Spring 2013
Industry Study

Final Report
Biotechnology Industry

The Dwight D. Eisenhower School for National Security and Resource Strategy
National Defense University
Fort McNair, Washington D.C. 20319-5062

BIOTECHNOLOGY INDUSTRY 2013

ABSTRACT: Biotechnology inspired innovations offer great promise for addressing a number of pressing 21st century economic and global security issues that the U.S. will face in the near future. As an industry that relies on complex science, involving the manipulation of living organisms, to develop a set of enabling technologies it is not without its challenges. Accordingly, the pursuit of marketable biotechnology products is often risky and capital intensive. In addition to the unpredictable nature of the biology, economic, social, political, and regulatory environments play an important role in influencing the industry. The dynamic relationship between the U.S. government, academia, and the private sector – also known as the triple helix – help shape these environments. This robust relationship and a uniquely innovative environment have made the U.S. the global leader in biotechnology. As such, the industry overall is healthy, but emerging trends in the economic, social, political, and regulatory environments introduce a level of volatility. If not mitigated these could affect the industry's ability to compete in the global marketplace, and in the long-term, impact its ability to commercialize products offering potential solutions to pressing national security issues, and limit the industry's ability to act as an engine for economic growth. While the industry is healthy overall, strengthening the relationship between the members of the triple helix and focusing the use of policy tools are essential to ensuring the future vitality, vibrancy, and competitiveness of the industry.

COL Chris Beveridge, US Army
COL Tony Coston, US Army
Mr. Christopher Echols, Department of the Air Force
Lt Col John Giles, US Air Force
COL Ross Guieb, US Army
Mr. John Hoeft, Department of the Air Force
Mr. Tim Huddleston, Department of Homeland Security
CDR Mike Jefferson, US Navy
Mrs. Nicola Johnson, Office of the Secretary of Defense
Lt Col Frank Latt, U.S. Marine Corps
COL Peter Lehning, US Army
Lt Col Alesia Quiton, US Air Force
Lt Col Karen Rader, US Air Force
Mrs. Doria Schauer, Defense Information Systems Agency
Mr. Nick Sifer, Department of the Navy
Mr. Tom Waters, Department of the Army

Dr. Faye Davis, Faculty
Mr. Bradley Calhoun, Faculty
CAPT Gerard Hall, US Navy, Faculty
Mr. Mike Lawrence, Faculty

PLACES VISITED

Domestic:
Sandia National Laboratories (Livermore, CA)
Boehringer-Ingelheim (Fremont, CA)
Bay-Bio (South San Francisco, CA)
Solazyme (South San Francisco, CA)
SRI International (Menlo Park, CA)
University of California, San Francisco QB3 Garage (South San Francisco, CA)
Arcadia BioSciences (Davis, CA)
Bio-Rad (Hercules, CA)
PaxVax (San Diego, CA)
BIOCOM (San Diego, CA)
NuVasive (San Diego, CA)
Takeda (San Diego, CA)
BioAlta (San Diego, CA)
Huya Pharma (San Diego, CA**)**
Biotechnology Industry Organization (Washington, DC)
Eli Lilly (Washington, DC)
Massachusetts Biotechnology Council (Cambridge, MA)
Broad Institute of MIT & Harvard (Cambridge, MA)
Harvard Stem Cell Research Institute Boston Children's Hospital, (Boston, MA)
Charles River Laboratories (Wilmington, MA)
Draper Laboratory, (Cambridge, MA)
Amgen, (Cambridge, MA)
U.S. Food and Drug Administration (Silver Spring, MD)
National Institutes of Health (Bethesda, MD)
Center for Biosecurity of University of Pittsburgh Medical Center (Baltimore, MD)
U.S. Army Medical Research Institute for Infectious Diseases (Frederick, MD)
Walter Reed Army Institute for Research (Bethesda, MD)

INTRODUCTION

When Francis Crick and James Watson introduced the double helix model of DNA in 1953, they ushered in a new era of scientific discovery. New techniques for "using the properties of living things to make products or provide services" shaped the evolving science of biotechnology.[1] Since that time, the numerous applications of biotechnology have inspired innovations which hold great promise for improving public health, protecting against harmful biological agents, addressing environmental issues, mitigating challenges in the developing world, and driving long term economic growth. Biotechnology innovations also hold great potential for "spillover" into other segments of the U.S. economy, resulting in increased economic productivity overall. However, the strong ties between a healthy biotechnology industry and U.S. national security go beyond the obvious benefits of a thriving economy. Biotechnology may provide solutions for many of the global challenges and trends which could drive conflict in the future.

Biotechnology is a producer industry defined by its reliance on complex science related to the manipulation of living organisms which results in a variety of enabling technologies.[2] A pioneering spirit; outstanding higher education; protection of intellectual property; failure tolerance through bankruptcy laws; a robust investment culture; and, a favorable regulatory environment foster a culture of innovation and risk-taking that have allowed the U.S. to maintain its position as the global leader in this field. Additionally, the robust and dynamic relationship between members of a triple helix of government, academia, and private industry has further served to advance the U.S. biotechnology industry.[3]

The industry, which is still in its growth phase, is already a net exporter with positive revenue and has the opportunity to expand its reach into a number of untapped markets in emerging countries. The White House has embraced the importance of biotechnology's applications and its potential to act as an engine for economic growth by producing the *National Bioeconomy Blueprint*, which seeks to establish conditions for a 21st century bioeconomy.[4] Despite its obvious potential, the numerous challenges facing the biotechnology industry necessitate effective coordination between the triple helix stakeholders to realize the vision of a vibrant bioeconomy.

Chief among the many challenges facing the biotechnology industry is access to capital in a struggling economy. The current fiscal environment portends reduced government funding for basic research and science. Further, the high risk of failure and long-lead times associated with the commercialization of a product have resulted in the flight of venture capital. These two sources of funding are the lifeblood for start-up biotechnology firms. The industry now faces the challenge of developing innovative business models and processes to overcome the present economic environment. Moreover, the political, social, and global landscapes introduce additional complexities and have the potential to hinder the industry's growth if not properly mitigated.

Despite these realities there are still immeasurable opportunities for biotechnology to provide solutions to a plethora of unmet needs and be an engine of economic growth. This report will examine the health of the biotechnology industry and provide insight into the competitive landscape, challenges, and opportunities using Michael Porter's "Five Forces" and the Strategic Game Board as analytical tools. Based on this analysis, the paper will offer policy recommendations aimed at ensuring the biotechnology industry remains healthy given its

importance to U.S. economic and national security; it is also imperative that the U.S. maintains its position as the global leader in biotechnology.

KEY ASSUMPTIONS

Several key assumptions inform the analysis and are instrumental in assessing unmet needs that will drive demand for biotechnology products and services. First, the major strategic demographic trends of aging populations in developed countries and population growth in poor and underdeveloped countries will fuel demand for health and medical services as well as technology to increase food production. Second, the growing middle classes in developing nations such as China and India will spur demand for protein rich food sources and place increased strain on water and other natural resources. Third, the combination of growing populations, increased production to meet their needs, and climate change will create demand for technologies to prevent and mitigate environmental impacts. Finally, the effects of globalization will cause these strategic trends to have increasing implications for U.S national security interests.

INDUSTRY AT A GLANCE

The biotechnology industry is comprised of a set of enabling technologies which address national and international security concerns in health, agriculture, industrial processes, and defense.[5] Yet, the complexity of the science, the unpredictable nature of the biology, and the regulatory and legal frameworks that provide oversight for the commercialization of biotechnology products prolong the industry's cycle of innovation and reduce its capacity to increase its time to market.

Despite these challenges, biotechnology has proven to be a source of great economic opportunity. In 2012 the biotechnology industry revenue was estimated at approximately $87.06 billion with profits of $4.7 billion from approximately 1,843 firms.[6] U.S. biotechnology products accounted for $6.3 billion in U.S. exports.[7] According to one industry study, the U.S. is the largest market and leading consumer of biotechnology products in the world. It boasts more than 1,300 firms involved in the biotech industry and from 2001 to 2010, the industry grew by 6.4 percent, adding more than 96,000 jobs. In contrast, the total employment for all private sector industries in the U.S. fell by 2.9 percent, losing more than 3 million jobs.[8] Moreover, there are more than 5.5 million scientists, engineers and technicians in the U.S.; 1.3 million people directly involved in biosciences; and another 5.8 million workers in related industry sectors.[9]

The industry's structure, conduct, and performance viewed through the lens of analytical tools of Porter's Five Forces and the Strategic Game Board theory, provide greater insight into this dynamic industry.

Structure

There are hundreds of small biotechnology companies, academic institutions, and a few mega-firms competing in this industry.[10] As a result, the market share concentration in the industry is low, with the top four firms accounting for only about 36.1% of revenue.[11] Industry analysts attribute this low market share concentration to the specialization of biotechnology products; the industry's position in the growth cycle, which allows for new firms to emerge in response to unmet needs; the high rate of technological change; the requirement for innovation which does not

translate well to big firms; and, the constant evolution of the biotechnology market, including a trend towards personalized medicine.[12] Based on these characteristics industry analysts assess competition in biotechnology to be medium, but intensifying.[13]

The structure of the biotechnology industry is also defined by the triple helix, or the dynamic relationship between the U.S. government, academia, and the private sector.[14] As part of the triple helix the government acts as a customer of biotechnology products and services, establishes policy and legal frameworks, invests in research and innovation, and provides regulatory oversight for the industry. The government faces many competing interests in its complex role as it must balance bio-economic innovation; support to the safety and efficacy of products; competition for scarce resources; an increasingly competitive global landscape; as well as other global market influences. The government's capacity to address these competing interests is managed through legislation, regulation, funding, and policy guidance as outlined below.

Legislation: Congressional legislation has played an important role in advancing the biotechnology industry through the enactment of laws aimed at protecting intellectual property, ensuring the availability of funding for research and development, and incentivizing innovation. U.S. patent laws have created a favorable environment for innovation by offering protection of intellectual property rights, which enables companies to attract investment and to better endure lengthy development timelines.[15] The 1980 Bayh-Dole Act further enabled researchers by allowing them to maintain rights on technologies discovered with federal funding.[16] More recently, the Affordable Care Act (ACA) increased data exclusivity for biologic drugs from 5 to 12 years, barring generic companies from producing biosimilars for that period of time.[17] The ACA also provides tax breaks to smaller firms and attempts to simplify elements of the regulatory process.[18] Lastly, bankruptcy laws in the U.S. provide failing companies an opportunity to exit the market more easily.

