

TURNING PLANTS INTO PRODUCTS

Delivering on the Potential
of Industrial Biotechnology

FINANCIAL INNOVATIONS LAB™ REPORT





MILKEN INSTITUTE

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This report was prepared by Mark Conolly and Joel Kurtzman.

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FINANCIAL INNOVATIONS LAB™ REPORT

Financial Innovations Labs™ bring together researchers, policymakers, and business, financial, and professional practitioners for a series of meetings to create market-based solutions to business and public-policy challenges. Using real and simulated case studies, participants consider and design alternative capital structures and then apply appropriate financial technologies to them.

This Financial Innovations Lab report was prepared by Joel Kurtzman, Senior Fellow, Executive Director of the Center for a Sustainable Energy Future, and Mark Conolly, Research Analyst.

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We are nonprofit, nonpartisan, and publicly supported.

TABLE OF CONTENTS

INTRODUCTION.....	1
ISSUES AND PERSPECTIVE	4
Substitutes From an Unlikely Source	
Competing With Petrochemicals	
Environmental Benefits	
Regional Benefits	
Financing and Development of Joint Ventures	
Scope of the Market	
Technical Benefits	
Conclusion	
OBSTACLES FOR INDUSTRIAL BIOTECHNOLOGY.....	12
Barrier 1: Policy uncertainty and complexity restrict firm activity	
Barrier 2: Industry lacks coordinated support from R&D through scale-up and commercialization	
Barrier 3: Long value chains asymmetrically distribute the gains from developing new products	
Barrier 4: Feedstock costs and energy prices are volatile	
Barrier 5: Short investment horizon does not match long gestation timeline	
Barrier 6: Cost of capital is restrictively high due to high risk premiums	
Barrier 7: Lack of capital became a crisis	
Barrier 8: Investors lack awareness, and consumer demand is undeveloped	
CRAFTING SOLUTIONS: FINANCIAL AND POLICY INNOVATIONS	18
Recommendation 1: Establish concrete, long-term government policies	
Recommendation 2: Create prize forums to bolster early-stage innovation	
Recommendation 3: Create partnerships to share development costs (and disseminate knowledge of the sector)	
Recommendation 4: Utilize established resources to lower costs, accelerate development, and reduce risk	
Recommendation 5: Upgrade infrastructure	
Recommendation 6: Create innovative securitization and de-risk equity investment	
Recommendation 7: Innovate financial instruments with government-backed investment options	
MOVING FORWARD: FUTURE POLICY CONSIDERATIONS	24
APPENDIX	26
ENDNOTES.....	27

Our goal as an administration
is to set up an economy that
is self-sustaining.

— Sarah Bittleman, senior advisor
to the secretary of agriculture

Introduction

As interest in sustainability grows in the United States and around the world, there is a push by policymakers and the industrial biotechnology industry to find replacements for petroleum. This is the case not only in transportation industries but also in the industrial and chemical sectors.

Industrial biotechnology uses such biological resources as plants, algae, marine life, fungi and microorganisms, and biosolids to produce a broad range of products from plastics and chemicals to face creams and detergents. Packaging materials and bottles made from non-petroleum-derived chemicals are already used by Coca-Cola, PepsiCo, and other large companies that have made a commitment to becoming more environmentally friendly. Bioplastics have also proved useful in medical implants and stitches that dissolve. Similarly, compostable mulch films used in agriculture can be left in the fields to biodegrade on their own.

These products, some of which require fewer steps, in some cases are easier on the environment. These substitutes, particularly bio-based plastics, offer a product that can be engineered to degrade more easily in landfills than traditional plastic, meets product needs that cannot be met through traditional plastic production, can be made to be more durable, can be tailored to be more precise compounds, and may require less energy to manufacture.

Instead of petroleum, industrial biotechnology uses homegrown biomass such as wood, plant waste, and biogas as the primary feedstock to make the base chemicals. Bio-based plastics are also used as supplements in plastic manufacturing, combining petro-based and bio-based plastics in different layers within the same product to expand the potential applications.

Making plastics and other consumer goods from living material can address many environmental and sustainability issues, depending on the specific product and taking into account all the inputs and outputs over the life of the product through a full life-cycle assessment (LCA) of its environmental impacts. However, the industrial biotechnology industry faces strong competition from petroleum. Petroleum-based products are often cheaper, and industrial biotechnology has the disadvantage of being a new industry with a short tradition of sparse investment. This may largely be due to short production runs and limited production capacity for bio-based products. Furthermore, petroleum prices do not include such negative externalities as polluted runoff and protecting the petroleum supply line from overseas. Therefore, prices for petroleum-based products underestimate the full market and environmental cost of their use.

Why Industrial Biotechnology?

- It provides new pathways to create **chemicals** and **substitutes** for existing consumer products.
- It provides **more efficient** means of creating popularly used chemicals and end products.
- It uses **renewable** biomass as a feedstock for chemical manufacturing.
- It creates **new market possibilities** for agricultural waste products.
- It **reduces dependence** on imported petroleum products.
- It provides a chemical production mechanism that may be **sheltered from the volatility** of the petroleum market.

