The U.S. Biopharmaceutical Industry:

Perspectives on Future Growth and The Factors That Will Drive It

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Executive Summary

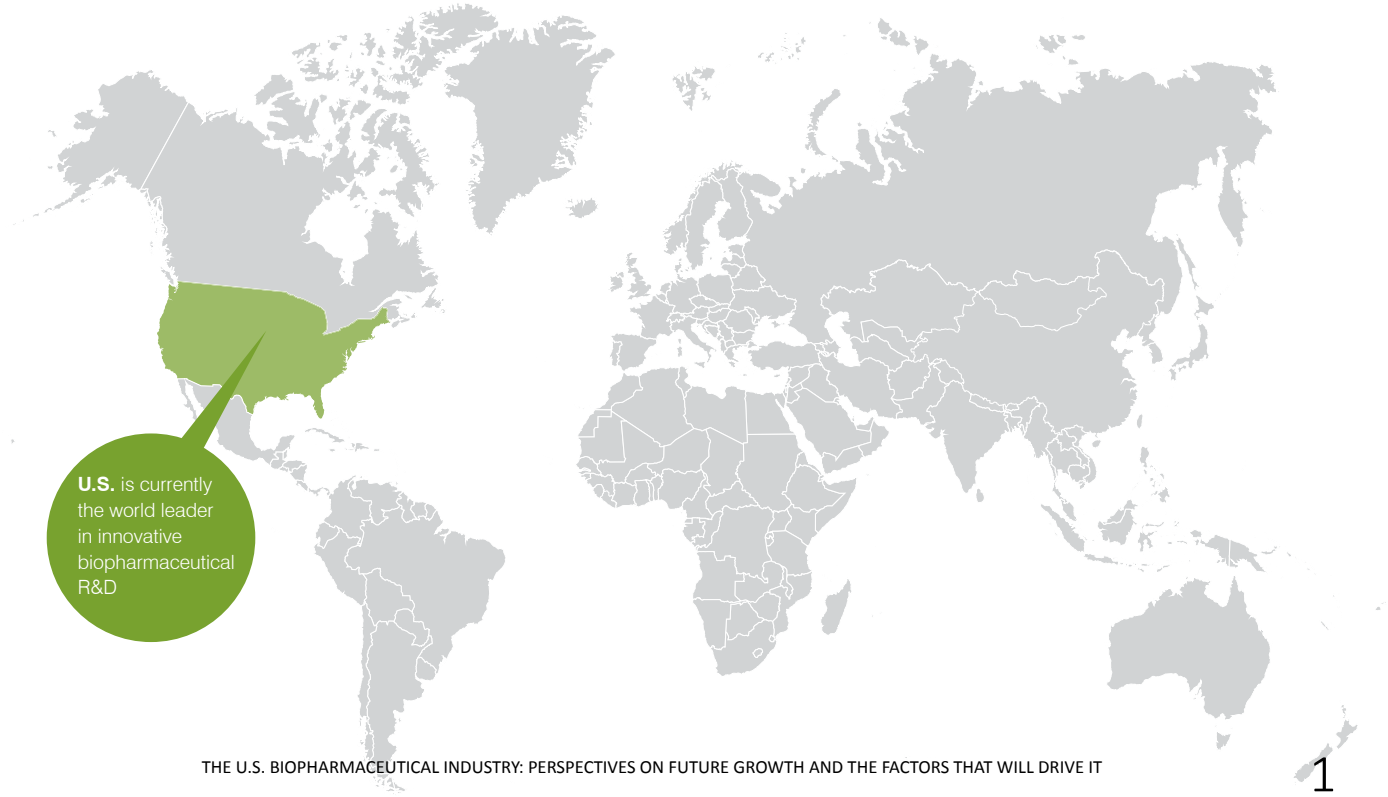
The capability to innovate is fast becoming the most important determinant of economic growth and a nation's ability to compete and prosper in the 21st century global knowledge-based economy.

The innovative biopharmaceutical industry stands out among high-value knowledge-based industries, including aerospace, automotive, and semiconductors, as a driver for future U.S. economic growth. Aging populations throughout the world and rising purchasing power for medical advances among emerging economies are expected to drive increased demand for prescription medicines in the coming years, providing opportunities to increase production and exports.

The large-scale supply chain for both research and development (R&D) and manufacturing and distribution translates into significant economic multiplier effects that further grow jobs and incomes. Moreover, this value chain continues to evolve, shaped by scientific advances that open up opportunities for new medicines to combat our most costly and challenging diseases.

However, while opportunities abound for advancing biopharmaceutical R&D and manufacturing in the U.S., future growth is not a given as other nations race to compete for the economic benefits that these innovative activities bring. Given the economic contributions of this and other R&D-intensive industries, the U.S. is now facing increasing competition not just from developed countries that want to expand their own innovative capacity in these areas, but also from emerging economies such as Brazil, China, and Singapore that are laying the groundwork for future growth.

This report focuses on some of the key measures of the U.S. innovative biopharmaceutical industry's economic contributions and explores policies critical to enabling future growth and sustainability in the years ahead. The report authors identified 10 broad policy areas central to improving the business climate for the biopharmaceutical industry, composed of a total of 38 sub-attributes. This report is unique in that it provides an assessment of the relative importance of these policy factors by combining a quantitative approach with a real-world perspective incorporating the knowledge and



Primary attributes key to advancing a more favorable business operating environment in the U.S.:

- Coverage and payment policies that value innovative medicines
- Strong, science-based regulatory system
- Robust intellectual property (IP) rights and enforcement in the U.S. and abroad
- Competitive corporate tax rate
- Access and robustness of private funding of R&D in early stage and emerging biopharmaceutical companies in the U.S.
- Robust government basic R&D funding and favorable technology transfer environment
- Strong R&D and STEM workforce
- Favorable trade policy environment for U.S. biopharmaceutical products
- Robust manufacturing workforce in the U.S.
- Competitive state-level incentives for innovation

insights of senior-level strategic planning executives from biopharmaceutical companies representing approximately 75 percent of U.S. biopharmaceutical sales.

These individuals are directly involved in making real-world decisions about where to locate biopharmaceutical R&D and manufacturing operations and have substantial expertise in identifying and evaluating the most critical factors shaping biopharmaceutical investment decisions around the world.

Key findings of the report include:

- **As the ability to innovate is increasingly becoming the most important determinant of a nation's future potential for economic growth and global competitiveness, the biopharmaceutical industry ranks among the most innovative advanced manufacturing industries in the U.S. economy.** This is reflected by a number of indicators including R&D investment, intellectual property (IP) generation, venture capital investment, and share of total R&D employment among manufacturing industries.
- **While the U.S. is currently the world leader in innovative biopharmaceutical R&D and manufacturing, industry executives expressed concern that U.S. leadership cannot be taken for granted.** Global trends suggest that U.S. leadership will be challenged as emerging economies implement more favorable policies to attract R&D investment and spur growth in their own innovative capacity in biopharmaceutical manufacturing to meet domestic demand.
- **The three policy factors identified as most critical for enabling innovation and the resulting economic contributions in biopharmaceutical R&D and manufacturing are: (1) coverage and payment policies that support and encourage medical innovation; (2) a well-functioning, science-based regulatory system; and (3) strong IP protections.** Of the 38 sub-attributes assessed, the single most important attribute identified as critical to driving future biopharmaceutical industry growth in the U.S. is a domestic IP system that provides adequate patent rights and data protection to sustain continued investment in the lengthy and costly R&D process needed to develop new medicines.
- **Insights from industry executives informed the development of two potential growth trajectories for the innovative biopharmaceutical industry in the U.S. over the next 10 years, with well over 300,000 retained and newly created jobs at stake between the two scenarios. The industry executives viewed the likelihood of achieving these alternative futures as highly dependent on policy choices made in the U.S.**
    - According to the industry executives, if negative trends in key policy areas continue, exacerbating uncertainties in the business climate, domestic R&D and manufacturing activities in the biopharmaceutical industry are expected to record only modest gains over the next decade. However, even with modest growth projections, jobs supported by the biopharmaceutical industry are expected to decline over the next 10 years due to continued productivity gains projected across all manufacturing industries. Accounting for expected productivity gains, up to 149,000 jobs may be lost across the economy over the next decade if there are little to no improvements in the key policy areas that foster biopharmaceutical innovation.