Regulation: The regulatory agencies in the U.S. ensure the safety and efficacy of products in an effort to protect public health. However, their role is also important in creating business value for the industry, by ensuring the public's trust and confidence. There are three agencies which regulate different sectors of the biotechnology industry: the Food and Drug Administration (FDA) provides oversight of food and biopharmaceuticals; the Environmental Protection Agency (EPA) maintains authority over the industrial and environmental biotechnology products; and, the U.S. Department of Agriculture (USDA) oversees bio-agriculture.[19]

Funding: Basic research funding institutionalizes a growing knowledge base that enables discovery and commercialization of products to address unmet needs. There are several government agencies authorized to fund varying elements of basic scientific research. The Department of Health and Human Services (HHS) and some of its supporting agencies such as the National Institutes of Health (NIH) and the Biomedical Advanced Research and Development Authority (BARDA) are important sources of funding for biomedical research. More than 80% of NIH funding is provided in the form of competitive grants for medical research.[20] BARDA and the Department of Defense (DoD) provide funding to support the development of medical countermeasures for biodefense. Additionally, DoD, the National Science Foundation, and other agencies invest in a variety of other technologies across the biotechnology sphere. This

government funding is essential to fill the void where private and philanthropic funding falls short or is non-existent.

Policy Guidance: The Obama administration's *National Bioeconomy Blueprint* outlines strategic objectives aimed at strengthening the U.S. bioeconomy and is a strong recognition of the potential biotechnology offers. The guidance calls for continuing investment in research and development; facilitating a more expedient bench to market process; reforming and clarifying regulatory pathways; improving education with a focus on science, technology, and mathematics (STEM); and capitalizing on public-private partnerships and collaboration.[21]

Conduct and Performance

Most biotechnology firms, at least initially, compete on differentiation due to the protections offered by strong intellectual property laws.[22] Additionally, product performance can provide a foundation for competing on differentiation if the product demonstrates clear advantages over existing products.[23] Ultimately however, with expiring patents and increasing competition, many biotechnology firms are forced to compete on price.

Though competition is said to be intensifying, barriers to entry in this industry also appear to be increasing. Capital requirements and risk are incredibly high, and strong intellectual property assets provide the foundation for industry success. As a result, firms are increasingly entering the biotechnology industry by acquiring established biotechnology companies, thereby reducing risk and time to market.[24]

Despite many of the challenges, the industry is expected to increase at an average annual rate of 8.7%. However, this assumes a favorable fiscal, political, and regulatory environment. It is noteworthy that the industry proved to be susceptible to the recession of 2008, which resulted in decreased venture capital investment, reduced government funding, and poor economic conditions overall.[25] The economic downturn caused many firms to cut back on research and development funding – the real life-blood of innovation – and revenues declined. Continued economic uncertainty, the coming wave of expiring patents, otherwise known as the "patent cliff," and high costs and risk, continue to drive mergers and acquisitions of many small biotechnology firms.[26] These factors greatly impacted the industry's operating costs relative to revenue, and only in 2009 did the industry record a profit.[27]

Bioclusters. The biotechnology industry has attempted to mitigate many of the challenges associated with its work by forming bioclusters, from which an ecosystem for a successful bioeconomy emerges and where all the elements within the ecosystem are geographically co-located. Advocacy organizations such as the Biotechnology Industry Organization (BIO) attribute much of the U.S. biotechnology industry's success to the advent of bioclusters. The co-location of academic institutions, venture capitalists, both start-up and large firms, and R&D incubator facilities have driven the industry to effectively organize around Boston, San Francisco, and San Diego, although many other states within the U.S. and foreign competitors are attempting to replicate the model. These bioclusters are also known for a talented human capital pool and great financial resources, but as the subsequent analysis will suggest the availability of human capital and financial resources are threatened by industries such as information technology, where cost

and risk are significantly less and there is a much shorter lead-time to commercialization and resulting return on investment.

INDUSTRY SECTORS

The major products and services of the biotechnology industry are: human health technologies; animal health, marine and terrestrial microbial technologies; environmental remediation and natural resource recovery; agriculture and aquaculture technologies; and industrial technologies.[28] The major markets are biopharmaceutical, biodefense, agricultural biotechnology, and industrial biotechnology. Although based on common technology, each of these markets is subject to different conditions, different challenges, and different future outlooks. The following discussion details these sectors, provides an analysis of these markets, and provides sector-specific recommendations; however, industry-wide recommendations will be found at the conclusion of this report.

Health Care: The majority of biotechnology firms participate in the health care sector, which comprises 57 percent of the market.[29] These firms compete in three distinct markets: biopharmaceuticals, medical devices, and diagnostics. Recent gains in biologics enable product differentiation as these type of products are more molecularly complex, susceptible to variances in manufacturing, and make them more difficult to duplicate by generic manufacturers. Biologics also are distinguished by their ability to target specific populations as opposed to the general population, increasing the demand for personalized medicine.

Agriculture and Aquaculture: Agricultural products make up another significant portion of the biotechnology industry, comprising 15 percent of market share.[30] Most commercial agricultural products have production-enhancing traits that complement or replace traditional chemical inputs.[31] Crops are designed to be pest-, drought-, and weed-resistant, making them the "crop of choice" in some regions. In livestock production, biotechnology is used to enhance growth and muscle mass, and improve disease resistance.[32] Biotechnology also has applications in promoting adaptability to extreme conditions, and promising applications are emerging in the use of microbes and synthetic proteins for use in diagnostics.[33]

Industrial and environmental biotechnology: Firms in this sector compete in markets that involve biologically created fuels and industry chemicals.[34] They use a variety of techniques or platforms to identify and improve natural enzymes as well as create synthetic enzymes for later use in manufacturing processes. These products are differentiated by the superior enhancements they bring to the manufacturing process.[35] Additionally, firms in the environmental remediation and resource recovery market apply various techniques involving biotechnology to make new discoveries for the use of enzymes and microbes in environmental clean-up activities.

Biodefense: Firms in this sector use bio-technology to create products in markets such as prevention, detection, remediation and treatment of naturally occurring and man-made biological threats. Techniques used in this sector are similar to those used in other sectors, except they are used to support national defense goals.

Health Care

The largest segment of the health care sector is made up of the biopharmaceutical product market, which consists of drugs that are biological in nature and often involve genetically engineered products and processes, such as monoclonal antibodies and recombinant proteins. Major industry players include Amgen, Inc., Biogen Idec, Celgene Corporation, and Eli Lily. These firms often operate in multiple product industries, including the traditional small molecule pharmaceutical market.

Biopharmaceuticals account for 57% of the global revenue generated by the larger biotechnology industry.[36] The market operates globally and is often segmented along differing areas of grievous diseases or disorders (e.g. oncology support, nephrology, anti-inflammatory). The buyers within this market include healthcare providers (physicians and clinics), hospitals, pharmacies and drug distributors. Within the U.S., biopharmaceutical products fall under the regulation of the FDA. These products cannot be marketed and sold until they receive approval from the FDA after several rounds of clinical trials aimed at proving safety and efficacy. Many foreign nations have similar, though possibly less stringent, regulatory bodies.

Current Condition of the Market. Rivalry within the biopharmaceutical market is moderate. Firms initially tend to compete largely on product differentiation in the early life stages of a new product. Intellectual property protection enforces this market structure as patents prevent other companies from marketing and selling drugs with similar chemical structures. Thus, competitors within the market develop and release differentiated drugs designed to provide similar effects or treat similar diseases. After patent expiration, firms experience intensified competition due to the entrance of biosimilar products that compete largely on price with the original biological drug compounds. Biosimilars are similar though not identical products to the original drug and are analogous to more commonly referred term 'generic' drugs used within the small molecule drug market. These drugs rapidly reach the market once the patent protection of the initial biopharmaceutical product expires.

There are significant barriers for companies attempting to enter the biopharmaceutical market. The largest barriers include federal regulation, significant capital requirements, and high failure rates in clinical trials. The average cost to bring a new biopharmaceutical to market exceeds $1.3 billion.[37] These barriers have increased investor risk and have made it more difficult for both new and small companies to bring products to market. However, recent US regulations have reduced both the time and the cost to bring biosimilar products to market, making it easier for new entrants to attack existing market segments resulting in even more market competition.

Buyer bargaining power within the market is moderate. Most biopharmaceutical drugs are sold primarily to a small concentration of large distributors that then resell and distribute the products to pharmacies. Federal and private healthcare regulation has aided in increasing the buying power of these large buyers as the regulations stipulate policies that set caps on the amount of reimbursement healthcare providers receive for healthcare services and drug administration. Supplier bargaining power is low to moderate. Biopharmaceutical firms rely on specialized labor pools and equipment for research, development, testing, and manufacturing. However, firms often have the advantage to backward integrate or buy smaller companies to gain control over required

resources or services. Access to adequate supply of specialized labor pools will continue to be an issue within the market.

The overall power of substitute products is high. End users are faced with an increasing number of treatment choices due to advances in small molecule drugs and surgical care. The growing wave of biosimilar manufacturers has further fueled price competition within the larger pharmaceutical market.

Market Outlook. The global biopharmaceutical market remains healthy in terms of business value creation. Firms within the industry have achieved returns on investments (ROIs) that match or exceed the weighted average cost of capital both in 2012 and over the last five years. The current and 5 year ROI figures further indicate that the industry is fairly resistant to global economic downturns, highlighting the strong demand for biopharmaceutical products. The global biopharmaceutical industry captured roughly $50B of the estimated $87B in global revenue of the biotechnology industry.[38] Biopharmaceutical firms are currently valued at over $145 billion dollars according to research conducted by BioPlan Associates, with projected value exceeding $167 billion by 2015.[39] Growth will be fueled largely by increased global demand for biopharmaceuticals as population and standards of living increase.

Despite continued revenue growth projections, cost containment measures and entry of biosimilar products in developed markets continue to suppress growth. The industry continues to rely on a small concentration of blockbuster drugs with high profit margins rather than a wide base of products. However, long term prospects remain hopeful due to the higher potency and promise of biopharmaceuticals as compared to the capability of small molecule drugs.

Table 1. Biopharmaceutical Major Producer Return On Investment[40]

Company	Return on Investment% (year 2012)	Return on Investment% (5year)
AMGEN	10.10	11.80
BIOGEN	18.00	15.00
CELGENE	17.2	9.5
Eli Lily	20.20	18.30
NOVARTIS AG	11.50	12.60
JOHNSON &JOHNSON	13.80	18.30
TEVA	5.50	7.70

* Note: Many companies are composed of multiple business units in different markets

Challenges Facing the Market. The greatest short term challenge facing the biopharmaceutical industry is the wave of product patents that have recently or are due to expire in the next few years. The expiration of multiple product patents, referred to as the patent cliff, will likely result in dramatic and rapid declines in revenue streams. These declines lead many firms to cut costs such as research and development funding in order to remain attractive to investors. This in turn damages the longer term health of the industry's product pipeline and shifts the basis of product competition from differentiation

to pricing. Increased price competition is likely to lead to reduced revenues and value creation for the industry at large.

Over the long run, the cost and time requirements of the FDA approval process coupled with increasing competition from biosimilar manufacturers threaten to erode business value creation and sustainable investment levels within the market. Despite the large research and development investments made in the past, the annual number of biological drugs that receive FDA approval has not significantly increased. FDA annual biological licensing approval data indicates a maximum of 19 annual approvals over the last decade.[41] However, most of these approvals are for 'biobetter' or 'me-too' products that offer slightly better versions of existing drugs, indicating stagnation in development and approval of innovative products.[42] Thus, the market remains reliant upon revenues from development and recycling of a small number of blockbuster drugs rather than a large base of novel, though possibly less profitable products. The low quantities of blockbuster drugs coupled with the advent of biosimilars threaten to erode the overall revenue generation potential of this market.