BioPreferredSM Program

BioPreferred, a product of the 2002 and 2008 Farm Bills, directs spending on the part of government agencies to purchase products derived from renewable biomass feedstocks. The preferred procurement measure compels federal agencies and their contractors to purchase and expand the use of bio-based products. It also includes a component that allows products that meet environmental standards after a full life-cycle assessment to qualify for preferred procurement. The bio-based content of consumer products can be mixed with petroleum-based content at varying ratios depending on the severity of the performance requirements of the product. For instance, fuel lines that require a more resilient plastic are allowed to have a higher percentage content of petroleum-based plastic, as petroleum-based plastics can be stronger. Eventually, the BioPreferred designation will not be limited to just the final product, but will also include intermediary ingredients and feedstock chemicals that are derived from biomass.

The BioPreferred program also will have a fully developed voluntary labeling program to make it easier for bio-based products to be identified by government purchasers and general consumers. The labels are considered to be an incentive in the marketplace due to elements of consumer preference for renewable products.

Agencies may side-step the BioPreferred purchasing requirements under the following conditions:

- The product is not available within a reasonable time period.
- The product is available only at an unreasonable price.
- The product fails to meet the performance standard of the procuring agency.
- The agency is purchasing for combat or space-related use.

There is much appeal for policymakers to invest in expanding this industry. In the long term, it has environmental advantages and offers an alternative to foreign oil. It also has the immediate benefits of increased employment and diversified income streams in agricultural regions. As Sarah Bittleman, senior advisor to Secretary of Agriculture Tom Vilsack, recently said, agriculture is the only sector in which the United States has a positive trade balance with the rest of the world, and it provides rural employment opportunities as well as an alternative to foreign oil.

Developing the bio-based products industry will require not only the participation but also the organized cooperation of local, state, and federal governments, the investment community, trade organizations, and academia. Currently, the complexity of the industry and the immense investment required to commercialize a bio-based product, aside from joint ventures, have resulted in low investment participation and large attrition rates, particularly for underfunded biofuels start-up companies.

The industry needs to find the momentum to get companies past the funding gaps and on to commercial-scale production. This will require continued investment in R&D, supported by the government and public-private partnerships to make the investment less risky and to increase the efficacy of the technology in development.

Participants in the industry attribute some of the success of bio-based products thus far to the program that became BioPreferred—initiated in the 2002 Farm Bill, and then expanded in the 2008 Farm Bill. The program encourages federal agencies and contractors to purchase bio-based products, and provides a voluntary labeling program to promote the marketing of bio-based products. A growing desire by consumers for environmentally preferable products and by manufacturers for new and novel product applications has also spurred industry development.

However, preferred procurement eligibility is something of a moving target. To be labeled bio-based, a product's content must meet the required threshold of bio-based material for its designated category. If the product does not fall into a designated category, it must contain a minimum of 25 percent bio-based content for eligibility unless the applicant applies for and receives an alternative minimum bio-based content allowance. In addition, federal agencies are compelled to buy bio-based products only if the costs are reasonable and the products are functionally equivalent, but functional equivalence opens the door to flexible thresholds under which performance and the specific use determine the minimum bio-based content. For instance, plastics used in fuel lines must be robust and resistant to corrosion, so a higher petro-based plastic content is required for the fuel lines to be functional equivalents. Government inertia, comparable costs, functional equivalence, and lack of a competitive number of suppliers all present opportunities for government agencies to avoid this procurement requirement.

Despite these issues, the BioPreferred program has partially de-risked investment in biotechnology by assuring a minimum, consistent demand that will continue to grow as federal government procurement becomes more established.

How can the United States facilitate the flow of private capital into the production of bio-based products? To answer that question, a Financial Innovations Lab, developed and funded by the Milken Institute and the Office of Energy Policy and New Uses at the U.S. Department of Agriculture, was convened in July 2010 in Washington, D.C. This event gathered leading scientists and technologists, bio-based product producers, banks, institutional investors, venture capitalists, public officials, and representatives from think tanks and industry associations. Together they identified practical solutions for encouraging investment and helping this fledgling industry mature, building a greener economy in the process.