- The perspective of industry executives informed an alternative growth scenario – whereby modest improvements in key policy areas – e.g ., more favorable coverage and payment policies for medical innovation, improvements in regulatory policy to create efficiencies in the R&D process, and improvements in IP policy to incentivize R&D investment – would foster the continued growth of biopharmaceutical R&D and manufacturing capacity in the U.S. This could conservatively lead to the creation of more than 185,000 additional jobs across the U.S. economy over the next 10 years, resulting in well over 300,000 retained and newly created jobs when comparing the two scenarios.

As an industry rooted in science and propelled by advanced manufacturing, the innovative biopharmaceutical industry is uniquely positioned to help maintain U.S. leadership in new technologies and scientific breakthroughs that will continue to create high-quality, high-wage R&D and manufacturing jobs and enhance America's global competitiveness in the future. Today, the U.S. biopharmaceutical industry supports a total of 3.4 million jobs across the U.S. economy – including over 810,000 direct jobs – contributes $789 billion in economic output, and is responsible for about one in five dollars spent on domestic R&D by U.S. businesses.

However, as this report suggests, the continued growth and sustainability of this industry is not guaranteed and has the potential to shrink or shift to other countries if the business operating environment for the biopharmaceutical industry in the U.S. does not improve.

Introduction

The innovative biopharmaceutical industry stands out among high-value knowledge-based industries as a driver of U.S. economic growth.

By harnessing new scientific and technological advances and sophisticated advanced manufacturing capabilities, the industry develops novel medicines that result in substantial socioeconomic benefits from improved patient outcomes, reduced morbidity and mortality, and increased worker productivity. In addition, the industry is a generator of high-value, high-wage jobs that fuel local and regional economies around the country. The increasing market potential for new medicines to meet unmet medical needs, including the needs of aging populations throughout the world, as well as the rising purchasing power for medical advances among developing countries, provides additional opportunities to expand biopharmaceutical research and development (R&D) and advanced manufacturing capacity in the U.S.

This report sheds light on the economic value of the U.S. innovative biopharmaceutical industry and looks to the future to understand the factors that have the potential to foster future growth in the years ahead. It examines the standing of the U.S. biopharmaceutical industry compared to other U.S. advanced manufacturing industries and competing nations on a number of metrics. The report also combines a rigorous quantitative approach with the real-world knowledge and perspectives of senior-level strategic planning executives from biopharmaceutical companies representing approximately 75 percent of U.S. biopharmaceutical sales. These executives are directly involved in making real-world decisions about where to locate biopharmaceutical R&D and manufacturing operations.

An Economic Engine Powered by Innovative R&D and Manufacturing

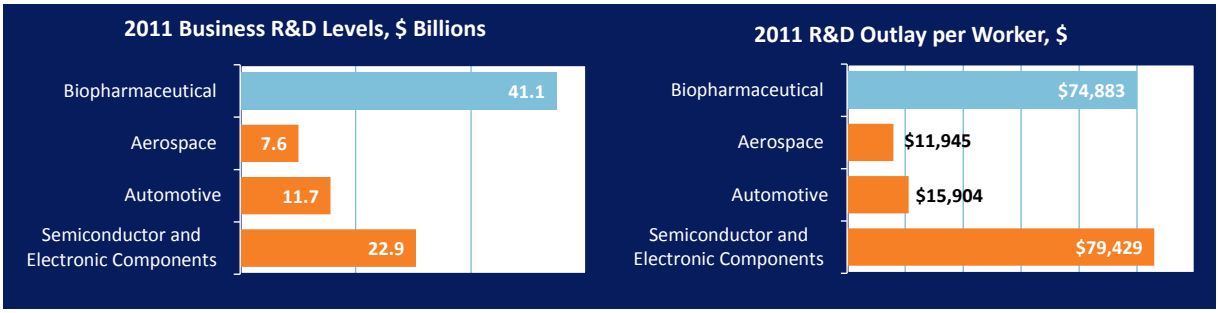
The U.S. has been the world leader in biopharmaceutical R&D and the development of new medicines over the past 30 years, a direct result of the nation's world-class life sciences ecosystem and the policies it has adopted to support innovation.

Today, the U.S. biopharmaceutical industry employs a total of 813,523 workers.[1] These workers span a wide range of occupations that offer high-wage, high-quality employment. When accounting for the total economic impacts of the industry, it is estimated (via the generally accepted methodology of input/output analysis) that it supports nearly 3.4 million total jobs and generates nearly $789 billion in U.S. economic output.

Studies of the industry have attributed its sustained competitive advantage to a number of factors including but not limited to a robust science-based regulatory system, strong public and private funding for biomedical research, a competitive free market system that provides companies with the potential to earn a return on their substantial R&D investments, and strong intellectual property (IP) rights and enforcement.

Government data shows that the biopharmaceutical industry is among the most innovative advanced manufacturing industries in the U.S. Three industries—the aerospace, automotive, and semiconductor industries—serve as particularly appropriate comparisons. Like the biopharmaceutical industry, these industries are capital-intensive, require a highly-skilled R&D workforce, look to innovation for increased productivity and continued growth, play a major role in the U.S. economy, and face growing global competition from countries that recognize the economic contributions of high-tech industries. Among these industries, the biopharmaceutical industry is a leader in innovation-related activity, as measured by R&D investment, IP generation, venture capital, and share of total R&D employment in manufacturing industries.

- **Investing in R&D:** The biopharmaceutical industry has the highest total amount of industry domestic R&D expenditures across all industries, accounting for approximately one in five dollars spent on R&D by U.S. businesses. It also has the second highest level of R&D investment per employee compared to the other capital-intensive, advanced manufacturing industries.



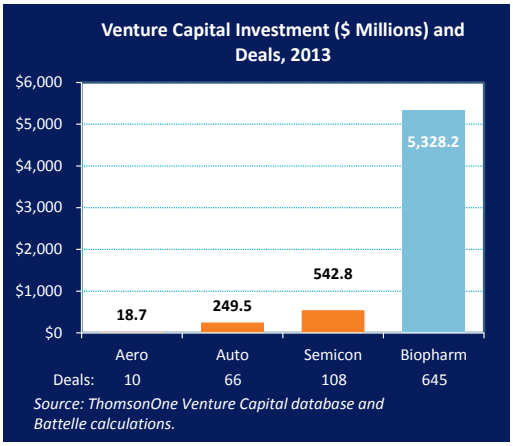
Source: National Science Foundation Business Research, Development, and Innovation Survey (BRDIS) 2011, and Calculations by Battelle.