Product innovation is critical to the long term growth of this market. Firms have recently made reductions in basic research and development funding in order to increase short term profitability or favor existing product lines. These cuts to basic research diminish the size and scope of future product pipelines. In addition, many of the innovative firms within the market are planning entry into the biosimilars product segment, leading to increased price competition and less product differentiation.

Policy Recommendations. Several policy recommendations are appropriate to maintain the strategic advantage the biopharmaceutical product market provides the U.S. Additionally, these policy instruments allow the U.S. government to correct a market failure by ensuring increased research and development in biopharmaceuticals.

First, the safety and efficacy of biopharmaceuticals and time to market is critically important to public health and ensuring the viability of the industry. As such, Congress should maintain historical levels of mandated funding for the FDA, but review these levels of funding annually to ensure they are sufficient. Simultaneously Congress should also provide the FDA with greater flexibility under the Prescription Drug User Fee Act (PDUFA); this legislation allows the FDA to collect fees from biopharmaceutical manufacturers during the review process. Increased flexibility also includes treating the FDA budget and PDUFA revenues independently, as PDUFA is currently subject to sequestration cuts as part of the FDA budget.

Allowing for greater PDUFA flexibility also includes authorizing an increased fee cap – a move supported by many in the industry as a means towards making the review process more effective, efficient, and predictable. The greater flexibility and increased revenue will cover potential funding shortfalls, allow the agency to modernize its system, hire additional staff with the appropriate expertise, and further streamline its processes. If adequately resourced and modernized the FDA will be better positioned to keep pace with the rate of technological change in the industry and allow the agency to engage manufacturers early, more frequently, and with the right expertise.

Second, we recommend increased funding for research in regulatory science and rapid, low cost diagnostic and clinical testing products and services. These costs could be off-set by finding efficiencies in the management and associated man hours required to provide oversight under the current system and increased PDUFA fees. The research should focus on technologies and processes to help identify and terminate failures early, while modernizing and shortening the clinical trial process that has remain unchanged for 30 years. This will offer more cost effective and efficient clinical trials, providing cost savings to both the firms and the regulatory and oversight bodies. This will also allow products to get to market in a shorter timeframe, but with the same efficacy and oversight.

Finally, we recommend providing tax credits for firms engaged in the research and development of biopharmaceuticals to offset the high capital costs. These costs coupled with the high probability of failure limit the funding available for firms to engage in more research and innovation. The sustained growth of this industry relies on a healthy pipeline of new products and services. A tax structure that provides credit for research costs associated with clinical trials may reduce investor and corporate risks for continued investment in development of new products. Ultimately, the costs of these tax credits could be offset by decreases in U.S. government mandatory health spending, as new products come to market better, faster, and cheaper.

Biodefense

The biodefense product market consists of medical countermeasures (MCM) including vaccines, drugs, therapies, and diagnostic tools to respond to natural or man-made chemical, biological, radiological, and nuclear (CBRN) threats. Since 2001, the U.S. government has apportioned more than $70 billion to address the threat of biological weapons and their related activities, focusing primarily on MCM research, development, and acquisition.[43] Given their expertise in the development of biologics, biotechnology firms are well positioned to develop MCMs for the purposes of biodefense. However, the unique conditions and challenges of this market result in limited commercial participation.

Current Condition of the Market. Unlike the market for biopharmaceuticals, biodefense is a "monopsony" with the government as sole customer. The market is almost exclusively dependent on government policy direction and funding for research and development and has no market based demand. The demand is instead derived from public policy decisions (usually based on threat assessments), and funded by federal research and development dollars. As a result, public policy drives quantity and production timelines. The lack of public demand for biodefense products combined with the positive social consequences of having adequate vaccines to counter natural and manmade threats mean this market experiences a market failure of a positive externality where there is increased need for research and development. Legislative and executive branch actions such as the Pandemic All Hazards Preparedness Act (PAHPRA), Project BioShield, and DoD's Transformational Medical Technologies Initiative have provided the majority of funding and policy direction for MCMs.

Despite the large number of biotechnology and pharmaceutical firms already in the business of developing biologics, there are only a limited number of firms currently operating in the MCM market. Accordingly, on the competitive spectrum this market is considered an

oligopoly. A Congressional Research Service issue paper on Project BioShield indicates that there are currently eight firms in the process of developing MCMs for a range of threats, including anthrax, smallpox, botulinum toxin, and radiological or nuclear events.[44] This amounts to approximately $2.63 billion obligated by HHS to this development effort thus far, and a little over $2 billion to replace MCMs already in the strategic national stockpile.[45]

A Five Forces assessment of the market provides further insight into the market conditions.[46] From the perspective of the policy maker the rivalry among existing competitors may appear healthy, as the biotechnology and pharmaceutical industry are already in the business of developing biologics. However, a closer look reveals that only a limited number of firms are willing to play in the MCM market given the lack of demand and challenges. These challenges include the high bargaining power of the buyer, the government, which has the ability to levy stringent requirements and price ceilings. While the expertise of the suppliers is high, there is also the risk that the government could invest its funds internally to develop MCMs – or "backwards integrate." The threat of substitutes is low, but the government does rely on intelligence and the projection of power to prevent a potential bioterrorist event, reducing the likelihood that one will occur. Finally, the threat of new entrants is mixed. Though the lack of a market demand and the burden of working with the government may deter some firms, the guarantee of funding may attract others; especially those who have previously worked with the government and are able to navigate the bureaucratic and regulatory hurdles.

Market Outlook. The outlook for biodefense is uncertain because of its dependence on federal funding and the challenging fiscal environment. Risk associated not only with biological weapons but also with infectious disease creates an imperative for continued funding and Congress has responded by renewing Project BioShield funding with passage of the Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) of 2013.[47] Although the funding extension is only for 5 years, it signals a commitment on the part of the federal government that could add stability to the sector. However, even with a short term funding guarantee, the fundamental force structure in this sector combined with the challenges discussed below create an uncertain outlook for the foreseeable future.

Challenges Facing the Market. The biodefense market faces many unique challenges. As previously discussed, biodefense is dominated by a sole buyer, and that buyer also provides the regulation and funding for the market. While our government has made great progress over the past decade in passing legislation to govern, organize, and fund biodefense initiatives, we still face significant challenges encouraging industry participation.

In the *Medical Countermeasures Enterprise Review,* HHS has challenged the nation with a unifying vision which states, "Our Nation must have the nimble, flexible capacity to produce MCMs rapidly in the face of any attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring emerging infectious disease."[48] Industry is often hesitant to enter the biodefense market because of the challenges associated with operating in a monopsony.

First, the high risk/low reward nature of the biotechnology industry in general is amplified in biodefense because there is no market guarantee for its products. The Project BioShield Act addressed this challenge, advanced appropriations of $5.6 billion dollars over ten years, and gave

HHS the authority to use milestone payments to fund products in development, even if they never make it to market.[49] While these payments help reduce risk, they do not mitigate it entirely and many products still fail to get through clinical trials.

Another risk compounding an uncertain market is the lack of dual use technology for biodefense products in the civilian market. Many MCMs are only used following a CBRN event. Absent a steady civilian consumer demand, there is little incentive to develop biodefense products outside of government funded projects. Additionally, biodefense lacks a clear demand signal for MCM products and quantities. HHS plans for contingencies and sources the Strategic National Stockpile with anticipated products and quantities, but not until an event occurs, true demand remains an unknown, and it is challenging for industry to ramp up or change production after an incident. Yet another challenge facing biodefense is the high level of regulation surrounding the safety and efficacy of products. The FDA testing requirements and clinical trials create additional barriers, although Congress has passed legislation to accelerate development including Emergency Use Authorizations when required.

Firms also face an immense number of challenges keeping pace with the number of requirements levied by the government grant and procurement processes. This is compounded by a lack of coordinated requirements among agencies in the biodefense community. Consequently firms often commit significant time and money to responding to government requests for information and tracking milestone requirements.

Perhaps the most significant challenge facing this market is maintaining a long-term commitment to funding research and development. Some critics find it difficult to justify funding and wonder whether efforts thus far have made the U.S. any safer. Project BioShield only protects against a limited number of potential threats, only acquires products in limited quantities for a portion of the nation's population, and ultimately MCMs on the shelf expires, requiring follow-on procurements. Although PAHPRA authorizes an additional $2.8 billion in funding for the next 5 years, ensuring adequate funding levels for the long-term may prove to be difficult in today's austere budget environment.

Policy Recommendations. The risk of natural or manmade biological threats necessitates the availability of MCMs and detection tools, so the U.S. government must use policy tools to overcome existing market failures. Even in an austere budget environment, it is critical that the U.S. government, as the sole customer, assure firms seeking to enter this market that long-term funding will be available. This becomes especially important as companies attempt to cross the "valley of death" from discovery to market. Incentivizing firms to enter this market requires a steady rhythm of long-term funding with a guarantee of milestone payments to encourage firms to engage in research and development of biodefense products.

Funding authorizations should be increased from $2.8 billion over five years to $5.6 billion over ten years, to be more consistent with the drug development timeline and ensure firms that the government remains committed to the development of MCMs. Moreover, because the availability of these funds is subject to annual appropriation laws, despite authorization levels, Congress should fence off the annual appropriations to ensure they are not raided to meet other requirements.

Simultaneously, the government should increase small business innovation and research funding administered by the NIH to invigorate innovation and discoveries in this field. Additional incentives should be geared towards firms that develop innovative processes to expedite the research, development and manufacturing processes. This has the dual benefit of making discoveries in MCMs, while also providing scientific advances for other areas of medicine and public health. Additionally, a guaranteed market for MCMs will continue to foster this emerging biotechnology sector, resulting in increased employment opportunities and greater innovation that has reach beyond the biodefense sector. While, resourcing this increase in an austere fiscal environment requires some tough trade-offs, the funding required is minimal and the benefits warrant advocating for the increase.

The government must also ensure that smaller firms will have the capacity to move into advanced development even if these firms depend on funding from agencies such as BARDA and DoD to procure biodefense tools. This effort will require that the oversight and regulatory agencies (i.e., HHS and FDA) are fully resourced with adequate capacity and expertise to provide the technical assistance to include timely reviews and feedback. Moreover, the FDA should continue its efforts to clarify regulatory pathways for MCMs in accordance with the recent reauthorization of PAHRPA.

Finally, the interagency should develop a strategic plan to establish coordinated priorities and funding. This would include breaking down stovepipes that often result in requirements differing from agency-to-agency. Additionally, the strategic plan should include a plan for reforming the funding mechanisms to allow for maximum flexibility and streamlining the contract management process.