Issues and Perspective

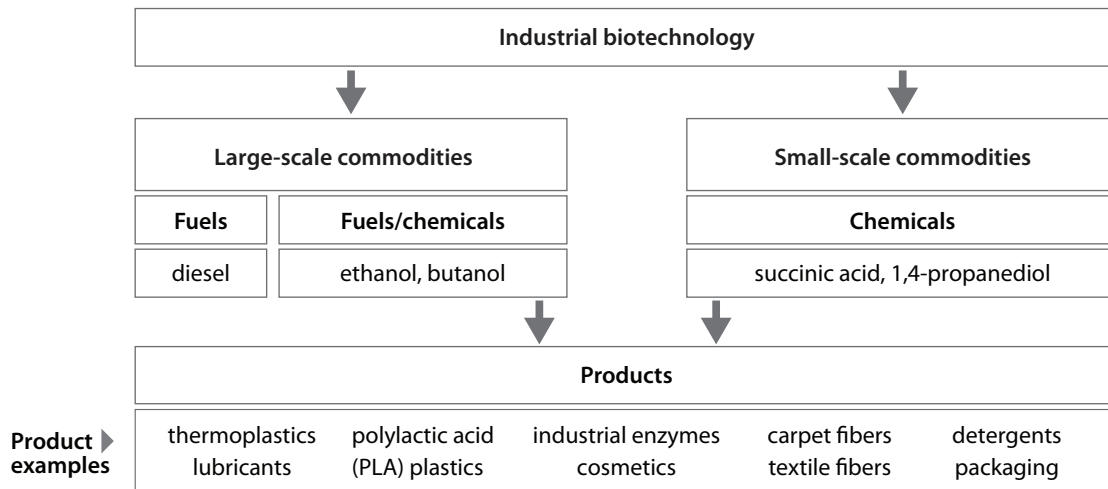
Substitutes From an Unlikely Source

The industrial biotechnology industry is involved in the production and processing of chemicals, pharmaceuticals, materials, and bioenergy using enzymes, bacteria, yeast, or other biological pathways with low energy requirements. It uses microorganisms and enzymatic catalysis instead of petrochemicals and high heat and pressure conditions. Feedstocks are from agricultural starches or lignocellulosic residues instead of petroleum-based products. Biotechnology has several subcategories, sometimes identified by color: Pharmaceuticals (red), agriculture (green), marine biotechnology (blue), and industrial biotechnology (white). The Financial Innovations Lab focused on white biotechnology as a replacement for petrochemical feedstocks with base chemicals that have been derived through biological pathways using biomass as feedstocks. These base chemicals are sold as commodities based on living materials and then polymerized into larger compounds that are fashioned into consumer goods like bottles.

FIGURE
1

What is industrial biotechnology?

Industrial biotechnology is the pathway through which enzymes and microorganisms are used to create chemicals, energy, and materials for industrial uses from a carbon feedstock of biomass and living materials.



Source: "White Technology: Ready to Partner and Invest In," Manfred Kirchner (2006).

The industry requires huge amounts of long-term investment while R&D is under way. The research requires access to expensive labs with large teams of highly skilled experts. The facilities to prove the technology also require large amounts of investment because they require all the resources and equipment of biological laboratories

and biorefineries at the same time. The average time from inception to commercialization of a technology is seven to 10 years—even longer than the timeline for pharmaceuticals—assuming the developers have secured funding for that amount of time.

The most successful businesses to date in industrial biotechnology have been joint ventures that match agricultural companies with established chemical companies that have developed agricultural products: Metabolix joining with Archer Daniels Midland to form Telles, a plastic biorefinery; Cargill and Dow partnering on Natureworks; and DuPont's pending acquisition of Danisco. While these operations are relatively successful in the biomaterials sphere, they still face a cost disadvantage compared to petroleum-derived products. For example, Telles produces its resins for \$1.50 per pound, while the traditional plastics industry can produce equivalent resins for 70 percent of that cost.¹ Bio-based polylactic acid (PLA) plastic costs 20 percent more to produce than the petroleum-based product it is meant to replace.² Other bioplastics can cost two to three times more than petroleum-based plastics. This is partially due to the fact that industrial biotechnology companies have not had the chance to perfect and streamline their processes or reach adequate economies of scale.

Competing With Petrochemicals

Unlike industrial biotechnology, the petrochemicals industry is well-established, with fully amortized facilities, economies of scale, and entrenched processes for operating efficiently. Because petroleum-based chemicals used in plastic manufacturing are derived from the refining process for petroleum, they are readily available—and will continue to be available as long as there is U.S. demand for gasoline and the refining is done domestically.

Contributing to biotechnology's price disadvantage is that petroleum prices don't take into account increased defense spending to secure petroleum shipping lines, potential effects on climate change, disturbances from unfriendly oil-producing countries, and the imbalance of international trade. Using domestic biomass feedstocks largely avoids these negative effects of fossil energy-based industrial product production.

Petroleum-based chemicals represent about 3 percent (1.2 gallons) of each barrel of oil,³ although the yields vary with the type of petroleum being refined (sweet crude, oil shale, etc.). Petroleum feedstocks are also derived from natural gas liquids before they enter utility transmission lines. In 2006, the United States consumed 7.55 billion barrels of petroleum, mostly to satiate the demand for gasoline. The refining process produced about 251 million barrels of petroleum-derived feedstock base chemicals, and roughly 80 million barrels came from natural gas liquids, for a total of approximately 331 million barrels of oil used for plastic and resin manufacturing.

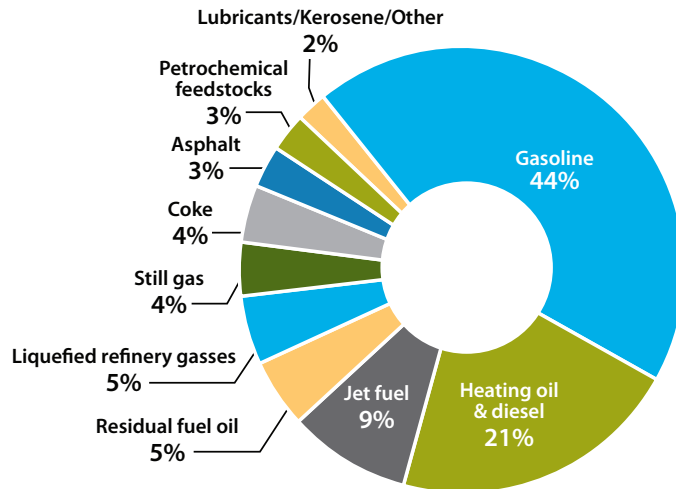
The degree of price competition varies by the cost and end-use value of the product itself, applicable subsidies, and the location of manufacturing. As one example, depending on the application, the performance and weight of some bioresins result in cost reduction compared to many petroleum-based substitutes. As another, high-octane fuels used in auto racing are more expensive than common retail gasoline, so these high-end fuels—which make up 10 percent of refined products—are one area where biofuels could capture part of the market because the prices of both are competitive.