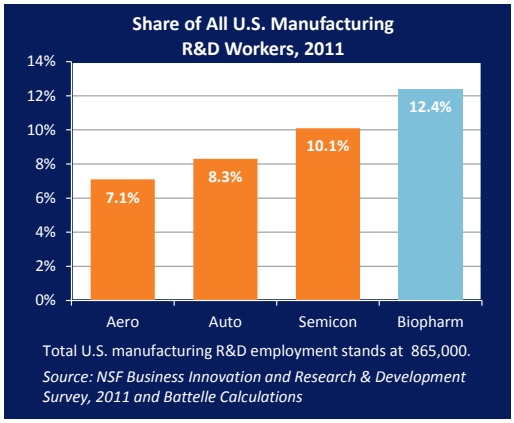
[1] The Economic Impact of the U.S. Biopharmaceutical Industry, July 2013, Battelle.

Patent Applications and Awards by Industry, 2011

	Applications	Awards
Semiconductor and Electronic Components	11,391	10,460
Biopharmaceutical	6,777	4,405
Automotive	4,368	2,679
Aerospace	2,814	1,905

Source: National Science Board, 2014 Science and Engineering Indicators, USPTO patent applications and grants, by industry: 2011.





- **Generating IP:** The biopharmaceutical industry stands 2nd to the semiconductor industry in both patent applications and patents issued, outpacing the automotive and aerospace industries. Based on R&D expenditures per issued patent, a reflection of the complexity of the technology and the level of investment needed to produce a patentable invention, the biopharmaceutical industry requires twice the level of investment per patent than the automotive industry, the next highest industry.
- **Ensuring access to financial capital, particularly for start-ups and emerging companies:** The biopharmaceutical industry leads the other industries in both venture capital deals and funding. The biopharmaceutical industry had 645 deals and raised $5.3 billion in venture financing in 2013 compared to a total of 184 deals and $811 million for the semiconductor, aerospace, and automotive industries together. Venture capital is often one of the few funding sources for start-up and emerging companies and is critical to helping companies translate medical innovations from promising ideas into new treatments.
- **Employing R&D talent:** Central to U.S. global leadership in scientific and technological innovation is a highly-skilled workforce. As the U.S. Department of Labor has noted, workers in the fields of science, technology, engineering, and mathematics (STEM) account "for more than 50 percent of the nation's sustained economic growth."[2] These workers comprise the R&D workforce needed by innovative, advanced manufacturing industries. The biopharmaceutical industry leads in its share of employment of R&D workers across all manufacturing industries, employing over 12 percent of the nation's manufacturing R&D workforce. This is the highest among the capital-intensive, advanced manufacturing industries analyzed, standing ahead of the semiconductor (10.1 percent), the aerospace (8.3 percent), and the automotive industries (7.1 percent).[3]
- **Translating scientific knowledge into new medicines.** In addition to its economic value, the biopharmaceutical industry benefits society and the economy through the development of new medicines that have enhanced the quality of healthcare, increased longevity, reduced disability, and improved quality of life for patients. Between 1999 and 2006 alone, medical advances, including new diagnostics, medicines, and devices, have helped cut the death rate from cardiovascular disease by 29 percent.[4] For HIV/AIDS patients, the introduction of

[2] U.S. Department of Labor, "The STEM Workforce Challenge: The Role of the Public Workforce System in a National Solution for a Competitive Science, Technology, Engineering, and Mathematics (STEM) Workforce," April 2007.

[3] National Science Foundation, "Worldwide, Domestic, and Foreign All and R&D employment, by Industry and Company Size: 2010," 2014.

[4] D. Lloyd-Jones, et al., "Heart Disease and Stroke Statistics 2010 Update: A Report from the American Heart Association," Circulation, published online 17 December 2009.

highly active antiretroviral treatment (HAART) in the mid-90s has meant that today patients diagnosed with HIV in their 20s can expect to live into their early 70s – a life expectancy close to that of the general population.[5] In addition to improving individual health and lengthening life spans, medical advances have contributed to substantial societal health gains, such as reducing disability and improving productivity. According to two University of Chicago economists, the estimated economic gains from declining mortality alone in the U.S. from 1970 to 2000 had a value to society of more than $3 trillion a year.[6]

As a source of unparalleled individual and societal benefits from improved health and a proven generator of high-wage, high-value jobs across the economy, the biopharmaceutical industry is uniquely positioned to be a driver of future economic growth in the U.S., even in the face of growing international competition. The industry has grown to support a broad and dynamic value chain from R&D to clinical testing to the manufacturing of new medicines and diagnostics to final distribution. This value chain will continue to evolve, shaped by scientific and technological advances that open up opportunities for new medical innovation in the future. Developing new treatments for our most costly and challenging diseases where patient needs are not fully met promises even greater benefits to families, society, and the economy, and ultimately, represents what sets this industry apart from other advanced manufacturing industries. As just one example, a breakthrough that could delay the age of onset of Alzheimer's disease by five years would mean 1.6 million fewer Americans would have Alzheimer's, and this in turn could save $50 billion a year in medical costs within five years of its availability and $111 billion over a decade.[7]

[5] H. Samji, et al., "Closing the Gap: Increases in Life Expectancy Among Treated HIV-Positive Individuals in the United States and Canada," PLosONE 2013; 8(12): e81355.

[6] Kevin M. Murphy and Robert H. Topol, "The Value of Health and Longevity," NBER Working Paper No. W11405, June 2005.

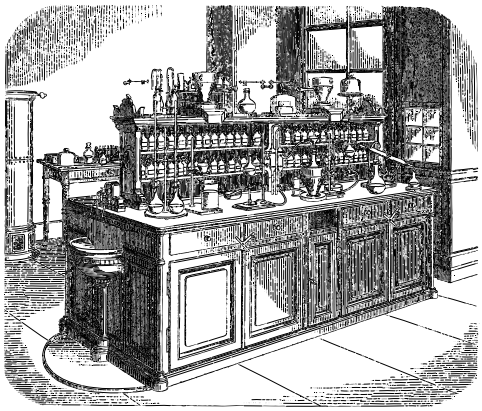
[7] Changing the Trajectory of Alzheimer's Disease: A National Imperative, Alzheimer's Association, May 2010.

Five Periods in the Development of the Biopharmaceutical Industry

FIRST PERIOD

1820 - 1880

Early pharmaceutical products: Medicines were natural products or simple chemicals that were dispensed by apothecaries who traded in plant and animal extracts and inorganic salts. In this first period, the focus of competition was primarily on improved formulation and quality.



SECOND PERIOD

1880 - 1930

Rise of vaccines and synthetic drugs: With rise of pharmaceutical chemistry and pharmacology as scientific fields, chemical companies established research laboratories and hired scientists to develop new drugs, largely by isolating new chemicals from medicinal plants or synthesizing them and testing for biological effects. This led to the first effective vaccines and synthetic drugs being developed.

Europe early leader in pharmaceuticals: Europe, particularly Germany, generated nearly all of the major innovations. Germany dominated through its chemical dyestuff industry, which possessed in-house research capabilities allowing for active collaborations with universities and public health institutes, and benefitted from progressive government policies, including effective patent laws and the establishment of medical research laboratories.

U.S. foundation for future success: During this time, many American pharmaceutical companies improved their scientific base and built strong ties with the rising universities. They made advances in medicine and the physical and life sciences, becoming leaders in physiological chemistry.