Agricultural Biotechnology

The biotechnology agricultural products market focuses on crop, vegetable, and fruit seeds which are developed using genetic modification (GM). There is also research and development ongoing to commercialize GM animals for food production. Biotechnology agricultural products market represents fifteen percent of the biotechnology industry. Within this macro-level market are several sub-markets, including herbicides, pesticides, and GM seeds (as well as a market for the traits used to complement or replace agricultural chemical inputs to further enhance crop production). Within the market for GM seeds, the primary products include row crop seeds (corn, soybean, cotton, and wheat), open field vegetable seeds (cucumbers, lettuce, broccoli, etc), and specific biological traits (via intellectual property license) that enhance the durability and production capacity of the seeds. These seeds can be genetically modified to resist pests, other more invasive plants, and extreme weather conditions such as drought. They can also be modified to enhance crop yield per acre and are designed to produce food, animal feed, basic materials and energy. The major producers include Monsanto, Dow AgroSciences, Du Pont (E.I.) de Nemours, BASF, Bayer CropScience, and Syngenta. The products fall under the regulation of the FDA, USDA, and EPA. The market operates globally with seeds tailored to specific regions.

Current Condition of the Market. The rivalry amongst existing competitors is moderate. Conventional seed and agricultural-chemical companies also compete in this market. There are a few major producers but there are hundreds of small regional seed companies. On a competitive spectrum, with perfect competition at one end and monopoly

at the other, this market has historically been somewhere between mid-range and monopoly with Monsanto maintaining the greatest market share. However, there are indications that the market's position is trending toward greater competition. There is increasing anti-competitive scrutiny due to the large market shares of the major producers. Competition is intensifying among major producers as products come off patent. As an example, in its Seeds and Genomics segment Monsanto has several patents expiring in 2014 which should open competition.

The bargaining power of suppliers is low. The major suppliers are labor, third party seed growers, raw materials and chemicals, research, development, and production equipment, and energy. While there is competition for talent, there are a limited number of companies hiring genetic scientists. There are low switching costs for the other suppliers. Suppliers are also unable to integrate forward and develop their own seeds due to the barriers to entry.

The bargaining power of buyers is moderate. Buyers include farmers, other seed companies, agricultural cooperatives, plant raisers, agricultural chemical producers, residential consumers, dealers, and agents. The GM seeds are differentiated from both other genetically modified seeds and non-GM seeds by yield, insect resistance and pest resistance. Some producers have established ecosystems of seeds and herbicides which work together to greatly diminish the amount of effort to grow crops such as corn and soybeans. These ecosystems make it more difficult for buyers to switch brands. Due to intellectual property protections buyer power is diminished because they are unable to integrate backwards. There is moderate to high price sensitivity which is offset by product yields and there is some public sentiment against GM food. As the market expands into the developing world the buyer power will be further reduced.

The threat of new entrants is low. The threats include small startup companies in partnership with larger corporations, foreign governments sponsoring new entrants, and expiring intellectual property protection. The barriers to entry include the capital-intensive and research and development intensive nature of the products, returns on investment taking years, intellectual property protections of existing firms, and extensive regulatory scrutiny. The major producers have large operations, well established processes for product development and approval, and well established distribution networks.

The threat of substitute products or services is moderate. Buyers will have access to generic seeds as products come off intellectual property protection. Buyers may choose to grow non-GM seeds such as organic due to customer sentiment against GM foods. For energy crops, biotech enzyme technology may substitute growing corn for ethanol.[50]

Market Outlook. The biotechnology agriculture products market is healthy with much of it focused on GM seeds and complementary products competing against conventionally bred seeds. The market is global and the demand for food will continue to increase as population and standards of living increase.

The biotechnology agriculture products market competes on differentiation with the first to the market gaining advantage over the others. By developing seeds with superior traits, focusing on customer service, and expanding to underserved regions it is possible to avoid a downward

price competition spiral. With the growth of using enzymes to produce ethanol, it might be opportune for the industry to enter that market to compensate when corn sales decline due to new sources of ethanol.

The leaders in the biotechnology agriculture products market compete when intellectual property is protected and by changing the game using innovation to create new products which add value. Innovations have included herbicide resistance which allows the field to be sprayed with herbicide which kills everything except the desired crop such as corn or soybean. Other innovations have included insect resistant sugar cane, drought tolerant cotton, and flood tolerant rice.

Another indication the biotechnology agriculture products market is healthy is in its financial data. The return on investment for the major producers exceeds cost of capital estimated at 10% with the exception of Dow AgroSciences as shown in table 1. These companies have also experienced growing sales with manageable debt, further demonstrating a healthy industry.

Table 1.2 Biotechnology Major Producer Return On Investment[51]

Company	Return on Investment% (1 year)	Return on Investment% (5 year)
Monsanto	16.10	14.60
Dow AgroSciences*	2.70	4.00
Du Pont (E.I.) de Nemours*	13.70	14.20
BASF*	Not Available	15.26
Syngenta	16.70	15.10

* Note: Many companies are composed of multiple business units in different markets.

Challenges Facing the Market. In the near term, sustainable value can be produced in the biotechnology agricultural product market. The intellectual property and human capital of major producers are sufficient to maintain position. The market demand for food continues while the demand for fuel is less certain.

In the long term it is probable the value will decline on the current path. There are potential issues with poor public perception of GM foods which may reduce demand, causing shortages and higher prices among non-GM food products. There is potential for intellectual property violations when farmers reuse seeds without paying royalties. With expiration of intellectual property protection for certain seeds, some philanthropists are supporting the development of generic GM seeds.[52] In addition there is always the possibility of increased regulation slowing approval of new products.

To compete in the biotechnology agricultural product market, companies need to counter rivalry competition by expanding to new markets. One example is China where population and increasing living standards is generating greater need for grain crops supporting food, livestock, and fuel needs and urbanization is decreasing available crop land. Companies should also focus on product differentiation, expand their research and development into new areas such as enzymes or aquaculture, and develop innovative products such as GM seeds for a larger range of fruits and vegetables. Companies also need to target the bargaining power of buyers by expanding into

underserved markets such as Asia and improve customer service to overcome intellectual property violations. In addition, companies need to mitigate the threat of substitute products through a strategic communications campaign to promote the safety of GM foods. In this effort they could leverage industry associations to develop and promote a unified GM food message.

Policy Recommendations. Although this sector is essentially healthy, there are several policy recommendations appropriate to maintain the competitive structure, enhance innovation, and maintain strategic advantage the biotechnology agricultural product market provides the U.S.

First, Congress should pass and implement the Expediting Agriculture Through Science (EATS) Act to establish a fixed 180 day timeline for approval or disapproval of certain biotechnology products. This would encourage innovation by giving firms a planning date for moving forward with their new products rather than indefinitely waiting for a government agency response. Passage of this act would not require additional government resources, but would work to counter a risk averse regulatory atmosphere.[53]

Second, the U.S. government should designate portions of current foreign aid to developing and drought-impacted regions such as Sub-Saharan Africa (SSA) as specifically for the purchase of GM seeds. In addition, the U.S. should help fund research and development of GM seeds derived from native crops to facilitate greater acceptance and sustainability of GM products. For example, the Obama Administration's FY2012 SSA bilateral aid request was $7.8 billion to support several broad-based objectives. Since this money is already designated, it would be budget neutral to designate some for GM, and it would bring needed technology to a region that so far has only marginally embraced it.[54]

Third, the government should maintain current levels of support for research and development in the biotechnology agriculture product market through continued funding of NIH. Because of the positive externality of decreased strain on natural resources of GM agriculture products, the government should consider increased tax incentives as fiscal constraints allow. The government should also consider federal land use agreements for crop development as this could make use of an untapped resource to encourage innovation.

Finally, the government, in coordination with industry stakeholders, must address the issue of public perception of GM foods. A strategic communications plan should be adopted as an objective of the Bioeconomy Blueprint, and the government should encourage voluntary versus mandatory labeling of genetically modified products.

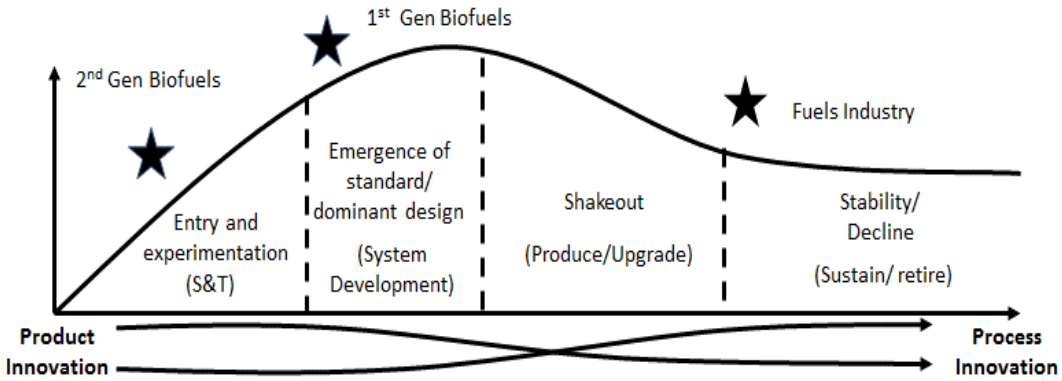
Industrial Biotechnology

The industrial biotechnology market is focused on the production of enzymes or micro-organisms that enable fuels and chemicals to be made from renewable sources, such as cellulosic biomass, or algae.[55] Most industrial applications involve process improvements to reduce waste products, energy consumption, and water consumption in textiles, energy, and chemical sectors.[56] One of the primary markets in this sector is biofuels, which is the subject of the remainder of this section.

Approximately 90% of the domestic fuels market includes non-renewables such as petroleum, coal, natural gas, and nuclear.[57] The global demand for non-renewable resources continues to grow as developing nations in Asia and Africa build domestic industrial capabilities. The U.S. is the leading global consumer of oil followed by China and Japan.[58] The U.S. Energy Information Administration expects dependence on non-renewable energy sources to continue to grow by about 10% through 2040.[59] The heavy use of non-renewable resources, coupled with concerns about the long-term supply and its price volatility have increased the desire to find renewable alternatives. Recent technological advances and government regulations have helped biofuels become the most consumed renewable energy source, comprising over half of the renewables market.[60] First generation biofuels include fuels derived from food products such as corn starch, sugar canes, or plant oils. Second generation biofuels are derived from non-food cellulosic biomass or the non-food waste bagasse from plants once food products are removed.

Current Condition of the Market. To appreciate the complexity of the biofuels market, one must first understand the overall fuels market, to gain insight into how competition drives and weakens the biofuels sub-market. Not only do biofuel firms compete against each other, they also compete against other types of renewable energy such as solar, wind, hydroelectric, geothermal, and tidal. Most importantly, biofuels also compete in the larger fossil fuels market against petroleum and natural gas firms. The larger fossil fuels market is an oligopoly on the competitive spectrum, and biofuel firms cannot compete in any significant manner without the continued support of federal, state, and local regulators. As a separate market, biofuels are perfectly competitive, but there is no single biofuel standard, and sellers have little influence over their pricing.

The biofuels market must be further dissected to understand where specific types of bioengineered biofuels are in their specific industry lifecycle. For example, first generation ethanol fuel is moving towards the "shakeout" phase of their life cycle as ethanol production is somewhat standardized in terms of its processing. Second generation biofuels show promise, but the saccharification process is inefficient and too costly to scale up with current technology. These second generation biofuels are still in the early phase of their industry lifecycle, as they are still experimenting with various types of engineered enzymes that will yield cost effective biofuels. Algal based fuels are also in the early phase of their industry life cycle, but are already showing great promise as the third generation of biofuels. Firms experimenting with algae derived biofuels, as well as various types of algal growth methods are still trapped in the entry and experimentation phase of their life cycle. The table below highlights the various stages of first and second generation biofuels, including the larger fuels industry.