FIGURE
2

How one barrel of refined petroleum is used

Petroleum Products

Contents of one barrel of refined petroleum
(44.2 gallons after refining)



Source: American Petroleum Institute.

The consistent supply of base chemicals for petroleum-based plastics makes these products inexpensive. In contrast, the bio-based materials industry transforms every unit of base chemical at relatively high costs with no gasoline-like by-product to sell. Biorefineries are relatively young and are forced to mature while competing with established petro-refineries.⁴

Chemical products are extremely sensitive to feedstock cost, so the more stable the price of biomass feedstocks for biotechnology, the lower the risk of investment and hence the lower the cost of capital—and vice versa. Cellulosic conversion of commodity-based chemicals offers a steadier supply of feedstocks and can help resolve the issue of feedstock sensitivity. A more robust industry will have a steadier agricultural feedstock market.⁵

The industry for petroleum-based products has achieved economies of scale over the past 100 years; meanwhile, the young technologies used in bio-based product manufacturing are still being developed. With increased scale and experience, lower costs can eventually be achieved. Instead of importing oil from countries that are not friendly to American interests, the nation could use its abundance of suitable homegrown organic material for biofuels and bioplastics.

Environmental Benefits

Replacing petroleum products with bio-based substitutes has many environmental benefits, including less processing, transportation, handling, and easier end-use disposal of compounds that are harmful to humans and habitats. Industrial biotechnology processing also requires less energy than petroleum-based products do. In fact, NatureWorks claims its products can be produced with 25 percent to 68 percent less energy than fossil fuel products use in the manufacturing process. In addition, products derived from biomass take up less space in landfills and can be engineered to break down faster than petroleum products do. When they do break down, there is no net addition to atmospheric carbon dioxide, unlike petroleum-based products. Industrial biotech products can be engineered for ease of disposal (biodegradability), or for strength and durability, as the use application requires.

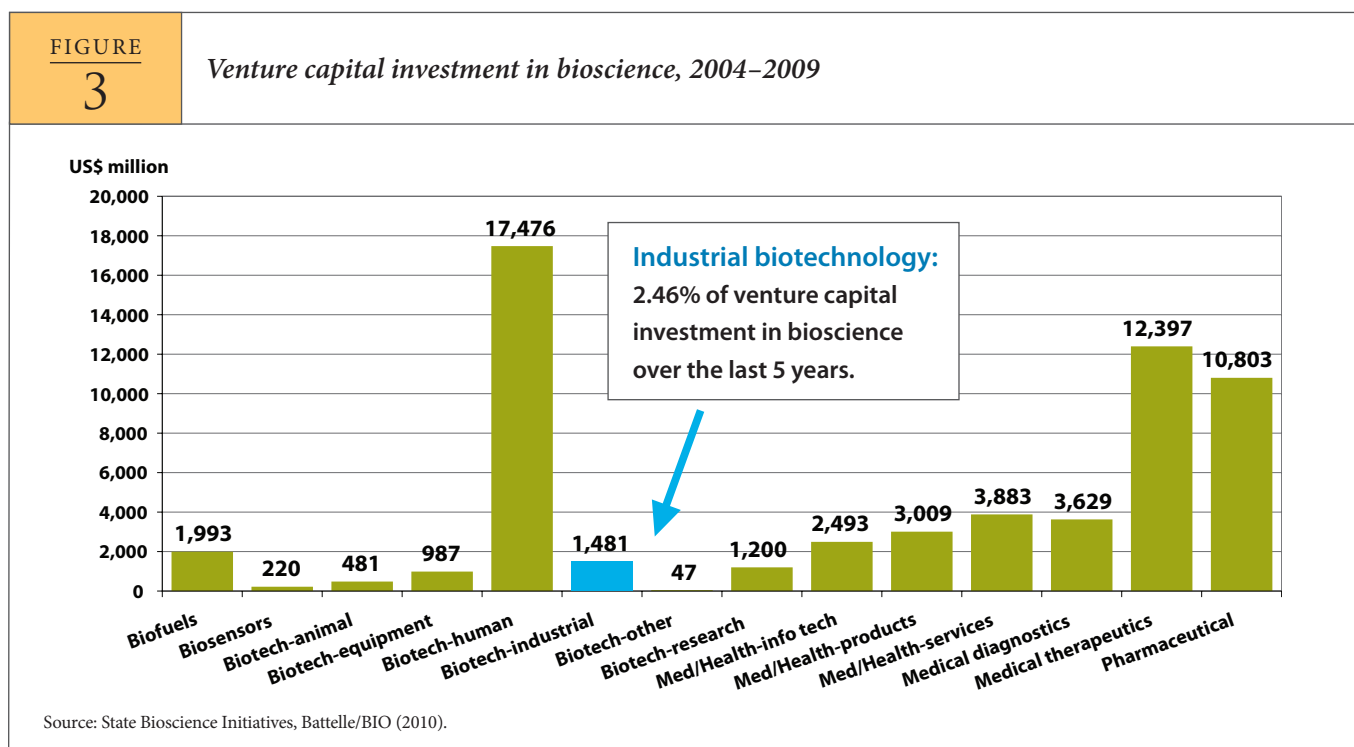
One caveat to biodegradability is that the more durable the product, the less biodegradable it is likely to be.⁶ But even if these products are not as biodegradable, they are valuable because they support the concept of producing substitutes for petroleum-based products.