THIRD PERIOD

1930 - 1960

New focus on innovation: The 1930s, 1940s and 1950s marked a watershed for the pharmaceutical industry with a new focus on innovation, as most pharmaceutical companies became committed to in-house research capabilities for new product development. The pharmaceutical industry became, for the first time, an important contributor to the economies of the U.S. and Western Europe.

New analytical techniques and instrumentation: These advances brought new knowledge into the relationships between molecular structure and bioactivity that facilitated the use of synthetic chemistry and made possible the first effective antipsychotics, tranquilizers, antidepressants and antihistamines.

Increased federal investment in basic research: U.S. pharmaceutical companies got a boost before and during World War II years from the U.S. government's program to hasten the development of antibacterials, antimalarials and anti-inflammatories. These government efforts encouraged several companies to enter the pharmaceutical field and others to step up their research capabilities. After WWII, the market for innovative pharmaceuticals expanded rapidly in the U.S.

FOURTH PERIOD

1960 - 1980

Increasing focus on chronic conditions: Advancing knowledge of the science behind causes of disease increased the pace of pharmaceutical innovations. Now focus shifted away from primarily countering disease-carrying organisms and was aimed increasingly at correcting illnesses caused by heredity, diet, and environmental factors including treatments for hypertension, anxiety, depression, cancer, and other chronic conditions. This era marked the emergence of U.S. global leadership in pharmaceuticals.

FIFTH PERIOD

1980 - Present

Rise of biotechnology: The emergence of the field of biotechnology gave rise to the modern biopharmaceutical industry in which molecular biology, genetics and genomics now play an integral part of drug discovery and development.

Convergence of science and technology: The integration of chemistry, biology and information technology led to new methods for high throughput screening of drugs and more scientific design of chemical entities.

Rise of venture capital industry: New funding sources emerged to advance early stage biopharmaceutical innovation through venture capital and other forms of private equity.

Evolving ecosystem for biopharmaceutical innovation: Mature biopharmaceutical industry showed signs of restructuring away from vertically integrated companies to a more diversified value chain inclusive of emerging companies advancing novel therapeutics, contract research organizations supporting pre-clinical and clinical trials, and contract manufacturing organizations for both biologics and chemical drugs.

Timeline compiled by Battelle from Landau, Achilladelis and Scriabine, ***Pharmaceutical Innovation: Revolutionizing Human Health,*** Chemical Heritage Foundation, 1999 and Daemmrich and Bowden, *Rising Drug Industry*, Chemical & Engineering News, June 20, 2005, Volume 83, Number 25.

Challenges to U.S. Global Competitiveness

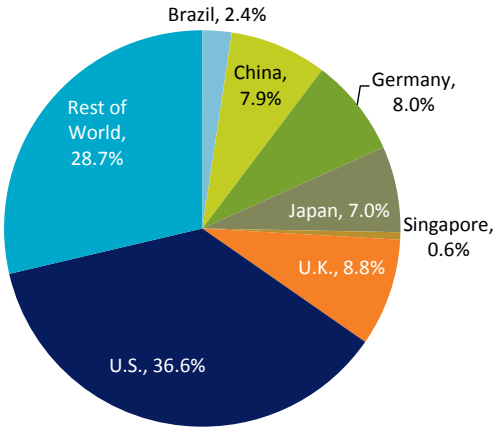
This section compares biopharmaceutical trends in the U.S. and six benchmark nations.

Three of these benchmark nations—Brazil, China, and Singapore—represent up and coming or emerging economies that are specifically targeting biopharmaceutical growth in both production and innovation. The other three benchmark nations—Germany, Japan, and the United Kingdom—comprise longstanding competitors from the developed world that continue to view an innovative biopharmaceutical industry as critical to their own economic growth and sustainability.

U.S. leadership in biopharmaceutical innovation remains firmly established as evidenced by the following:

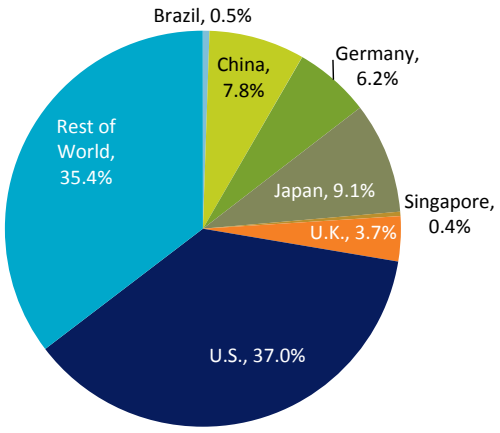
- The U.S. stands out in biopharmaceutical research, with 37 percent of the publications in peer-reviewed medical journals worldwide.
- The U.S. leads the world in biopharmaceutical IP generation, with 37 percent of biopharmaceutical patents.
- The U.S. leads the world in both overall clinical trial activity and early stage clinical research.
- Over 70 percent of worldwide venture capital investments in high-growth potential start-up biopharmaceutical companies are made in the U.S.

Biomedical Peer-Reviewed Publications by Country, 2011



Source: Thomson Reuters Web of Knowledge and Battelle calculations.

Share of Biopharmaceutical Patents Issued by WIPO, 2012

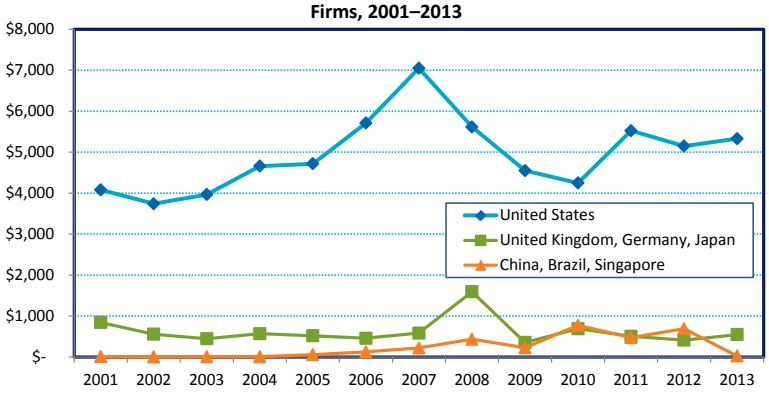


Source: World Intellectual Property Organization.

Active Clinical Trials, December 2012		
Country	**Phase I and II**	**Total**
U.S.	8,256	13,394
Germany	953	2,188
U.K.	805	1,798
China	363	1008
Brazil	202	819
Japan	290	779
Singapore	130	288

Source: Clinicaltrials.gov.

Venture Capital Investment (USD Millions) in Biopharmaceutical Firms, 2001–2013



Source: ThomsonOne Venture Capital database and Battelle calculations.

However, globalization has changed the competitive landscape for the biopharmaceutical industry. Two major external forces will impact the growth potential of this sector in the U.S.:

- The increasing capability in emerging economies in biopharmaceutical manufacturing to meet rapidly rising demand for new medicines to treat their own growing middle class populations.
- The intensified global race to attract research and development investment. Other nations have seen the success of the U.S. life sciences industry and are seeking to emulate it.

Given the substantial investments made by other countries to increase their R&D and manufacturing capacities, the continued success of the U.S. as a world leader in biopharmaceutical innovation cannot be taken for granted. Together, these two external forces are often reinforcing— as biopharmaceutical manufacturing capabilities advance in emerging economies, so does their focus on improving their innovation capacity through investments in their R&D infrastructure. As a result, the U.S. must assess its policies relative to other countries to ensure that the nation's ability to compete is not impeded.