Until biofuels moves into the shakeout phase of their life cycle, they will not be able to compete in the larger fuels market on price. Under these conditions some companies, like Solazyme, are instead competing in niche fuel markets, where product differentiation is more important to the customer than cost. Solazyme has demonstrated this effectively as they are able to engineer algae specific to a customer's needs, producing algal oils that when converted into biodiesel, meet strict customer specifications. One of the obvious benefits of this clean biodiesel derived from algae is that maintenance costs on sensitive combustion equipment may be reduced to a fraction as compared to its petroleum derived diesel fuel. This model serves to sustain and grow Solazyme's technology as they strive to improve product efficacy.

In order to create real market value, the collective biofuels industry must ultimately compete on price in the larger fossil fuels market, and focus less on product differentiation. Presently, fossil fuel is relatively cheap to produce and becoming cheaper through innovative extraction techniques. As a result, long-term fossil fuel prices will remain stable even if demand rises, thus creating a nearly impossible barrier for biofuel firms to enter the larger fuels market. In 2010 a U.S. Department of Energy report from the Lawrence Berkeley National Laboratory, Office of Science stated that scaling up algae production to compete in the larger fuels market would still cost around $240 to approximately $330 per barrel while crude oil is currently hovering around $95 per barrel. Many industry leaders also agree that cellulosic biofuels now and into the near future will remain somewhere near $200 per barrel. Should petroleum prices rise, it would expedite price competitiveness and drive biofuel R&D to close the price gap.

In examining Porter's Five Forces one will likely conclude that the threat of new entrants and substitutes is relatively low to the fossil fuel industry at large. While there is somewhat perfect competition in the oil service/extraction market, with thousands of companies competing to distribute their product, major fossil fuel suppliers, particularly petroleum suppliers, thrive in an oligopoly where price leadership is king. However, globalization is shifting moderate power to the consumers. For example, when the price at the gas pump goes up, consumers respond by driving less, or they look to more efficient means of transportation, which places considerable pressure on the suppliers to lower their prices. In consideration of the threat of substitutes, when petroleum prices go up, other fossil fuels become more competitive such as coal and natural gas. Think of substitute fuel sources as a ladder with biofuels rounding out the bottom rungs along with solar, wind, and other renewable energy sources. Consumers of fossil fuels will look to the next cheapest fuel, and so on. Consequently, while fossil fuel extraction technology is making it

cheaper to extract these fuels, competitive rivalries are all but squashed under the weight of their inability to compete simply on price.

Market Outlook. The global biofuels market will grow substantially over the next ten years, but will not displace fossil fuels in any significant manner. Additionally, the majority of biofuel firms will require continued financial and regulatory support from the federal government. In August 2012, Hart Industries presented their analysis on the outlook of the biofuels industry to the US Department of Energy's, Energy Information Administration. They found the following:

- Global biofuel will increase by 70% by 2020 and nearly double by 2025
- In 2020 88% of biofuel demand will come from North America, Latin America and Europe
- U.S. and Brazil will account for ¾ of ethanol produced.
- By 2020 biofuel potential to reach 7% of gasoline plus transportation diesel demand
- Difficulty meeting far reaching program goals in EU and US[61]

At best, by 2020 biofuels have the *potential* to supplant 7% of the transportation fuels industry. That said, it cannot be overstated that fossil fuel extraction is becoming cheaper and new areas are opening up where fuel was once unreachable. As a result, the viability of the industry depends on the larger fossil fuel industry, and therefore will remain largely dependent on governmental support in the short term. Much like the Solazyme model, the Hart Industry Analysis concludes that biofuels will remain costly, but incremental introduction into niche markets will open up opportunities to sustain and grow biofuel technology.

Challenges Facing Biofuels in the Market. Several issues pose challenges to the biofuels sector including cost, the lack of maturity in the market, lack of adequate biomass to produce biofuel, and public perception of using food products for fuel. Presently, no company is producing first or second generation biofuels at competitive prices without significant help from regulation. The first generation biofuels industry receives an estimated $7 billion per year in tax credits, tariffs and other incentives in order to make them competitive.[62] Second generation fuels are from non-food sources but have not produced at commercial volumes or at competitive prices in the U.S. Even in nations like Brazil that heavily use 1st generation biofuels, production and consumption of biofuels is decreasing due to market competition from fossil fuels.[63]

The biofuels market is very young and competitive with over 12 companies in direct competition in the research and development of the next generation biofuels. No one is producing viable fuel at commercial quantities. This wide-open field is financially fragile as funding and long-term sustainability of most companies is in question. Most of these companies rely on a large business partners to underwrite their research and development and lack long-term financing.

Currently, the U.S. lacks adequate cellulosic biomass to mass produce biofuels. According to an industry expert, if 100 percent of cellulosic biomass in the US were available for conversion to bio-fuel, it would produce only 20 percent of the current US fuel demand.[64] However, not all biomass is available for conversion, and there are not enough crops producing biomass for biofuels to overtake fossil fuels, either in the short or mid-term future.

Compounding all of this, public perception is driven by the food for fuels debate. The most prominent posture for those against the use of food products for fuel is that the redirection of corn leads to higher demand and therefore, higher prices. Since the summer of 2012, disappointing corn yields, worldwide loss of wheat crops, and growing U.S. and international corn demand have increased corn prices from $3.50 per bushel to more than $7.50 per bushel, according to the Energy Policy Research Foundation.[65] Many sources have recognized biofuels production as a major driver of these food prices. The *World Economic Outlook 2008* published by the IMF states: "Although biofuels still account for only 1.5% of the global liquid fuels supply, they accounted for almost half of the increase in the consumption of major food crops in 2006-2007, mostly because of corn-based ethanol produced in the U.S."[66] Global production of biofuels is projected to nearly double by 2021 and consumes a growing share of the global production of sugarcane, vegetable oil, and coarse grains.[67] Therefore, many argue that it is both immoral and inefficient to use food for fuel when so many in the world are malnourished.

Policy Recommendations. Given the challenges to the fuels and biofuels markets, there are several policy recommendations that would help the market sector remain healthy and sustain U.S. leadership for the future.

Negative externalities, such as environmental impact and dependence on foreign oil in the fossil fuels market indicate that market equilibrium delivers the product at a marginal cost to the consumer which is less than the marginal social cost. Biofuels have the potential to eliminate those externalities, but the sector lacks the ability to produce sufficient capacity to meet demand as a fossil fuels substitute. As a result, policy intervention to allow biofuels to compete on price would be premature.

However, given the ability of biofuels to compete in some areas on differentiation, and the potential for it to eventually compete on price, the government should continue to act as the early adopter of biofuels technology, incorporating lessons from countries like Brazil.

The Renewable Fuels Standard is an effective policy tool to allow the biofuels industry to develop. It should be maintained, and coupled with a requirement for renewable energy to meet price targets to determine its future potential to compete on price in the fossil fuels market. In the meantime, the government should maintain federal funding for research and development to encourage innovation in this area.

CHALLENGES AND INDUSTRY TRENDS

Changing demographics and other trends in the U.S. and the world will increase the demand for biotechnology products. An aging population, coupled with longer life expectancy and the increase in chronic conditions such as diabetes, Alzheimer's, and heart disease will continue to drive the global demand for medical biotechnology goods and services. In emerging countries, population growth and scarce resources, such as water and food, will also greatly increase demand.[68] Compounding the challenge of already scarce resources is climate change, which threatens to have significant environmental impacts with implications for agriculture, but also presents an opportunity to advance bioindustrial products as a substitute for fossil fuels. Finally, emerging infectious diseases and the threat of weaponized biological agents also demand solutions from the biotechnology industry.

Biotechnology offers numerous opportunities and potential solutions to these threats, which pose challenges to both U.S. national security and prospects for economic growth and prosperity. However, economic, political, and social trends and emerging industries in Asia introduce risk that affect the ability of the U.S. to remain the global leader and ensure the vitality of the industry.

Economic Trends

The biotechnology industry remains vulnerable to changing economic conditions because of its heavy reliance on federal funding and venture capital, both of which decreased following the 2008 economic downturn. Also, because the industry is still in the growth phase the lack of availability of capital is one of the primary threats to the viability and vitality of the industry.

Investor Uncertainty & Flight of Capital. In discussions with experts in the industry many noted that the flight of capital is the biggest threat to biotechnology. Venture capitalists and biotechnology experts attribute much of the strength of the biotechnology industry to the robust venture capital community in the U.S. While many of the large firms have consistent revenue streams, the majority of small, start-up, and pre-commercial biotechnology firms rely on venture capital investment. However, these firms are facing an environment of increasingly savvy investors who have set the bar higher in terms of the scientific and reimbursement data necessary to support an investment decision.[69] Moreover, the total amount of capital available to the venture capital industry has decreased substantially over the past few years. Consequently, companies desiring access to that smaller pool of capital face competition from other industries that hold the promise of faster returns. While the total announced venture capital dollars invested in the sector is consistent with prior periods, the investments in early-stage companies is dwindling, with a large fraction of the total funding received only after meeting additional milestones.[70]

The decline in venture capital funding has significant implications for biopharmaceutical firms attempting to cross the "valley of death," the chasm between initial discovery and the successful commercialization of a product.[71] With the average cost of a new drug estimated at $1.2 billion over a 10-12 year timeframe, the need for long-term research and development funding remains critical.[72] On the positive side however, one venture capital expert suggests that changing business models, such as the move to "virtual biotechnology," the growth of patient advocacy groups, and a more favorable regulatory environment could help reverse some of these trends.

Government Funding. The U.S. government's role in funding scientific discovery cannot be overstated. The government has directed tens of billions of dollars towards basic research, directly contributing to the ability of the U.S. to lead the globe in biotechnology by providing the seed funding for initial discoveries.[73] However, the current fiscal and political environments have already resulted in a decrease of available funding through legislation such as the Budget Control Act. For example, the NIH took a $1.6 billion budget cut and as the world's largest funder of biomedical research, these budget cuts are already said to be impacting advances in medical research.[74] Additionally, in areas such as biodefense, government funding is the sole source of funding. As a result, reduced budgets will greatly impact the industry's ability and incentive to pursue research and development of MCMs to protect against the threat of a weaponized biological agent or emerging infectious disease.

Even if government funding was available, the lack of flexibility of government funding tools also presents a concern to the industry. Industry officials contrast the notoriously rigid terms, milestones, and requirements of government funding with the more flexible funding available through private sources. Additionally, most note that the unyielding rules that come with government funding are a failure to recognize the pace of change and unpredictable nature of biotechnology.