Regional Benefits

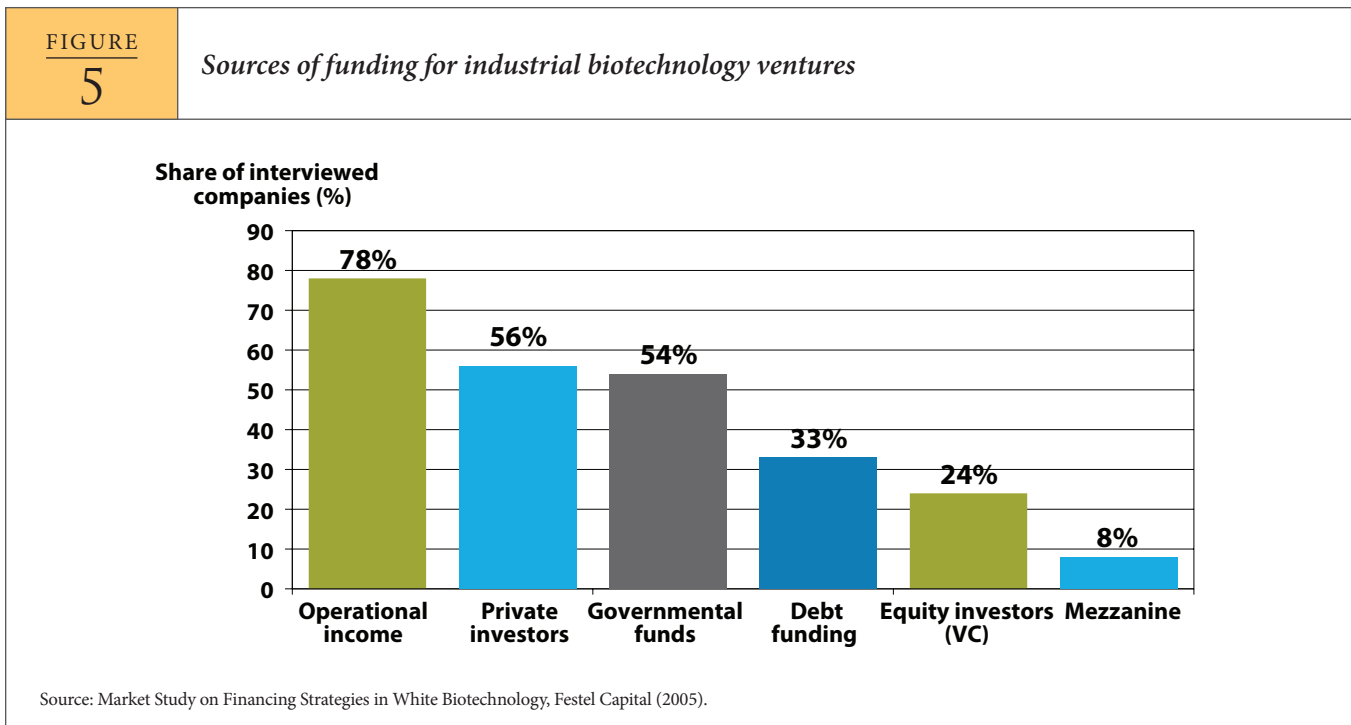
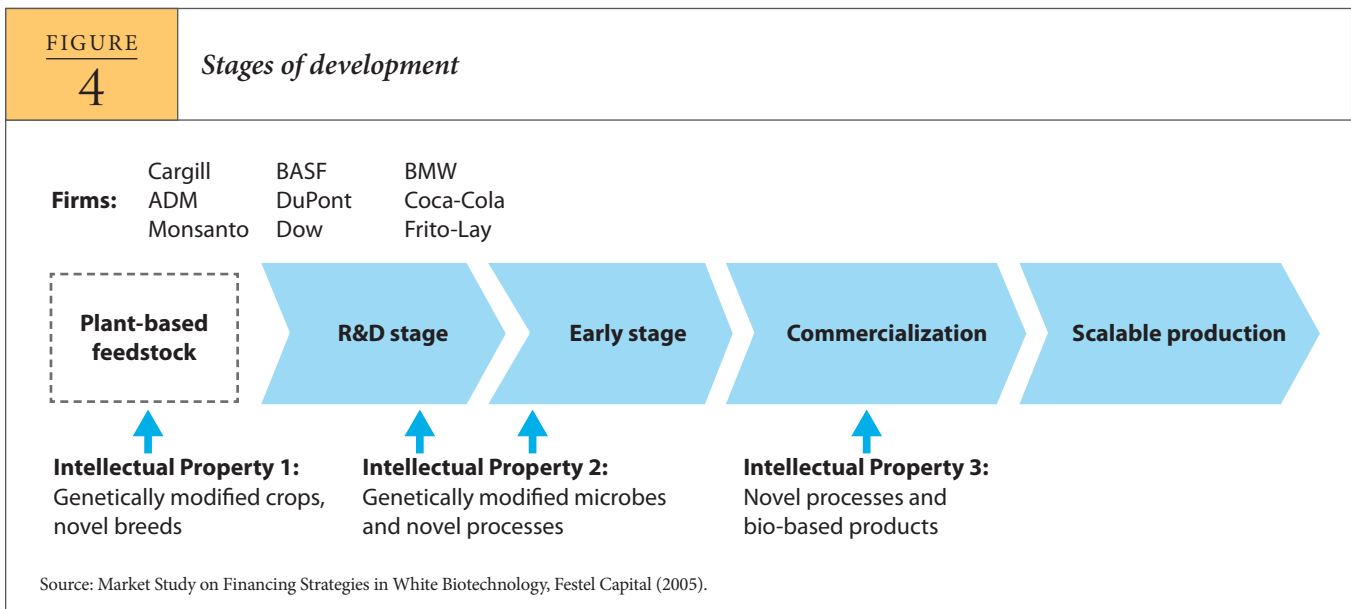
The industrial biotechnology industry provides opportunities in agriculture because it diverts consumers' money away from foreign petroleum producers to domestic producers of renewable feedstock crops. It is inherently more efficient to have biorefineries in agricultural areas, closer to their feedstocks, than the current system of purchasing petroleum from foreign sources and refining it near the ports where the petroleum arrives by tanker. U.S. policy should attempt to keep that money in the regional economy, especially when it can benefit domestic agriculture. The proliferation of industrial biotechnology to create bio-based products can lead to significant rural development through investment in new production facilities, job creation, and ancillary economic activity.