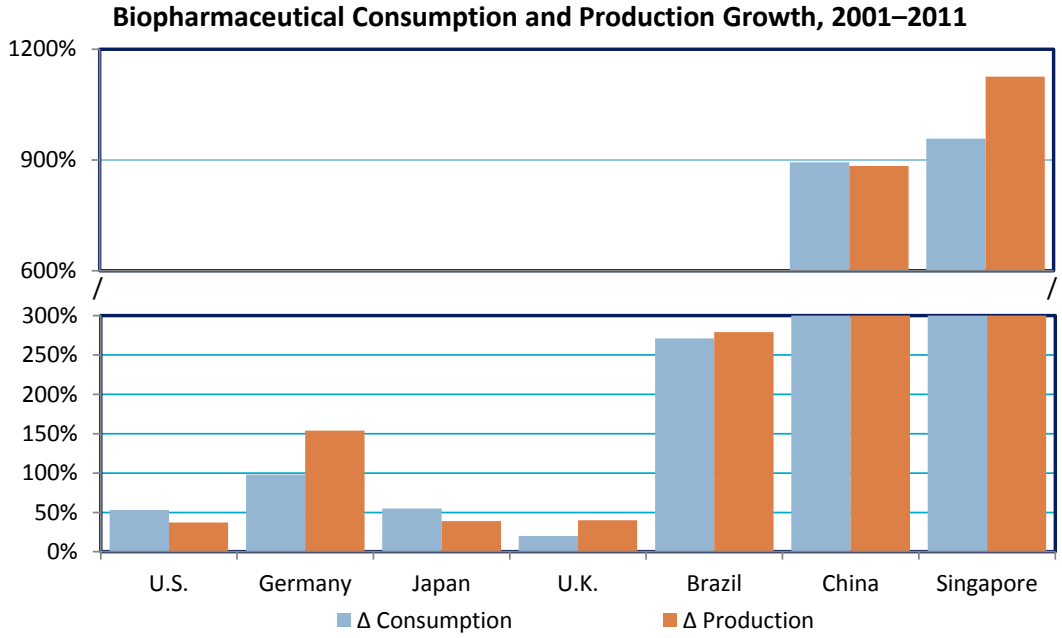
On the world stage, the global biopharmaceutical industry remains a high-growth industry. From 2001 to 2011, biopharmaceutical production worldwide rose a robust 140 percent, while overall economic activity across all industries worldwide grew by only 117 percent.[8] Still, the pattern of growth in biopharmaceutical industry production is starting to shift between developed and emerging nations. With slower population growth and well-established biopharmaceutical markets, developed nations continue to post gains, albeit at a slower rate than emerging nations. A significant component of the growth in biopharmaceutical production in emerging nations stems from their rapidly growing internal markets for biopharmaceutical medicines (dominated by generics) fueled by a rising middle class.

In terms of economic activity, trends in two measures are considered: one is biopharmaceutical consumption and the other is biopharmaceutical production. The fast growth of internal biopharmaceutical consumption of emerging nations stands out. For example, China's domestic biopharmaceutical consumption (independent of the source of production) increased by an astounding 894 percent from 2001 to 2011, while its production kept pace growing 884 percent from 2001 to 2011. Similarly, the emerging economies of Singapore and Brazil each had strong growth in both consumption and production of biopharmaceuticals over the past decade.

[8] For biopharmaceutical worldwide production, IHS Global Insight Global Pharmaceutical Industry Data and Forecasts, World and Selected Countries, 2012. For worldwide total economic activity, International Monetary Fund, World Economic Outlook Database, Gross Domestic Product data by Country in U.S. dollars, downloaded February, 2013.

By comparison, while U.S. growth in biopharmaceutical consumption was sizable at 53 percent, and the average for the other developed nations was 58 percent over the past decade, the U.S. and other developed countries are not keeping pace with worldwide growth rates. As a result of the lower growth rates of internal consumption of biopharmaceuticals (largely reflecting the difference in population size), growth in total production of biopharmaceuticals was generally much lower in the U.S. than found in emerging economies.

At the same time, these emerging nations are rapidly increasing their innovation capacity, though still remaining far behind the U.S. in absolute size. But while the U.S. is currently the leader in innovative biopharmaceutical production and R&D activity, it risks ceding ground as emerging countries grow their capability in biopharmaceutical manufacturing and R&D capabilities. The challenge for the U.S. is that an emerging country's growing capacity for biopharmaceutical production is a precursor for growing R&D capabilities in the future. As the next section suggests, the U.S. environment for innovation is showing signs of relative weakening compared with other nations and there is a need to assess how to strengthen U.S. global standing.



Source: IHS Global Insight Global Pharmaceutical Industry Data and Forecasts, World and Selected Countries, 2012.

Insights from Senior Biopharmaceutical Executives

Senior biopharmaceutical industry executives with strategic planning and commercial development responsibilities were asked to assess the favorability of the U.S. and the selected benchmark nations (Brazil, China, Singapore, Germany, Japan, and the U.K.) on a variety of measures that have been found to impact: (1) the quality of the operating environments for R&D activities and manufacturing activities in those countries, and (2) the costs of doing business in those countries.

The insights of the executives help in understanding how these external trends influence investments in R&D and manufacturing. The key aspects are listed below and are consistent with various indicators of global competitiveness and innovation, as well as with prior work conducted by the authors on strategies implemented by various countries to develop an innovative biopharmaceutical sector.[9]

Key Quality Aspects
Private funding of R&D in early-stage and emerging companies
Trade environment
Market opportunities
Government basic R&D funding and technology transfer environment
Regulatory system
Health care coverage and payment
IP protections
Scientific R&D workforce
Manufacturing workforce

Key Cost Aspects
Cost of R&D operations
Cost of manufacturing operations
Taxation rates for industry

[9] *The Biopharmaceutical Research and Development Enterprise: Growth Platform for Economies Around the World*, Prepared for PhRMA by Battelle Technology Partnership Practice, May 2012 – can be accessed at http://www.phrma.org/sites/default/files/2290/phrma_growthplatformforeconomiesaroundtheworld_20120508.pdf.

The quality-cost trade-off applies a well-established business analytics tool that measures the key attributes underlying the choices made by customers in selecting between competing suppliers, known as Customer Value Analysis. For this report, the customers are the biopharmaceutical industry who are "shopping" for ideal locations for locating R&D or manufacturing facilities, and the competing suppliers are the U.S. and other benchmark nations who are "selling" their operating environments as location candidates. A further explanation of customer value analysis is provided by William J. Feuss, then Director of Market Research and Analysis at AT&T, at http://www.williamfeuss.com/Inc-1.pdf