Industry Consolidation. Facing an austere fiscal environment, many small companies -- which are known to be the main source of innovation in the industry -- are forced to merge or be acquired by larger firms with greater access to capital.[75] Additionally, with many large companies hoping to diversify their portfolios, expand into emerging markets, and generate new sources of revenue because of the impending "patent cliff," mergers and acquisitions will continue to increase.[76] The fiscal environment and increased start-up costs, driven up by the cost of capital, the pace of change, and regulatory requirements, may also limit the entry of small firms.[77] These are potentially worrisome trends for an industry where much of the innovation is generated by small and emerging firms.

Human Capital. Though many industry experts did not identify the lack of human capital as a near-term threat, they agree it is a threat in the longer term. Some attribute this to a decreased focus and interest on STEM education, a critical area outlined by the *National Bioeconomy Blueprint.* Biotechnology industry advocacy organizations also noted the potential for scientists to seek careers in other technology-based industries which may promise greater profit and less risk. However, some advocacy organizations pointed to immigration reform as the key to unlocking even greater potential in the human capital arena, if reform eases entry-and-stay requirements.

Political and Social Environment

In addition to the immense pressure to decrease government spending and reduce the U.S. debt, the biotechnology industry often runs into challenges related to the regulatory pathways and public perception of biotechnology products and services.

Regulatory Pathways. Most industry experts cite unclear, slow, and burdensome regulatory pathways – particularly in pharmaceuticals – as a major challenge for the biotechnology industry. Industry often cites the FDA's inability to keep pace with technological change as a significant hurdle, which results in a lengthy and complex regulatory process that hampers innovation and the development of new biotechnology products. Those familiar with the regulatory apparatus also conclude that personnel turnover at the highest levels of the organization results in inconsistent and ever-changing policies and requirements.

The emergence of biotechnology industries in Asia and elsewhere also presents a unique challenge to U.S. regulatory agencies. While it is important for the U.S. to remain the global leader in biotechnology, it must not set aside safety and efficacy for expediency. Although industry often laments the challenges of working with the FDA, it is still considered to be the "gold standard" for food and drug regulation worldwide.

Public Perception. The public's perception of biotechnology products and services can also threaten the industry because of the disproportionate relationship between the public's knowledge level and their ability to impact funding, policy, and regulation. A 2006 survey asked 800 voters about their opinions of the biotech industry. Participants were first asked about their impressions of the industry, then read a short description of the industry and again asked about their impressions. Prior to being provided additional information, only 13% reported having a *very favorable* view of the industry compared to 12% which had an *unfavorable* view. After being provided additional information, the number of respondents with a *very favorable* view increased to 34% while those with an *unfavorable* view dropped to 11%.[78] This study indicates increased education on biotechnology has a positive effect on an otherwise uninformed public.

The lack of knowledge coupled with the fact that some of the industry's research areas are at the center of on-going political debates (such as stem cell research) can have a significant impact on the industry if regulation is further tightened in response to public outcry.[79] Despite this evidence, the industry has failed to implement a large-scale strategic communications campaign to inform the public and generate political discourse surrounding biotechnology.

Emerging Industries & Emerging Opportunities

In the near-term the U.S. is well-positioned to maintain its role as the global leader in biotechnology. The robust biopharmaceuticals sector will remain the largest biotechnology sector because of the growing market for drugs. However, growth of other biotechnology sectors is expected and significant opportunities exist for capitalizing on emerging markets. Additionally, the potential for disruptive technologies such as personalized medicine may provide even greater room for growth of the U.S. biotechnology industry. However, other governments have also recognized the potential of biotechnology not only as an engine for economic growth, but also as a solution for many pressing social challenges.

Emerging Industries. While a number of foreign governments have staked their future in the growth of a biotechnology industry, China's commitments are particularly noteworthy. As part of a five year plan for economic growth, the Chinese government is pledging $11.8 billion to advance biotechnology innovation.[80] Additionally, the Chinese government has sought to repatriate many of its students studying in the U.S. to work in biotechnology.

Currently, the growth of China's biotechnology industry is predicated on the development and manufacturing of biosimilars.[81] The Chinese government is working to establish regulatory and legal frameworks to support this growth, but the risk calculation for safety and efficacy of new drugs and the lack of adequate intellectual property protections must be overcome going forward. That said, as the industry evolves business leaders will likely make an even more aggressive push to establish the conditions necessary to have a thriving bioeconomy in China.

Emerging Opportunities. The growth of emerging markets presents immense challenges but also opportunities for the U.S. biotechnology industry. First, many U.S. firms, through subsidiaries, are conducting work in nations with lower labor cost such as China and India.[82] Although this allows U.S. firms to lower their operating costs, there are risks involved because many of these countries lack the strict regulatory framework of the U.S. This is evidenced by the recall of a Baxter pharmaceutical drug that was tainted during manufacturing in China and is a

clear sign of some of the vulnerabilities that exist in the supply chain.[83] Additionally, the lack of strict intellectual property protections in many emerging markets increases the risk of illicit technology transfers.

The potential for a growing market of personalized medicine has the potential to positively impact the biotechnology industry. Personalized medicine is a model that suggests medical treatments should be personalized to each individual patient, largely based on genetic information. As this field evolves it may help address some of the systemic problems in the industry, mostly by reducing cost and risk of drug development. Such advances may include more targeted clinical trials with participants being selected based on genetic make-up rather than representing a cross-section of the population. Additionally, personalized medicine provides the potential to increase efficacy and decrease side-effects because therapies will be tailored for each patient. With the appropriate support from the regulatory agencies, advances in personalized medicine could reduce the cost and time of bringing a drug to market by compressing the clinical trial timelines and costs. At a more macro-level, personalized medicine also has the potential to reduce healthcare costs by focusing care and eliminating unnecessary treatments and therapies. This offers a great opportunity for the industry to impact one of the major drivers of increases to U.S. mandatory spending.

Austerity and Innovation. Finally, although the fiscal environment is largely perceived as a negative for the industry, arguably fiscal austerity may force greater innovation. Even in an austere budget environment, the demand for biotechnology continues to grow. As a result, pressure may increase to develop more products, faster, better, and cheaper. Potential opportunities for innovation include changing business models; finding efficiencies in the development and manufacturing processes; encouraging a "fail sooner, earlier, and more often" model; and, adopting regulatory processes to support more efficient reviews. Greater innovation in these areas will not only ensure the health of the industry, but will also allow the U.S. to maintain its position as the leader in biotechnology. However, if industry and the government fail to respond to these changes, the austere fiscal environment will have a negative impact on biotechnology innovation.

CONCLUSIONS AND RECOMMENDATIONS

The biotechnology industry is extremely diverse and cuts across several areas related to U.S. economic growth, prosperity, and security. The industry's disruptive and sustaining innovations in health care, agriculture, defense and energy will continue to be instrumental in addressing U.S. national security issues. Moreover, biotechnology will continue to be a catalyst for innovation and contribute to U.S. economic growth and productivity. This industry has historically provided enormous opportunities for employment, has been a positive net exporter, and continues to grow at a steady rate. While the industry overall remains relatively healthy, it is imperative for the government to take steps to ensure the U.S. maintains its position as the global leader in biotechnology. A key aspect of U.S. leadership is to continue to foster an environment where greater innovation can to contribute to both economic growth and the development of solutions for pressing security issues.

The recommendations that follow provide policymakers with tools needed to address market failures and competitiveness of the industry overall. Acknowledging the austere fiscal

environment, these recommendations are designed to stimulate further growth in the industry assuring increased economic growth, greater prosperity, and an increased capacity to maintain global security. These recommendations should be evaluated in the context of a long-term view. The role as a global leader in this industry comes with a cost, but the immense benefits to U.S. national security and economic growth justify the government's attention.

Recommendation # 1: Begin implementation of the White House's *National Bioeconomy Blueprint* and assign a champion to provide oversight and develop metrics to measure progress against its strategic objectives.

The *National Bioeconomy Blueprint*, if implemented, provides a strong signal that the U.S. government is committed to building the nation's capacity to innovate through the growth of a vibrant bioeconomy. This focus on the industry must include strengthening the relationship among the members of the triple helix. The *Blueprint* must be leveraged as a unifying document that attempts to break down the stovepipes between the various stakeholders in the government's biotechnology community. However, the current document requires revisions to develop further detail for how to achieve its overarching objectives. As a part of this review, policy makers should assess industry-related regulation and policy to ensure they do not run contrary to the stated objectives. For example, the ACA aims to provide consumers with greater equity in the biopharmaceuticals market by placing price caps on drug products, and thereby reducing the total cost paid by the consumer. However, these regulations have significant and negative ramifications for the biopharmaceutical producers since price caps reduce revenue and ultimately decrease the research and development expenditure required to fuel innovation.

In conjunction, the White House should immediately begin engaging the appropriate Congressional committees and executive agencies to make the strategic objectives in the document actionable and enduring beyond the current administration. These objectives provide overarching guidance for ensuring the health of the industry and maintaining the U.S.'s position as the global leader in biotechnology.

Resources will be required to ensure effective implementation of the *Blueprint.* However, we believe these costs will ultimately be offset by biotechnology solutions that result in reduced costs in health care, energy, and agriculture, while also growing the domestic biotechnology base. Additionally, investments in biotechnology will spur innovations in a variety of other segments of the economy where benefits will also be realized.

Recommendation # 2: Implement aggressive campaign to revamp the regulatory framework to improve its alignment with the speed of the 21st century scientific innovation; and to work with international partners to ensure U.S. access to emerging markets.

The U.S. regulatory system is considered to be the world's "gold standard," with an exceptional safety and efficacy record. Despite this, its processes are still woefully out of date and have not kept up with the pace of technological change in the biotechnology industry. This legacy system has a negative impact on firms in the industry as it drives up risk, costs, and lead times to bring a product to market. In an industry where the rate of failure is extremely high, government efforts to facilitate a more simple and timely regulatory pathway is key to attracting investment and mitigating capital costs for firms.

Additionally, successful efforts to address the U.S. regulatory framework may also open up markets and opportunities across the globe for U.S. companies. For example, under the Trans-Pacific Partnership (TPP) diplomatic and trade agreements, the U.S. will work with its partners to standardize regulations, facilitating the commercialization of U.S. products abroad. The TPP also provides for access and trade agreements and calls for strong intellectual property protections among signatories. These are important elements to keep the industry globally competitive, the latter being critical to U.S. firms seeking adequate protections which will allow them to take advantage of emerging markets.

Recommendation #3: Maximize limited federal funding for research and development by prioritizing areas for government funding, eliminating duplication among federal research and development organizations, and adopting dual-use policy to make the most of every dollar.

As a science-based industry, all biotechnology sectors are dependent on research and development to aid the discovery process. The last 5 years have seen a decrease in industry research and development expenditures and a decrease in venture capital. In addition, venture capital tends to be focused later in the development phases to reduce risk. Although research and development funding is projected to increase marginally through FY15, it is then projected to dip again.[84] This underscores the critical role of federal research and development funding, but the current fiscal crisis is likely to continue to impact federal spending in all areas for the indefinite future. As a result, federal agencies must maximize every dollar in the budget. Biotechnology firms have multiple funding streams from government agencies such as NIH, FDA, DARPA, DoD, DOE and many times these programs and goals overlap with each other and also with academic, private, and philanthropic funding goals. While sometimes overlap and duplication is needed, a clear lack of communication and rampant duplication seemed evident even in our limited firm visits. At present, other than the 2010 *Bioeconomy Blueprint*, there is no guiding document to prioritize federal funding in biotechnology, and no mechanism to eliminate duplication of effort among federal agencies. By incorporating these elements into a revised guidance document, policy makers can improve unity of effort among federal agencies to make the most of limited funding.

