until recently, very few drugs or devices had been commercialized out of Japanese universities due to a lack of clear regulations on the ownership of intellectual property. But Japan instituted a Technology Organization Law and its own version of Bayh-Dole, and in 1998, technology licensing offices were first established. Japan has been funneling more funding into biotechnology and the life sciences in recent years, primarily at its universities and research institutes. Between 2003 and 2006, the number of biomedical startups rose by over 50 percent. Japan now has an extensive network of small- and medium-sized firms that are attractive for larger firms seeking to invest in niche areas. While there are still challenges to obtaining regulatory approval, reimbursement, and intellectual property protection, positive steps have been made to reduce barriers to biomedical innovation.

China is focusing its knowledge-based economic development efforts in the biomedical area. Chinese universities have long been highly centralized, but the government is attempting to break down bureaucratic barriers and provide greater incentives to support R&D and biotechnology commercialization. China's National Development and Reform Commission initiated 20 venture capital funds in 2009, involving seven provincial governments. Biomedical innovation is a key target for these funds.

Another Chinese strategy involves encouraging the reverse migration of human capital from the United States. Beginning in the 1970s, thousands of native Chinese sought graduate degrees in the biomedical sciences in the U.S. In 2008, there were approximately 2,500 native Chinese life sciences faculty at U.S. universities, and 10 to 20 percent of scientists at U.S. drug and biotech companies were native Chinese. China is targeting this diaspora of biomedical talent and providing opportunities that will encourage these workers to bring their skills and training home. Some have dubbed returning Chinese scientists "sea turtles."

China is addressing the diaspora of its biomedical talent and providing opportunities that will encourage these workers to bring their skills and training home. Some have dubbed returning Chinese scientists "sea turtles."

Singapore, in addition to developing indigenous biomedical talent through excellent science education, has pursued a strategy of attracting top international biomedical researchers with experience in commercialization—including U.S. talent. It has developed the physical infrastructure to house and centralize these resources at an ambitious, modern facility called the Biopolis. Additionally, Singapore is seeking to create a more business-friendly environment by fostering public-private collaborations, enhancing its R&D infrastructure, and improving IP rights.

India has been encouraging Western multinational biomedical firms to make investments by demonstrating its commitment to funding and developing 20 biopharmaceutical research parks throughout the country. IKP Knowledge Park in Hyderabad, recognized as a world-class applied research center, includes a life science incubator. Several incentives for biotech R&D have been implemented, including a fully refunded rebate on private investment, fast-track clearance for foreign direct investment, and a 25 percent rebate for privately funded research in a publicly funded institution.

The rising research productivity of China and India can be seen in the growing numbers of inventions coming out of these two nations. Pharmaceutical patents that credit at least one inventor in China or India rose four-fold between 1996 and 2006—China held 8.4 percent and India 5.5 percent of worldwide patents. Other countries in Asia and around the world are also making advances, among them Taiwan, South Korea, Malaysia, Australia, Canada, Brazil, and Chile.

Public Policy and Regulatory Reforms

In several public policy areas, such as funding for the National Institutes of Health (NIH), the U.S. has been holding steady, while other countries have been improving. In regulatory areas, such as the predictability and efficiency of FDA drug and device approvals, the complexity of pre- and post-approval requirements, and clinical trial costs, the U.S. has seen declines in performance while other countries are gaining ground.

The NIH

The NIH (comprised of 27 separate institutes and centers) funds much of the basic biomedical science in the U.S., and in recent years, substantially more translational research. Under both Democratic and Republican administrations, Congress doubled the NIH budget between 1998 and 2003. However, since 2004, NIH funding has declined in real terms (excluding the $10 billion appropriated to NIH in 2009 for short-term stimulus under the American Recovery and Reinvestment Act); it stood at $31.2 billion in nominal terms in FY2010. In the

recently approved FY2011 budget, NIH funding was cut by $260 million. Other countries are increasing government support of biomedical research, while the U.S. is not.