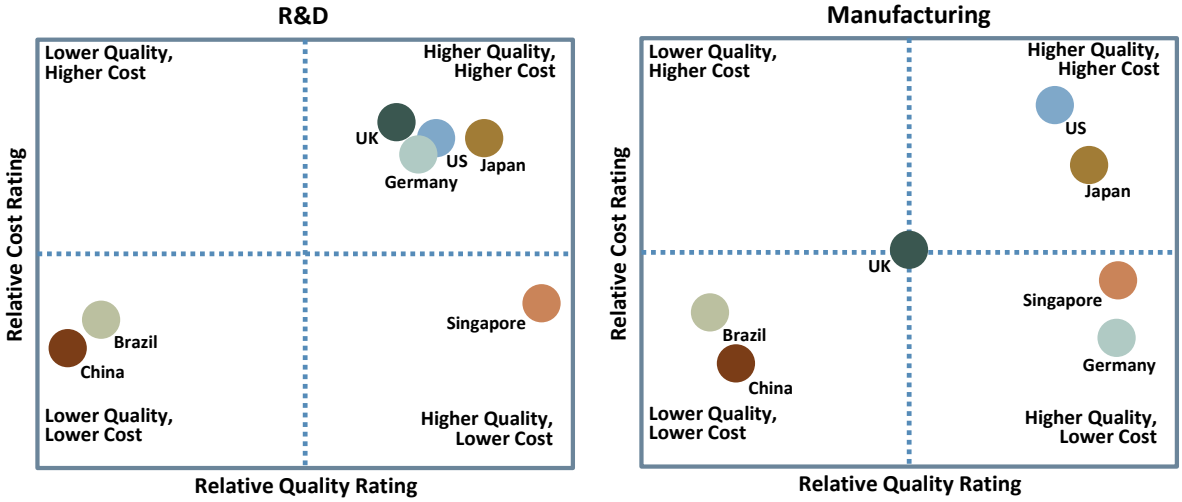
Often across products, there is relative quality-cost tradeoff such as for automobiles between family and luxury cars or for air travel between first class and coach. This report considers that relative quality-cost tradeoff in the business environment for biopharmaceutical R&D and manufacturing activities across the U.S. and benchmark nations based on the perspectives of the executives. Based on each nation's rating across quality and cost factors, an assessment was developed regarding whether a nation offers a more or less desirable environment in terms of R&D or manufacturing quality and the corresponding cost of carrying out R&D or manufacturing efforts.

This relative quality-cost tradeoff is presented in the graphic in terms of key quadrants that outline characteristic profiles of each country's standing in terms of these two attributes. Countries that are most aligned with the "fair value" tradeoff between quality and cost will appear in the bottom left and upper right hand quadrants. These two quadrants correspond to the two endpoints of the classic quality-cost tradeoff—lower quality environments that cost less to operate in versus higher quality environments that cost more. From the standpoint of biopharmaceutical R&D and manufacturing activities, this can be interpreted as the necessity of paying more in terms of investment cost for high quality R&D or manufacturing outcomes in developed countries with well-established infrastructure and technical expertise. Conversely, lower cost operations may be more attractive from the standpoint of investment but come with the added risk of potential lower quality outcomes in terms of product quality.

Countries that are not aligned with a "fair value" tradeoff relationship will appear in the upper left or lower right quadrants – these represent the worst and optimal business operating environments. High cost operations with low quality are clearly undesirable under any circumstances, while low cost operations with high quality are the most desirable and will be most attractive to biopharmaceutical companies (although this type of environment is not often sustainable in the long run as the market adjusts to this information).

As illustrated in the pair of graphics showing market perception with regard to R&D, China and Brazil are rated as low cost-low quality relative operating environments. Given their lower (and thus desirable) cost of doing business, their quality is significantly lower than developed countries as expected from a traditional tradeoff standpoint. Similarly, all of the developed nations – the U.S., Germany, Japan, and the U.K. — are rated as relatively high cost-high quality operating environments, where given their high quality they are more costly to operate in as expected from a traditional tradeoff standpoint. The one nation outperforming the fair value tradeoff of quality to cost is

Perceived Quality vs Perceived Costs – R&D and Manufacturing



Source: Senior Industry Executives response to survey, Calculations by Battelle.

Singapore, which executives viewed as offering a high-quality operating environment at a much lower cost than expected. This places Singapore in an optimal position relative to other nations that are more aligned with the traditional quality-cost tradeoff, but a number of factors including capacity to handle large volumes of operations are potential limiting constraints on its ability to capture significant portions of the market from other developed countries in the short term.

In manufacturing, biopharmaceutical executives assessed Singapore as continuing to offer a favorable environment in terms of quality versus cost, as well as Germany, which offers a lower than expected cost relative to its high quality. The U.K. is rated as having a fair value in its high manufacturing quality compared to its cost. The U.S. and Japan were considered by executives to have relatively high quality-high cost operating environments in manufacturing, while China and Brazil were again viewed as having relatively low quality, but also lower costs.

The assessments provided by the industry executives underscore the changing global environment and the extent to which U.S. competitors are actively seeking to improve their comparative advantage. These findings should serve as a wake-up call to the U.S. For the U.S. to maintain its competitiveness in biopharmaceutical development, it needs to pay close attention to bolstering capabilities in both R&D and manufacturing, while creating a business environment that allows companies in this and other R&D-intensive sectors to become more efficient and effective.

Bolstering the U.S. Biopharmaceutical Industry

While the U.S. has dominated globally over the past 30 years, many developed, and increasingly, emerging countries are making substantial infrastructure investments and seeking to implement policies aimed at securing increased biopharmaceutical R&D and manufacturing activity.

Primary attributes key to advancing a more favorable business operating environment in the U.S.:

- Coverage and payment policies that value innovative medicines
- Strong, science-based regulatory system
- Robust intellectual property (IP) rights and enforcement in the U.S. and abroad
- Competitive corporate tax rate
- Access and robustness of private funding of R&D in early stage and emerging biopharmaceutical companies in the U.S.
- Robust government basic R&D funding and favorable technology transfer environment
- Strong R&D and STEM workforce
- Favorable trade policy environment for U.S. biopharmaceutical products
- Robust manufacturing workforce in the U.S.
- Competitive state-level incentives for innovation

Historically, the U.S. has been characterized as the gold standard for its robust life sciences ecosystem, but a range of factors underpin a country's global competitiveness. As all of the countries examined are implementing policies and practices in the same key areas, the U.S. needs to assess where additional progress can be made to improve the U.S. long-term economic position.

The views of senior-level biopharmaceutical executives were sought to help examine the many issues shaping the environment for innovation and the future growth of the U.S. biopharmaceutical industry. The executives were surveyed regarding the leading factors that would be most significant in improving the business operating environment in the U.S. and result in generating higher growth for the U.S. biopharmaceutical industry. The results of the survey offer a unique insider's view of what it will take for the U.S. industry to stay competitive and maximize growth.

The executives were asked to weight the relative importance of 10 primary attributes for advancing biopharmaceutical business operations in the U.S. over the next 10 years (see text box for listing). These attributes of the business operating environment were selected based on previous studies which have suggested that they are essential for providing the level of certainty needed by biopharmaceutical companies to make R&D and manufacturing investment decisions.

Three broad attributes stand out as critical to the competitiveness of the U.S. business operating environment for biopharmaceutical innovation:

- **Coverage and payment policies that value and support the use of new medicines** – New medicines not only save and extend patients' lives by halting or slowing disease progression, they also improve quality of life, prevent unnecessary hospitalizations, reduce side effects, and provide options for patients with previously unmet needs. Often the full value of a medicine is not known upon Food and Drug Administration (FDA) approval as value evolves over time with new indications and uses, including demonstrated benefits in other disease areas, at earlier stages of disease, or in different patient populations. There is a perception among the executives that U.S. payers increasingly are not adequately valuing new treatments and are narrowly focusing on reducing prescription drug

costs or creating cost-offsets in the short-term. The uncertainty regarding whether a payer will provide coverage and adequate payment for medical innovation can make companies more risk adverse and impact R&D decisions now and in the future.