Financing and Development of Joint Ventures

From 2004 to 2009, industrial biotechnology took in just \$1.48 billion in venture capital investment (figure 3). For comparison, the pharmaceutical industry took in \$10.8 billion in venture capital in that same period. Reflecting the change in investment climate after the economic downturn, venture capital investment in all biosciences plunged 36.7 percent between 2008 and 2009, from \$12.27 billion to \$7.77 billion. Industrial biotechnology represents about 8 percent of the bioscience sector's employment, and about 10 percent of the sector's net income, earning \$7.73 billion in 2009. Average total investment per company in the biosciences sector is \$10.3 million in the early stage and \$30.5 million when a company is eventually acquired.⁷



In industrial biotechnology and tech in general, start-ups are starved for investment, particularly between stages of development (figure 4). Biotech firms, among the most idea-intensive businesses, depend heavily on intellectual content that is costly to produce.⁸ According to a study concluded in 2007, R&D spending for all U.S. industries over a 25-year period was 3 percent of total firm assets, compared to 38 percent for biotechnology companies over the same period.⁹ Once a product is developed, smaller companies then must scale up to production. To finance R&D and production, companies often license their intellectual property to bigger companies or seek strategic equity investment from larger companies like BASF Plant Science, Cargill, and DuPont.¹⁰



Life-Cycle Assessment

Life-cycle assessment (LCA) is a critical assessment of the environmental footprint of a manufactured product that takes into account all inputs and outputs of all stages of production. It is a comprehensive calculation that allows producers, policymakers, and consumers to understand whether there are effective environmental benefits to using one product over another and to what degree it may be beneficial. LCA follows products from “cradle to grave” using an analytic framework to capture the the environmental impact of any product, including bio-based products.

The USDA uses standardized life-cycle assessment tools established under BEES (Building for Environmental and Economic Sustainability) to determine the eligibility of products for preferred procurement under the BioPreferred program. LCA methodology considers the economic externalities in terms of environmental footprint in four steps. First the goal and scope are defined, and then the inventory analysis compiles the inputs and outputs through a product’s life-cycle, which includes inventory flows of water, energy, air emissions, and land and resource use. The third step calculates the impact of all the components of the inventory. In the final step, the impacts are interpreted according to the goals of the study and can be compared to identical assessments of other products.

Securing financing has become even more difficult for start-ups since the recent financial crisis. The gaps in funding that occur between academic research and commercialization are numerous and potentially fatal to a small company. This is due not only to sparse funding options but also to a lack of strategic partners for R&D.¹¹

Scope of the Market

Bioplastics currently make up less than 1 percent of the U.S. plastics market.¹² Carving out a bigger piece of the market is an uphill battle for bioplastics because price competition among existing products is fierce, the profit margin is narrow, and the supply of feedstocks from petroleum refining is steady and plentiful.

While prices for intermediate products such as PLA and succinic acid are competitive, other products’ pricing can be problematic. If price competition were resolved, bioplastics could become a functional substitute for 10 percent to 20 percent of all plastics by 2020. In fact, with the right regulatory and market conditions, bio-based fibers and other polymers have the potential to replace 90 percent of these petroleum-based equivalents.¹³ In 2007, analysts at Jefferies & Co. believed that just one bioplastics producer, Metabolix, would create a significant niche in the disposable plastics market—which is 20 percent of the entire plastics market—solely because of customers looking for a greener, more sustainable product.¹⁴

Biologically derived chemicals also have applications in cosmetics, food production enzymes, and an assortment of specialty chemicals. A report estimated that 2004 sales of biologically derived chemicals were 5 percent of the global chemicals market.¹⁵ In 2007, biochemicals represented 3.5 percent of Europe’s total chemical sales and

were expected to reach 15 percent by 2017.¹⁶ Bio-based materials could hypothetically replace up to 55 percent of petroleum-based materials.¹⁷ The U.S. can optimize its competitive position in this global market by increasing its rates of adoption and becoming an early provider of these products in the marketplace.