While prioritizing efforts and eliminating duplication will be of great benefit, federal agencies must also have a strategy to guide the types of technology being developed to further leverage every research and development dollar. One example is to incorporate a strategy of developing dual use technology. That is, approach discovery and development efforts with the intent to maximize crossover of processes, instrumentation, and technologies to other areas of biotechnology. This will promote a cost sharing culture, further reduce waste in federal efforts, and allow for the potential commercialization of the product. This is of particular benefit for biodefense where the market failure of public goods means the sector is almost exclusively dependent on federal funding to replace the lack of consumer demand.

Recommendation #4: The United States must take action to ensure availability of Science, Technology, Engineering, and Mathematics (STEM) human capital in the innovation pipeline.

The United States' global leadership in the biotechnology industry, relies on its capacity to sustain access to the human capital needs of the industry. International competitors such as China are increasingly recruiting U.S. educated students to return home in an attempt to improve their own ability to innovate. In 2011, the proportion of science and engineering doctorate recipients holding temporary visas was 36% coming primarily from China, India, and South Korea. Within the U.S., students are increasingly entering undergraduate institutions with substandard primary and secondary math and science foundations.[85] In 2009, H1B or temporary skilled worker visa holders constituted only 0.06% of the total American civilian labor force and the cap for H1B visas types has steadily declined in recent history.[86]

Maintaining the skilled workforce necessary to feed the innovation pipeline means enacting policy that encourages U.S. students to enter STEM education programs. It also means partnering with private sector, government, nonprofit organizations, and universities to find creative ways to promote education and careers in science and technology. Finally, policy makers should continue efforts to reform immigration policies to allow H1B and student visa holders to remain in the U.S. after graduation.

Recommendation # 5: Leverage biotechnology capabilities as a national security instrument to address global trends, such as resource scarcity and global health issues which have the potential to cause conflict and regional instability around the globe.

The 2010 National Security Strategy (NSS) states that promoting dignity by meeting basic needs is one of America's values. It further explains that pursuing a comprehensive global health strategy, promoting food security, and leading efforts to address humanitarian crises are actions required to enact that value.[87] The NSS clearly recognizes the national security risk posed by strategic trends such as population growth in poor countries, the spread of infectious diseases, and climate change, all of which will place strain on food, water, and public health resources. As a science with unique capability to mitigate some of these issues, policy makers should embrace biotechnology as a national security instrument. The U.S. position as the global leader in biotechnology is already of incredible economic benefit, but it can also be a tremendous national security benefit if it is integrated with other national security efforts.

These five recommendations taken together set the conditions for realizing the potential of biotechnology as a driver for 21st century economic growth and as an instrument to address national security challenges.

ENDNOTES

[1] Eric Grace, *Biotechnology Unzipped: Promises and Realities*, 2nd ed. (Washington, DC: Joseph Henry Press, 2006), 2.

[2] Yali Friedman, *The Business of Biotechnology: Profit from the Expanding Influence of Biotechnology*, 3rd ed. (Washington, DC: Logos Press, 2008), 3.

[3] Stanford University, "The Triple Helix Concept," accessed May 9, 2013, http://triplehelix.stanford.edu/3helix_concept.

[4] The White House, *National Bioeconomy Blueprint* (Washington, DC: The White House, 2012).

[5] Friedman, *The Business of Biotechnology*, 3.

[6] Sophia Snyder, *IBIS World Industry Report: Biotechnology in the US* (Santa Monica, CA: IBISWorld, August 2012), 3.

[7] Snyder, *IBIS World Industry Report*, 3.

[8] Battelle and Biotechnology Industry Organization (BIO), "Battelle/BIO State Bioscience Industry Development 2012," last modified June2012, accessed March 28, 2013, http://www.bio.org/sites/default/files/v3battelle-bio_2012_industry_development.pdf.

[9] Ibid.

[10] Snyder, *IBIS World Industry Report*, 31.

[11] Ibid.

[12] Ibid.

[13] Ibid., 34.

[14] Stanford University, "The Triple Helix Concept."

[15] Friedman, *The Business of Biotechnology*, 106.

[16] Patent and Trademark Law Amendments Act of 1980, 35 U.S.C. § 200-212 (1980), accessed May 5, 2013, http://www.law.cornell.edu/uscode/text/35/part-II/chapter-18.

[17] Emily P. Walker, "Lawmakers Defend Biologics' 12-Year Exclusivity," *MedPage Today*, last modified October 18, 2011, accessed May 5, 2013, http://www.medpagetoday.com/Washington-Watch/Washington-Watch/29108.

[18] Snyder, *IBIS World Industry Report*, 12.

[19] Friedman, *The Business of Biotechnology*, 109-132.

[20] National Institutes of Health (NIH), "NIH Budget," accessed May 5, 2013, http://www.nih.gov/about/budget.htm.

[21] The White House, *National Bioeconomy Blueprint*.

[22] Snyder, *IBIS World Industry Report*, 34.

[23] Ibid.

[24] Ibid., 35.

[25] Ibid., 5.

[26] Ibid., 9.

[27] Ibid.

[28] Ibid., 2.

[29] Ibid., 17.

[30] Ibid.

[31] Ibid., 19.

[32] Ibid.

[33] Ibid.

[34] Ibid.

[35] Ibid.

[36] Ibid., 4.

[37] Avik Roy, "How the FDA Stifles New Cures, Part I: The Rising Cost of Clinical Trials," *Forbes*, last modified April 24, 2012, accessed May 5, 2013, http://www.forbes.com/sites/aroy/2012/04/24/how-the-fda-stifles-new-cures-part-i-the-rising-cost-of-clinical-trials/.

[38] Snyder, *IBIS World Industry Report*.

[39] "Biopharmaceutical Industry: Market Research Reports, Statistics and Analysis," *Report Linker*, accessed May 5, 2013, http://www.reportlinker.com/ci02235/Biopharmaceutical.html.

[40] The Street, "Sectors and Industries" in "Market Overview", accessed March 2012, http://www.thestreet.com.

[41] U.S. Food and Drug Administration (FDA), "Biological Approvals by Year," accessed March 8, 2013, http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicalApprovalsbyYear/ucm289008.htm.

[42] Ronald Rader, "Approvals Increase from Last year, But Innovation and Health Care and Market Impacts are Limited," *FDA Biopharmaceutical Product Approvals and Trend: 2012*, accessed May 5, 2013, http://www.biopharma.com/approvals_2012.html.

[43] Crystal Franco and Tara Kirk Sell, "Federal Agency Biodefense Funding, FY2012-FY2013," UPMC Center for Health Security, accessed March 24, 2013, http://www.upmcbiosecurity.org/website/resources/publications/2012/biofunds_tables/2012-06-12-biofundsTable01.html.

[44] Frank Grotton, "Project BioShield: Authorities, Appropriations, Acquisitions, and Issues for Congress," *Congressional Research Service*, last modified May 27, 2011, accessed March 27, 2013, http://www.fas.org.ezproxy6.ndu.edu/sgp/crs/terror/R41033.pdf.

[45] Ibid.

[46] Michael E. Porter, "The Five Competitive Forces that Shape Strategy," *Harvard Business Review*, January 2008, 80.

[47] Bryan Cohen, "Senate and House pass PAHPA reauthorization bill," *BioPrep Watch*, last modified March 5, 2013, accessed March 25, 2013, http://www.bioprepwatch.com/news/senate-and-house-pass-pahpa-reauthorization-bill/327986/

[48] U.S. Department of Health and Human Services, Assistant Secretary for Preparedness and Response, "The Public Health Emergency Medical Countermeasure Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs," accessed February 15, 2013, https://www.medicalcountermeasures.gov/media/1138/mcmreviewfinalcover-508.pdf.

[49] Robert Kadlec, "Renewing the Project BioShield Act: What Has it Bought and Wrought?" Center for a New American Security, last modified January 25, 2013, accessed March 23, 2013, http://www.cnas.org/RenewingtheProjectBioShieldAct.

[50] Porter, "The Five Competitive Forces that Shape Strategy," 79-93.

[51] The Street, "Sectors and Industries."

[52] Mark Stevenson, "World's richest men aid 'Green Revolution' center," *Associated Press*, February 13, 2013, accessed March 2, 2013, http://bigstory.ap.org/article/green-revolution-center-sees-future-gm-seeds.

[53] Sara Sendeck, "Fincher Introduces Expediting Agriculture through Science Act," May 27, 2011, linked from *Congressman Stephen Fincher Home Page*, accessed May 8, 2013, http://fincher.house.gov/press-release/fincher-introduces-expediting-agriculture-through-science-act.

[54] Congressional Research Service, *U.S. Foreign Assistance to Sub-Saharan Africa: The FY2012 Request* (Washington, DC: Congressional Research Service, May 20, 2011), 1.

[55] Codexis, Inc., *2012 Annual Report on Form 10K* (Washington, DC: U.S. Securities and Exchange Commission, April 2, 2013), 5.

[56] Snyder, *IBIS World Industry Report*, 17.

[57] U.S. Energy Information Administration, *Monthly Energy Review: February 2013*, February 25, 2013, accessed March 10, 2013, http://www.eia.gov/totalenergy/data/monthly/pdf/sec10_3.pdf.

[58] "Countries: Overview Home Page," U.S. Energy Information Administration, accessed March 10, 2013, http://www.eia.gov/countries/index.cfm?topL=con.

[59] U.S. Energy Information Administration, *Annual Energy Outlook 2013 Early Release Overview*, December 5, 2012, accessed March 10, 2013, http://www.eia.gov/forecasts/aeo/er/pdf/0383er(2013).pdf.

[60] U.S. Energy Information Administration, *Monthly Energy Review: February 2013*.

[61] Ibid.

[62] David Biello, "Can Ethanol from Corn Be Made Sustainable?" *Scientific America*, February 20, 2013, accessed March 10, 2013, http://www.scientificamerican.com/article.cfm?id=can-corn-ethanol-be-made-sustainable.

[63] Claudio Angelo, "Growth of ethanol fuel stalls in Brazil," *Nature*, November 27, 2012, accessed March 10, 2013, http://www.nature.com/news/growth-of-ethanol-fuel-stalls-in-brazil-1.11900.

[64] Interview with representatives from a San Francisco, CA biotechnology firm, April 9, 2013.

[65] "Food Prices," Smarter Fuel Future, accessed March 30, 2013, http://smarterfuelfuture.org/impacts/food-prices.

[66] Anuradha Mittal, "The 2008 Food Price Crisis: Rethinking Food Security Policies," *United Nations Conference on Trade and Development's G-24 Discussion Paper Series, no. 56* (2009): 6, accessed February 23, 2013, http://unctad.org/en/Docs/gdsmdpg2420093_en.pdf.