- **A well-functioning, science-based regulatory system** – While the FDA has long been viewed as the gold standard for a science-based regulatory system, the number and complexity of regulatory requirements has increased over time. Some of the executives expressed concern that U.S. efforts to create efficiencies and improve R&D effectiveness may not be moving fast enough and they are concerned that the U.S. regulatory process may soon be less favorable than that of other countries. The European Medicines Agency, for example, is seeking to expand its collaboration with industry to improve the regulatory review and approval process. The emerging nations, as their regulatory systems evolve, have the potential to compete with the leadership position historically held by the FDA, according to interviews with the executives. The executives' comments make it clear that, similar to other operating factors, the regulatory environment is becoming a competitive issue, not just with Europe and Japan, but increasingly with China and other emerging economies. It is not sufficient for the U.S. regulatory environment merely to improve—it must improve relative to the regulatory environments of other nations to remain competitive.
- **Strong IP protections in the U.S. and abroad** – While the executives surveyed viewed IP rights and enforcement as an area that the U.S. was fairly competitive in, they were particularly concerned with increased uncertainty related to patent challenges occurring earlier and more frequently and continued efforts by the Administration and some policymakers to reduce the favorability of IP rights in the U.S., such as efforts to reduce the data protection period for biologic medicines. The respondents noted that the importance of IP protection cannot be overemphasized because it is directly linked to their ability to potentially recoup the significant investments needed for biopharmaceutical R&D and to provide the revenues needed to make up for the many R&D failures and continued investments in the future. Likely in response to generally flat government agency budgets and the impact of sequestration, executives expressed concern that increased emphasis should be placed on ensuring that the U.S. Patent and Trademark Office can function effectively and efficiently.

While each of these broader attributes may have stood out for different reasons among the executives, a review of the specific sub-attributes associated with each area is valuable for identifying those which were, in their view, most critical to advancing a more favorable business operating environment in the U.S. and therefore, key to fostering the continued growth of the biopharmaceutical industry in the U.S.

From a policy perspective, these sub-attributes reflect more specific directions about issues that need to be prioritized to strengthen the U.S. biopharmaceutical industry. Altogether, respondents rated the importance of 38 sub-attributes across the 10 primary attribute areas. The sub-attributes (and their rank) viewed as most critical to the future growth and sustainability of the U.S. biopharmaceutical sector were:

- Ensuring a robust IP system that provides adequate patent rights and data protection. (1)
- Supportive U.S. government health policies and regulations to account for and encourage biopharmaceutical innovation in coverage and payment policies. (2)
- Similarly, ensuring broad patient access to new medicines in public programs, such as through payment and coverage policies that recognize the value of innovative medicines (e.g., Medicare and Medicaid). (3)
- High level of certainty in FDA review and approval process. (4)

Other leading sub-attributes focused on the following areas:

- Having a globally competitive tax system – Tax policies ranging from corporate tax rates to the favorability of R&D tax credits are an increasingly common policy tool used by countries to foster R&D investment. Executives have expressed the need to assess the adequacy of U.S. tax policies to ensure a level playing field globally.
- Availability of venture capital and other private financing – The ability of firms, particularly start-ups and emerging companies, to access venture and other sources of funding is a prerequisite for countries seeking to grow an innovation-based economy. Access to capital for early stage innovative biopharmaceutical companies is a critical advantage for the U.S.
- Building human capital – Two critical sub-attributes related to the work force were noted for their importance: (1) a robust pipeline of U.S. students pursuing masters and doctorates in STEM fields, and (2) a high-quality U.S. K-12 education system. A recent report by the authors highlights the growing STEM gap in the U.S. and notes the recent decline in U.S. STEM rankings compared to other countries.

The key policy areas and sub-attributes are largely consistent with those noted in various rankings of global competitiveness and reinforce the need to assess the adequacy of U.S. policies and infrastructure given the increasingly competitive global environment. The next section explores how modest improvements in public policies may impact the potential growth of the U.S. biopharmaceutical industry based on input from the executives.

Exploring Two Potential Economic Futures

Insights from senior-level executives were sought to gain a real-world view of what is at risk for the U.S., given concerns regarding U.S. competitiveness for future biopharmaceutical industry growth.

These executives were surveyed to gain their views and inform projections for the future growth of the biopharmaceutical industry across R&D and manufacturing activities – both at the U.S. and global levels. The input from the executives was used to develop a statistically adjusted distribution of future growth probabilities. These fitted distributions were then used to provide an estimate of the probability of two different growth scenarios for the U.S. biopharmaceutical industry over the next decade. These different potential futures for domestic growth in biopharmaceutical R&D and manufacturing activities are dependent on policy choices made in the U.S. See the appendix for full explanation of the methodology used to develop the two growth scenarios.

Under the current trajectory where negative trends increasing business uncertainty continue, U.S. R&D expenditures and manufacturing output will grow modestly over the next 10 years. The responses from the executives suggest a potential growth of 19 percent in domestic biopharmaceutical R&D activities and a slightly higher 21 percent increase in domestic biopharmaceutical manufacturing activities over the next decade. However, while biopharmaceutical production is projected to grow, fewer workers will be needed as efficiencies in productivity are achieved across all manufacturing industries. As a result, under this "status quo" scenario, there is the potential for a decrease of 4.5 percent in industry employment, translating to over 140,000 total jobs lost across the U.S. economy over the next decade. This current trajectory is the growth rate with the highest statistical likelihood of occurring based on the executives' responses, and it can be interpreted as their expectation of future growth levels given all currently available market information.[10]

This would be much lower than the industry's job growth rate of about 4.3 percent over the past 10 years and would lag behind the 4.8 percent projected growth of pharmaceutical manufacturing jobs forecast by the U.S. Bureau of Labor Statistics over the 2012 to 2022 period, suggesting a somewhat pessimistic view from industry executives as to the current trajectory of the business operating environment in the U.S.

In contrast, the alternative trajectory represents a scenario under which *reasonable improvements are made to the U.S. business operating environment.* Based on the probabilities derived from the executives' responses, such a scenario has less than a 20 percent chance of taking place within the current U.S. business environment, driving home the importance of realizing real improvements to policies related to the U.S. business climate. This alternative growth scenario would translate into a 36 percent increase in U.S. biopharmaceutical R&D activities and a 31 percent increase in U.S. biopharmaceutical manufacturing output over the next decade (see the figure comparing the alternative growth scenario to the current trajectory). As expected, the estimated increase in R&D is substantially higher than the current trajectory for U.S. R&D growth, reflecting the

[10] Statistically, this corresponds to the 50th percentile in the probability distribution.

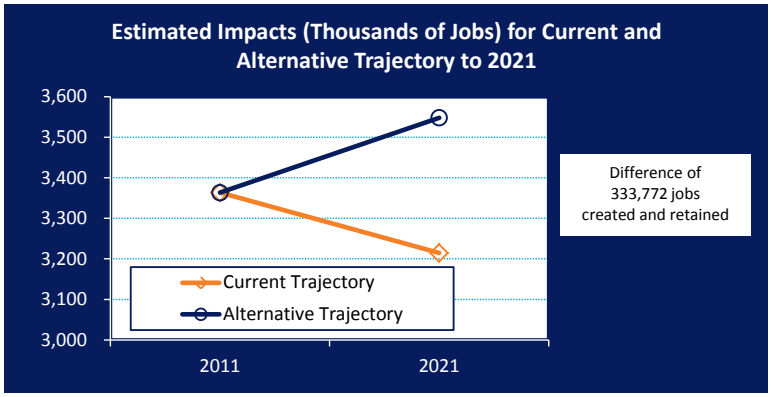
executives' view that through innovation the U.S. still has the potential to grow and expand the biopharmaceutical industry and to compete effectively against both developed and emerging economies through the continued introduction of new treatments.