Technical Benefits

Compared to the petroleum refining process, the industrial biotechnology pathway has the advantage of being able to produce chemicals more precisely. The microbes used to digest the agricultural carbon source can be designed to produce specific chemicals and do so with lower levels of unwanted by-products than traditional methods produce.¹⁸ When chemicals are produced, they present in the desired form or in their enantiomeric opposite, which has the same atoms but is configured in the molecular mirror image of the desired chemical. In producing enzymes and other specialty chemicals, it is important to get the enantiomerically pure chemical because enantiomeric purity results in significant cost savings. This advantage of industrial biotechnology will be further improved by efficiency gains as the industry expands.

Conclusion

The debate continues over whether biomaterials are better for the environment than petroleum-derived products, accounting for energy consumption on the front end of production. Opponents argue that, while industrial biotechnology offers the opportunity to eliminate fossil fuels from certain products, petroleum is still required for servicing farm vehicles, transporting crops, spreading fertilizer, and moving irrigation equipment. But this argument, previously used against biofuels, is based on old data and faulty assumptions. In fact, the net energy balance for corn-based biofuels is over 2.3 times more than the energy input,¹⁹ and that return is rising as the industry gains experience and efficiencies of scale.

In addition, jobs will be created domestically as a result of growing this industry. Some other benefits include applications for the end of the product's life such as composting, in addition to creating a new market for agricultural by-products.

Policymakers and investors know little about the industry. Disparate efforts and poor coordination in incubating the technology continue to hamper the industry's efforts to become self-sustaining. Policymakers can organize the research and execution of the industry starting with repurposing elements already in existence from the biofuels industry. This provides assistance not only in capital investment but also in the logistics of the permitting process. Overcoming these challenges requires careful coordination between academia and the different stages of the value chain that require R&D and intellectual property resources.²⁰ There are efforts to streamline the policies that will affect industrial biotechnology on an international level. The Organisation for Economic Co-operation and Development (OECD) is developing a set of alternative metrics that will allow for accurate comparisons of cost and sustainability, including such externalities as the energy consumed during production. This will create a better understanding of the differences in the true cost and social impact of each product.

TABLE
A

Petroleum-based and bio-based plastics

PETROLEUM-BASED PLASTICS	
Polyethylene terephthalate (PET or PETE):	Beverage bottles, food containers, luggage, carpet, furniture
High-density polyethylene (HDPE):	Flexible liquid chemical containers, grocery bags, milk cartons
Polyvinyl chloride (PVC):	Pipes, windows, siding, insulation film, medical tubing
Low-density polyethylene (LDPE):	Produce bags, cling film, flexible lids
Polypropylene (PP):	Packaging, ketchup bottles, automobile battery casings, medicine bottles
Polystyrene (PS):	Egg crates, fast-food restaurant trays
OTHER PLASTICS	
Nylon in toothbrushes and clothing, Teflon for non-stick pans, and light covers for vehicles and traffic lights	

Source: American Chemistry Plastics Overview

BIOPLASTICS	
Poly-lactic acid (PLA) plastics	PLA is a transparent plastic produced from cane sugar or glucose. It not only resembles conventional petrochemical mass plastics (like PE or PP) in its characteristics, but it can also be processed easily on standard equipment that already exists for the production of conventional plastics. PLA and PLA blends generally come in the form of granulates with various properties and are used in the plastic processing industry for the production of foil, molds, tins, cups, bottles, and other packaging.
Poly-3-hydroxybutyrate (PHB)	The biopolymer PHB is a polyester produced by certain bacteria processing glucose or starch. Its characteristics are similar to those of the petroplastic polypropylene. PHB produces transparent film at a melting point higher than 130 degrees Celsius and is biodegradable.
Polyamide 11 (PA 11)	PA 11 is a biopolymer derived from natural oil and is not biodegradable. Its properties are similar to those of PA 12, although emissions of greenhouse gases and consumption of nonrenewable resources are reduced during its production. Its thermal resistance is also superior to that of PA 12. It is used in high-performance applications like automotive fuel lines, pneumatic airbrake tubing, flexible oil and gas pipes, control fluid lines, sports shoes, electronic device components, and catheters.
Bioderived polyethylene	Polyethylene is comprised of the basic building block (monomer) ethylene. Ethylene is one chemical step from ethanol, which can be produced by fermenting sugar cane or corn. Bio-derived polyethylene is chemically and physically identical to traditional polyethylene; it does not biodegrade but can be recycled. It can also significantly reduce greenhouse gas emissions.

Source: Biodegradable Plastics 2010.

Obstacles for Industrial Biotechnology

Industrial biotechnology ventures face intense competition from petrochemical companies in the consumer goods industry. These ventures are particularly sensitive to institutional and financial barriers that prevent growth and a smooth transition to commercialization.

In order to properly define and assess potential solutions that may help industrial biotechnology ventures overcome financial gaps, the Milken Institute, in conjunction with the U.S. Department of Agriculture's Office of Energy Policy and New Uses, convened a Financial Innovations Lab in Washington, D.C. The group included stakeholders in the industry, including the top scientists and economists in academia, institutional investors, policymakers, biotech company representatives, and industry association representatives. These experts were brought together to design models that leverage public efforts for research and funding with private investments to generate a sustainable business climate for industrial biotechnology.