[67] Food and Agriculture Organization of the United Nations, *OECD-FAO Agricultural Outlook 2012-2021*, (Rome, Italy: FAO Publications, 2012): 3, accessed February 23, 2013, http://www.oecd.org/site/oecd-faoagriculturaloutlook/.

[68] Tracy T. Lefterohf, "Biotech Financing Blues," *Pharmtech.com*, July 2, 2011, accessed March 29, 2013, http://www.pharmtech.com/pharmtech/BioForum/Biotech-Financing-Blues/ArticleStandard/Article/detail/729983?contextCategoryId=49700.

[69] Ibid.

[70] Ibid.

[71] John M. Clerici, Esq., *Taking Measure of Countermeasures (Part 1): Testimony before the U.S. House of Representatives Committee on Homeland Security, Subcommittee on Emergency Preparedness, Response, and Communications*, April 13, 2011.

[72] Ibid.

[73] Michael Lawlor, "Biotechnology and Government Funding," *Challenge*, vol. 46, no. 1, (January/February 2003): 15.

[74] Sarah Bacon, "Medical Research Cuts Have Immediate Health Effects," *The Atlantic*, April 17, 2013, accessed May 5, 2013, http://www.theatlantic.com/health/archive/2013/04/medical-research-cuts-have-immediate-health-effects/275045/.

[75] Snyder, *IBIS World Industry Report*, 11.

[76] Ibid.

[77] Ibid.

[78]Thomas Hawk, "What Do Voters Think About the Biotechnology Industry?" *Biotechnology Industry Organization*, July 29, 2013, accessed March 6, 2013, http://www.bio.org/articles/what-do-voters-think-about-biotechnology-industry.

[79] Snyder, *IBIS World Industry Report*, 7.

[80] James Greenwood, "Biotech in China," *European Biopharmaceutical Review*, January, 2013, accessed May 5, 2013, http://www.bio.org/sites/default/files/Biotechnology-Industry-Pg62-64.pdf.

[81] Ibid.

[82] Snyder, *IBIS World Industry Report*, 36.

[83] Ibid.

[84] Ibid., 6.

[85] Livia Racz, "Stem in Biotechnology" (lecture, National Defense University, Washington, D.C., March 1, 2013).

[86] "Top H1B Visa Sponsor," My Visa Jobs, accessed March 27, 2013, http://www.myvisajobs.com/Reports/2012-H1B-Visa-Category.aspx?T=IN.

[87] The White House, *National Security Strategy* (Washington, DC: The White House, 2010).

BIBLIOGRAHPY

Angelo, Claudio. "Growth of ethanol fuel stalls in Brazil." *Nature*. Last modified November 27, 2012. Accessed March 10, 2013. http://www.nature.com/news/growth-of-ethanol-fuel-stalls-in-brazil-1.11900.

Bacon, Sarah. "Medical Research Cuts Have Immediate Health Effects," *The Atlantic*. Last modified April 17, 2013. Accessed May 5, 2013. http://www.theatlantic.com/health/archive/2013/04/medical-research-cuts-have-immediate-health-effects/275045/.

Battelle and Biotechnology Industry Organization (BIO). "Battelle/BIO State Bioscience Industry Development 2012." Last modified June, 2012. Accessed March 28, 2013. http://www.bio.org/sites/default/files/v3battelle-bio_2012_industry_development.pdf.

Biello, David. "Can Ethanol from Corn Be Made Sustainable?" *Scientific America*. Last modified February 20, 2013. Accessed March 10, 2013. http://www.scientificamerican.com/article.cfm?id=can-corn-ethanol-be-made-sustainable.

"Biopharmaceutical Industry: Market Research Reports, Statistics and Analysis." *Report Linker*. Accessed May 5, 2013. http://www.reportlinker.com/ci02235/Biopharmaceutical.html.

Codexis, Inc. *2012 Annual Report on Form 10K*. April 2, 2013.

Cohen, Bryan. "Senate and House pass PAHPA reauthorization bill." *BioPrep Watch*. Last modified March 5, 2013. Accessed March 25, 2013. http://www.bioprepwatch.com/news/senate-and-house-pass-pahpa-reauthorization-bill/327986/.

Arieff, Alexis et al. "U.S. Foreign Assistance to Sub-Saharan Africa: The FY2012 Request." *Congressional Research Service*. Last modified May 20, 2011. Accessed May 13, 2013. http://www.fas.org/sgp/crs/row/R41840.pdf.

Food and Agriculture Organization of the United Nations. "OECD-FAO Agricultural Outlook 2012-2021." Accessed February 23, 2013. http://www.oecd.org/site/oecd-faoagriculturaloutlook/.

Franco, Crystal and Tara Kirk Sell. "Federal Agency Biodefense Funding, FY2012-FY2013." UPMC Center for Health Security. Accessed March 24, 2013. http://www.upmcbiosecurity.org/website/resources/publications/2012/biofunds_tables/2012-06-12-biofundsTable01.html.

Friedman, Yali. *The Business of Biotechnology: Profit from the Expanding Influence of Biotechnology.* 3rd ed. Washington, DC: Logos Press, 2008.

Grace, Eric. *Biotechnology Unzipped: Promises and Realities.* 2nd ed. Washington, DC: Joseph Henry Press, 2006.

Greenwood, James. "Biotech in China." *European Biopharmaceutical Review*. Last modified January, 2013. Accessed May 5, 2013. http://www.bio.org/sites/default/files/Biotechnology-Industry-Pg62-64.pdf.

Grotton, Frank. "Project BioShield: Authorities, Appropriations, Acquisitions, and Issues for Congress." *Congressional Research Service*. Last modified May 27, 2011. Accessed March 27, 2013. http://www.fas.org.ezproxy6.ndu.edu/sgp/crs/terror/R41033.pdf.

Hawk, Thomas. "What Do Voters Think About the Biotechnology Industry?" *Biotechnology Industry Organization*. Last modified July 29, 2013. Accessed March 6, 2013. http://www.bio.org/articles/what-do-voters-think-about-biotechnology-industry.

Interview with representatives from a San Francisco, CA biotechnology firm, April 9, 2013.

Kadlec, Robert. "Renewing the Project BioShield Act: What Has it Bought and Wrought?" Center for a New American Security. Last modified January 25, 2013. Accessed March 23, 2013. http://www.cnas.org/RenewingtheProjectBioShieldAct.

Lawlor, Michael. "Biotechnology and Government Funding." *Challenge*. January/February 2003.

Lefterohf, Tracy T. "Biotech Financing Blues." *Pharmtech.com.* Last modified July 2, 2011. Accessed March 29, 2013. http://www.pharmtech.com/pharmtech/BioForum/Biotech-Financing-Blues/ArticleStandard/Article/detail/729983?contextCategoryId=49700.

Mittal, Anuradha. "The 2008 Food Price Crisis: Rethinking Food Security Policies." *United Nations Conference on Trade and Development's G-24 Discussion Paper Series, no. 56* (2009). Accessed February 23, 2013, http://unctad.org/en/Docs/gdsmdpg2420093_en.pdf.

My Visa Jobs. "Top H1B Visa Sponsor." Accessed March 27, 2013. http://www.myvisajobs.com/Reports/2012-H1B-Visa-Category.aspx?T=IN.

National Institutes of Health (NIH). "NIH Budget." Accessed May 5, 2013. http://www.nih.gov/about/budget.htm.

Patent and Trademark Law Amendments Act of 1980. 35 U.S.C. § 200-212 (1980). Accessed May 5, 2013. http://www.law.cornell.edu/uscode/text/35/part-II/chapter-18.

Porter, Michael. "The Five Competitive Forces that Shape Strategy." *Harvard Business Review*, January 2008.

Racz, Livia. "Stem in Biotechnology." Lecture presented at the National Defense University, Washington, D.C., March 1, 2013.

Rader, Ronald. "Approvals Increase from Last year, But Innovation and Health Care and Market Impacts are Limited." *FDA Biopharmaceutical Product Approvals and Trends: 2012*. Accessed May 5, 2013. http://www.biopharma.com/approvals_2012.html.

Roy, Avik. "How the FDA Stifles New Cures, Part I: The Rising Cost of Clinical Trials." *Forbes*. Last modified April 24, 2012. Accessed May 5, 2013. http://www.forbes.com/sites/aroy/2012/04/24/how-the-fda-stifles-new-cures-part-i-the-rising-cost-of-clinical-trials/.

Sendeck, Sara. "Fincher Introduces Expediting Agriculture through Science Act." Last modified May 27, 2011. Accessed May 8, 2013. http://fincher.house.gov/press-release/fincher-introduces-expediting-agriculture-through-science-act.

Smarter Fuel Future. "Food Prices." Accessed March 30, 2013. http://smarterfuelfuture.org/impacts/food-prices.

Snyder, Sophia. *IBIS World Industry Report: Biotechnology in the US.* Santa Monica, CA: IBISWorld, August 2012.

Stanford University. "The Triple Helix Concept." Accessed May 9, 2013. http://triplehelix.stanford.edu/3helix_concept.

Stevenson, Mark. "World's richest men aid 'Green Revolution' center." *Associated Press.* Last modified February 13, 2013. Accessed March 2, 2013. http://bigstory.ap.org/article/green-revolution-center-sees-future-gm-seeds.

Taking Measure of Countermeasures (Part 1): Testimony before the U.S. House of Representatives Committee on Homeland Security, Subcommittee on Emergency Preparedness, Response, and Communications (April 13, 2011) (statement of John M. Clerici, Esq.).

The Street. "Sectors and Industries" in "Market Overview". Accessed March 2012. http://www.thestreet.com.

The White House. *National Bioeconomy Blueprint.* Washington, DC: The White House, 2012.

The White House. *National Security Strategy.* Washington, DC: The White House, 2010.

U.S. Department of Health and Human Services, Assistant Secretary for Preparedness and Response. "The Public Health Emergency Medical Countermeasure Enterprise Review: Transforming the Enterprise to Meet Long-Range National Needs." Accessed February 15, 2013. https://www.medicalcountermeasures.gov/media/1138/mcmreviewfinalcover-508.pdf.

U.S. Energy Information Administration. "Annual Energy Outlook 2013 Early Release Overview." Last modified December 5, 2012. Accessed March 10, 2013. http://www.eia.gov/forecasts/aeo/er/pdf/0383er(2013).pdf.

U.S. Energy Information Administration. "Countries: Overview Home Page." Accessed March 10, 2013. http://www.eia.gov/countries/index.cfm?topL=con.

U.S. Energy Information Administration. "Monthly Energy Review: February 2013." Last modified February 25, 2013. Accessed March 10, 2013. http://www.eia.gov/totalenergy/data/monthly/pdf/sec10_3.pdf.

U.S. Food and Drug Administration (FDA). "Biological Approvals by Year." Accessed March 8, 2013. http://www.fda.gov/BiologicsBloodVaccines/DevelopmentApprovalProcess/BiologicalApprovalsbyYear/ucm289008.htm.

Walker, Emily. "Lawmakers Defend Biologics' 12-Year Exclusivity." *MedPage Today*. Last modified October 18, 2011. Accessed May 5, 2013. http://www.medpagetoday.com/Washington-Watch/Washington-Watch/29108.