The significance of realizing this alternative level of growth is substantial. Under this alternative growth scenario, industry jobs would increase by 5.4 percent, translating to a gain of 180,000 total jobs across the economy over the next decade.

This analysis demonstrates that by making selected improvements in the policy areas most directly linked to the ability to innovate, future growth rates would exceed growth rates of the past decade and make up for projected job losses due to increased productivity across all manufacturing industries, such that over 300,000 jobs could be retained and created in the U.S. economy over the next decade.

Current Trajectory vs Alternative Growth Rate of U.S. Biopharmaceutical R&D

	Growth (%) over 10 Years	
	Current	**Alternative**
R&D	19.1%	35.5%
Manufacturing	21.2%	30.8%



Looking to the Future

The innovative biopharmaceutical industry continues to be an important contributor to U.S. economic growth and sustainability, but faces significant challenges in the years ahead.

Compared to other capital-intensive, advanced manufacturing industries in the U.S., the biopharmaceutical industry is a leader in R&D investment, IP generation, venture capital investment, and R&D employment. Policies and infrastructure that helped foster these innovative activities have allowed the U.S. to seize global leadership in biopharmaceutical R&D over the past 30 years.

However, as this report details, other countries are seeking to compete with the U.S. by borrowing and building upon some of these pro-innovation policies to improve their own operating environment and become more favorable to biopharmaceutical companies making decisions about where to locate their R&D and manufacturing activities.

A unique contribution of this report was the inclusion of the perspective of senior-level strategic planning executives of biopharmaceutical companies regarding what policy areas they see as most likely to impact the favorability of the U.S. business operating environment. The executives cited the following factors as having the most impact on the favorability of the operating environment and hence, potential growth of the innovative biopharmaceutical industry in the U.S.:

- Coverage and payment policies that support and encourage medical innovation
- A well-functioning, science-based regulatory system
- Strong IP protection and enforcement in the U.S. and abroad

The top sub-attribute identified as driving future biopharmaceutical industry growth in the U.S. cited by executives was a domestic IP system that provides adequate patent rights and data protection. Collectively, these factors underscore the need to reduce uncertainties and ensure adequate incentives for the lengthy, costly, and risky R&D investments necessary to develop new treatments needed by patients and society to address our most costly and challenging diseases.

With more than 300,000 jobs at stake between the two scenarios, the continued growth and leadership of the U.S. innovative biopharmaceutical industry cannot be taken for granted.

Continued innovation is fundamental to U.S. economic well-being and the nation's ability to compete effectively in a globalized economy and to take advantage of the expected growth in demand for new medicines around the world. Just as other countries have drawn lessons from the growth of the U.S. biopharmaceutical sector, the U.S. needs to assess how it can improve the environment for innovation and continue to boost job creation by increasing R&D investment, fostering a robust talent pool, enhancing economic growth and sustainability, and continuing to bring new medicines to patients.

Appendix: Note on Methodology

This report assesses the growth potential of the U.S. biopharmaceutical industry by incorporating the knowledge and "on-the-ground perspectives" of senior level strategic planning executives from innovative biopharmaceutical companies.

The in-depth survey developed by Battelle addressed four key areas to complete the analysis found in this report: (1) industry perspectives on the weighting of attributes and subattributes of the U.S. operating environment for biopharmaceutical companies; (2) industry weighting of the trade-off of quality vs cost for locating research and development activities and manufacturing activities; (3) industry weighting of the current performance of benchmark nations against the attributes of a biopharmaceutical operating environment; and (4) industry expectations of growth in R&D and manufacturing activities for the U.S. under alternative scenarios.

With assistance from PhRMA, senior level executive responsible for strategic planning were identified and then directly contacted by Battelle. The survey responses were directly sent to Battelle and treated as confidential. Once the survey responses were received Battelle then reached out to learn more about the perspectives of these senior industry executives relating to their responses. Altogether, the companies responding represent approximately 75 percent of U.S. biopharmaceutical sales.

The industry executives are directly involved in making real world decisions about what to expect in terms of demand as well as assessing key business environment factors driving biopharmaceutical manufacturing and R&D operations. As part of the in-depth surveys and follow-up interviews, these industry executives provided their projections for the future growth of the biopharmaceutical industry across R&D and manufacturing activities in the U.S. Each of the industry executives was asked to quantify the expected growth in economic activity (equivalent to gross domestic product) over the next ten years under three scenarios:

- Worst case
- Most likely under currently available operating conditions and market information
- Best case if improvements were made to current U.S. business environment conditions

Battelle developed a statistically adjusted or normalized distribution of future growth probabilities based on the distribution of these future growth rates and how much, on average, the individual scores varied from the current trajectory. These fitted distributions were then used to give an estimate of the probability of observing different growth rate scenarios in the biopharmaceutical industry over the next ten years.

To convert these estimates of economic activity into jobs generated, Battelle further refined the data to consider and account for likely growth in biopharmaceutical productivity. Over the past ten years, productivity gains in the biopharmaceutical industry have been strong. To estimate future productivity changes, Battelle used the U.S. Bureau of Labor Statistics 2010–2020 industry employment and output projections to develop a long-range forecast of changing output per

worker (using the compound annual growth rate from 2010–2020 to extend it to 2021 for analytical purposes). This estimated output per worker measure for the pharmaceutical manufacturing sector is projected to increase from $1.0 million in 2011 to nearly $1.3 million in 2021 (in constant 2011 dollars).

For the purposes of this report, two specific data points in the statistically adjusted distribution of future growth probabilities were considered to inform likely growth over the next ten years.

One estimate is the current trajectory of U.S. growth in biopharmaceutical R&D and manufacturing. This "current trajectory" is the growth rate with the highest statistical likelihood of occurring based on the industry executives' responses. It can be interpreted as the industry's expectation of future growth levels given all currently available operating conditions and market information.

An alternative scenario was also identified to assess a feasibly achievable higher growth scenario. Using the normalized distribution of future growth probabilities, the attainable growth rate given positive improvements to the expected business environment was estimated to be one standard deviation above the mean or current trajectory. Standard deviation is one measure of the variability of the scenario projections from the industry executives that can be used to baseline the probability of observing actual growth rates that differ from the estimated industry expectations. From the perspective of senior executives, there is only a 16% probability that the actual growth rate will meet or exceed this higher one standard deviation level trajectory, which drives home the importance of realizing real improvements to policies related to the U.S. business environment for the biopharmaceutical industry.

To estimate changes in the level of output and jobs ten years out for the biopharmaceutical industry, Battelle used its 2011 measurement of the size of the biopharmaceutical industry incorporating pharmaceutical manufacturing, drug merchant wholesale, biopharmaceutical-related scientific R&D services, and management of companies/enterprises (including stand-alone biopharmaceutical corporate headquarters operations) as reported in The Economic Impact of the U.S. Biopharmaceutical Industry: 2011 (see http://www.phrma.org/sites/default/files/pdf/The-Economic-Impact-of-the-US-Biopharmaceutical-Industry.pdf).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