Emerging Technologies

The U.S. continues to play a leading role in innovative fields such as advanced DNA sequencing, new imaging modalities, computational biology, and nanotechnology. Personalized medicine, using genetic and clinical information to develop customized solutions, provides an opportunity to revolutionize the way that drugs are discovered and prescribed. However, the current system of drug discovery and approval is not designed to support this type of innovation. Notably, although the U.S. produced 30 percent of the world's nanotech-related patent publications between 1996 and 2008, countries such as China and Japan are also performing well, with 24 and 15 percent, respectively.

In stem cell science, other nations with sophisticated biomedical research infrastructure in place— including the U.K., Japan, France, Switzerland, and several others— have instituted more flexible government funding guidelines than the U.S. These nations have been attracting leading embryonic stem-cell researchers from countries with more restrictive policies. For example, American stem cell pioneer Roger Pedersen left U.C. San Francisco for Cambridge, England, in 2001, shortly after President Bush's executive order limited the scope of government funding. More recently, he has been active in stem cell efforts in Singapore.

President Obama lifted federal restrictions on developing new stem cell lines in March 2009 and instructed the NIH to review and update guidelines for funding "responsible, scientifically worthy" research. But as of this writing, legal challenges continue to cloud the issue. The U.S. is far behind where it might have been in developing stem-cell scientific and therapeutic breakthroughs, and substantially higher federal funding may be required to play catch-up.

Tax Environment

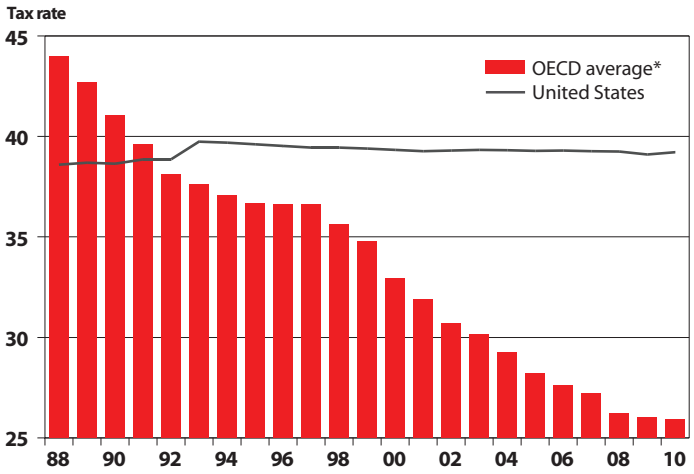
Research and development activities in the biomedical industry carry substantial risks. The sizable cost of undertaking these risks can be mitigated by effective R&D tax credits that encourage firms to invest in innovation. Many countries have introduced tax incentives to support sustained investments in R&D, and considerable evidence also shows a high association between R&D tax credits and R&D activities.

According to figures from the Organization for Economic Cooperation and Development (OECD), 12 member countries had these incentives in place in 1995, but that number was up to 20 by 2007. Although the U.S. pioneered this policy, it has not kept pace with other leading biomedical countries. It now ranks 17th out of 21 OECD members in the effective rate of the R&D tax credit. European countries have increased the size of their credits, while Asian competitors have initiated aggressive programs as well. Furthermore, while most other countries focusing on the biomedical arena have made the R&D investment tax credit permanent, the U.S. has failed to do so, creating a climate of greater investor uncertainty. This is a particular issue for R&D-intensive industries; in the case of the biopharmaceutical industry, it takes 10 to 15 years to develop a new medicine.

Variations in tax policies, particularly corporate income tax rates, between countries can influence where firms choose to locate their R&D activities, production facilities, distribution networks, and even headquarters. As of 2011, the U.S. has the second-highest corporate tax rate (a 39.2 percent federal and state average) across OECD countries. Most disconcerting for the U.S. is that many European nations and other members of the OECD have been slashing rates over the past 20 years. The OECD average corporate tax rate fell from 47.5 percent in 1981

to 25.4 percent in 2011, undermining the competitiveness of U.S.-headquartered biomedical firms. Other European countries offer more attractive corporate tax rates than the U.S.: Switzerland (21.2 percent), the U.K. (26 percent), Germany (30.2 percent), and France (34.4 percent). Even China cut its corporate income tax rate to 25 percent in 2008. In addition, other countries are implementing a range of other R&D and tax incentives to attract foreign direct investments as a part of economic growth strategies.

Statutory corporate income tax rates
OECD average vs. United States



Sources: OECD, Milken Institute.

*OECD average includes Chile from 2000 onward

FDA and Regulatory Approvals

In drug, device, and diagnostics approvals, the FDA has recently become more risk averse. Increasing complexity and rigidity has raised R&D costs and added a layer of uncertainty to the review and approval process. The FDA has been tightening safety requirements partly in response to legitimate public concerns over adverse drug reactions and their legal implications, along with pressure from Congress.

According to a study by the Tufts Center for the Study of Drug Development, unique procedures per protocol increased by 6.5 percent between 1999 and 2005. Clinical trials conducted between 2003 and 2006 were 69.6 percent longer than those held between 1999 and 2002. This translates to an extension of 460 to 780 days. The median number of procedures per clinical trial increased by 49 percent between the periods 2000-2003 and 2004-2007, with a corresponding increase in total work burden per protocol of 54 percent. Volunteer enrollment and retention decreased by 21 and 30 percent, respectively, between the same periods.

The U.S. approval process tends to be rigid, with little transparency throughout the process. In the current system, clinical trials require the use of consistent methods, including statistical tests and sample sizes. Given the length of clinical trials, it is common for researchers to discover new developments that could alter the original methods and promote better and faster results, but they have not been allowed to change parameters midway through the process. Today there is a growing call for speedier expansion of a system of "adaptive trials" that can potentially increase efficiency and effectiveness by allowing for mid-course adjustments. Adopting more flexible practices would be beneficial when there is high uncertainty involved in the earlier stages, thereby increasing the success of Phase III trials. This may be especially applicable to novel therapeutics, diagnostics, and devices that have limited prior data. While the FDA is beginning to accept a limited number of adaptive clinical trial designs, the current regulatory regime is not set up for implementation of adaptive trials on a broad basis, thus slowing innovation.

While the FDA has seen an increase in average review times, the European Medicines Agency (EMA) has been streamlining. After declining to 12.3 months in 2007, the average FDA review time for new drugs increased to 17.8 months in 2008. This number does fluctuate, and while it improved in 2009, anecdotal evidence suggests that the 2010 numbers will reflect a slow-down. Meanwhile, the EMA has reduced its drug approval time to 15.8 months. To maintain its position as the world's leading regulator, the FDA will need additional resources to meet the twin goals of making reviews more efficient while maintaining the highest standards of patient safety.

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Medical device approvals from the FDA have become even more problematic than drug approvals. In Europe, many devices are approved in half the time it takes for similar approvals by the FDA. The onerous pathway to FDA approval can inflict unnecessary regulatory burdens and discourage innovation in medical technologies. The opacity of the device approval process inhibits startup medical device firms from accessing private capital markets and adds to development costs, as companies must hire seasoned experts just to navigate the approval labyrinth.

Developing countries are not only modernizing their drug and device approval processes to meet international standards, but they're also capitalizing on their ability to offer more cost-effective clinical trials than the U.S. Clinical trial costs in China and India are approximately one-half of those in the U.S. China is increasingly willing to streamline regulatory processes for clinical trial approvals. In addition, the government is enforcing stricter intellectual property protections, pledging to eliminate the copying and counterfeiting of drugs through reverse engineering—a practice that had made international firms leery of entering the Chinese market. Both China and India are coming into better alignment with international standards to bolster their ability to attract multinational firms.

Actions and Policy Recommendations to Retain U.S. Leadership

The U.S. remains the leading center of biomedical research and production. But innovation is not constrained by borders. It will follow future scientific breakthroughs wherever they occur, as long as the originating nation has the correct policies in place to support commercial application and production. Those include the right R&D infrastructure, economic and policy incentives, and an overall environment that encourages innovation. It's entirely possible that biomedical innovation could quickly diminish in the U.S. and grow elsewhere.

But the U.S. can retain the retainable by making forward-thinking changes in policy, regulation, and government funding. These include:

Increase R&D Tax Incentives and Make Them Permanent

Research and development activities in the biomedical industry carry substantial risks of product failure and investment losses. Tax incentives can mitigate these risks and encourage innovators and investors to commit time and resources to the cause. The United States should make its R&D investment tax credit permanent and increase it by 25 percent in addition to exploring other incentive proposals and approaches that promote greater domestic R&D investment.

Cut Corporate Tax Rates to Match the OECD Average

All other things being equal, countries that impose higher corporate tax rates will lose investments to competitors with lower rates. A major revamp of the U.S. corporate tax structure would address this issue. We recommend cutting the federal corporate tax rate by 13 percentage points to 22 percent—essentially matching the OECD average.

Extend Support for Emerging Biomedical Research Fields

The U.S. can extend and enhance its global competitive position by supporting cutting-edge areas like nanotechnology, personalized medicine, and stem cell research, all of which hold immense potential. Additional laboratory and market creation initiatives are needed to spur discovery and commercialization.

Supporting R&D will give the U.S. the best chance of establishing a strong and sustainable foothold in the regenerative medicine arena. Adaptive trial design, the use of surrogate endpoints, and ensuring adequate scientific expertise at the FDA and NIH will also help ensure a platform for the applications of novel technologies. A viable and effective policy framework can facilitate the development of new frontiers that may provide the greatest financial and societal returns in the decades ahead.

Provide Adequate Resources for the FDA and the NIH to Expedite Regulatory Reviews and Clinical Trials

The FDA needs additional resources to hire staff, better manage the review process, and improve the system of review. Congress should commit to robust funding for both the NIH and the FDA. Providing resources for the broader adoption of flexible approaches such as adaptive trials can address the rigidity of existing practices and create more efficient regulatory reviews, particularly for emerging fields with limited prior research. Beyond that, the NIH must be given additional resources to support clinical trials and translational research; increased funding for translational efforts at the NIH could improve research productivity throughout the scientific community. In addition, PDUFA should be reauthorized prior to its scheduled 2012 expiration.

Leverage Existing Strength in Medical Devices

The FDA must again be given a firm mandate to create an efficient system for medical device approvals. This is necessary to ensure medical device companies are not deterred from seeking approvals in the U.S. Streamlining approvals for export licenses to developing countries such as China and India could improve U.S. export performance in medical devices even further.

Build Human Capital for Biomedical Innovation

Building a 21st-century workforce requires a renewed commitment and funding to improve science, technology, engineering, and math (STEM) education in the United States, as well as providing skills enhancement and retraining in STEM fields for incumbent workers. Making STEM education a national priority will nurture homegrown talent, encouraging American students to become the scientists and innovators of tomorrow.

Additionally, the U.S. should provide an expedited pathway to permanent residence status and then a green card to foreign researchers in exchange for their participation in biomedical R&D over a stipulated period of time. Such changes could bring about international collaborations that leverage the foreign contacts of these global talents.

Promote and Expand the Role of Universities: Adopt Best Practices in Technology Transfer and Commercialization

The U.S. has the most productive university technology transfer process in the world, but there is a high degree of variation in efficiency across universities. Convening university medical scientists and tech transfer officials together with industry experts and investors could focus U.S. efforts to adopt existing best practices more widely and enhance the interaction between universities and biomedical companies. Universities could play a more prominent role in early-stage biomedical discovery, helping the U.S. develop a new and sustainable model for R&D and enhance its competitive position.

However, there are increasing obstacles to collaborations between the private sector and academic research centers. Recognizing that such collaborations are foundational to the U.S. ecosystem of innovation, we need to explore ways to promote partnerships and remove the barriers preventing their success. This has to start with acknowledging the problem and recognizing the unintended chilling effects of conflict-of-interest and related policies.

To reiterate, the United States continues to dominate the global biomedical playing field. It still has the means to compete, but other countries are increasingly developing the kind of strength that could one day seize the lead. The seven recommendations detailed here are critical to the continued growth, sustainability, and preeminence of a vital U.S. industry.

Complete references are available in the full report, which is available for download at www.milkeninstitute.org.

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