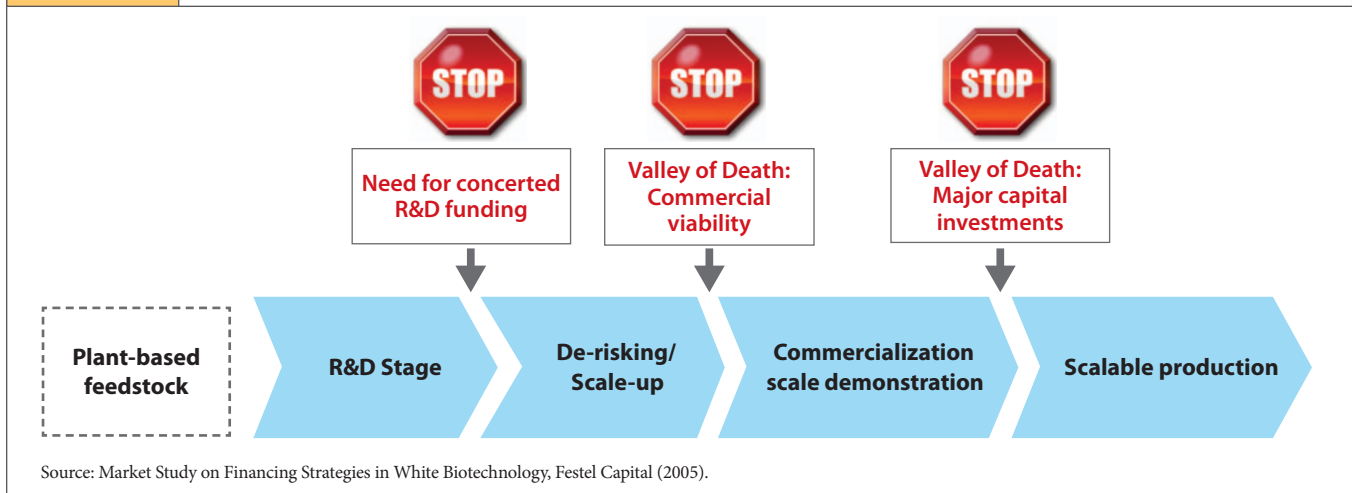
Dr. Marvin Duncan, senior agricultural economist at the U.S. Department of Agriculture, discussed the importance of industrial biotechnology in providing chemicals and cited several benefits. He noted that biological innovation in new products has grown rapidly, that the industry uses feedstocks that are more secure than petroleum, and that the market for environmentally friendly products is expanding. But if the industry is to be competitive in world markets, increased public investment to stabilize funding in basic research and product development will be required.

Bobby Bringi, CEO of the not-for-profit Michigan Biotechnology Institute, highlighted the need to effectively and rapidly bridge the gap between promising research and practical application. He suggested that "de-risking" technologies could attract private investment to augment public efforts. For example, bundling intellectual property and sharing its value equitably with all players spreads both the benefits and the risks during the most uncertain stage in technology development.

Brent Erickson, executive vice president of the Biotechnology Industry Organization, spoke of increasing market entry and introduced the optimistic notion that we are at the beginning of a "biorefinery evolution." He outlined the challenge presented by the economic downturn, the inconsistent deployment of government assistance, and the shrinking government budgets that will have to support the fragile industry.

Recurring themes also emerged, including the importance of industrial biotechnology in solving national security problems by reducing demand for petroleum, increasing and stabilizing jobs in rural America, and increasing government involvement to spur successful activity for the industry in its infancy.

Based on a comprehensive review of the financial implication of the stages of production and the entities involved at each stage, we have identified several barriers to success in this industry as the technological concepts scale up from R&D to commercialization of a product.

FIGURE
6*Funding gaps between stages of development (called 'Valleys of Death')*

Barrier 1: Policy uncertainty and complexity restrict firm activity

The road to commercial success for biotechnology processes and products is extensive, technical, and not guaranteed. The firms are regulated by one of several agencies, depending on the product, and some products are regulated by more than one agency. The Coordinated Framework of Regulation of Biotechnology assigns which parts of the biotechnology industry are regulated by the three federal agencies involved: the USDA, EPA, and FDA.

The USDA's Animal and Plant Health Inspection Service (APHIS) is tasked with ensuring that genetically engineered organisms do not pose a risk as a plant pest. APHIS also works with the EPA and FDA to administer the rigorous approval process. The EPA uses its authority under the Toxic Substances Control Act to regulate new microorganisms that are used in the commercial production of industrial enzymes and specialty chemicals. The FDA regulates the safety and labeling of all foods, feeds, and additives, including those derived from genetic engineering and biotechnology pathways, and FDA approval must be received prior to marketing.

This complexity can dissuade firms and investors alike from entering the market or investing, and it can impede diversification of production within a firm. Putting products through different regulatory processes creates an additional barrier for firms branching into different markets with different products.

The process also confuses the provision of government funding. For example, biorefineries that focus on biofuels receive more assistance from Congress than facilities that focus on other bio-based materials, which also sends a confusing message to investors.

Barrier 2: Industry lacks coordinated support from R&D through scale-up and commercialization

Unlike in the Silicon Valley—where universities, private research institutions, production facilities, industry advocacy groups, and investors are clustered in the same geographic region—biotechnology interests are spread across the country.²¹ This lack of proximity can act as a barrier to the industry. Clusters contribute to successful R&D and eventual commercialization because they expedite the dissemination of technical information, create cohesive industry partnerships for lobbying and other efforts, open access to larger amounts of capital, and make the cluster's companies more visible to venture capital firms.

Though the industry's players remain far-flung, more research and production have recently emerged in agricultural areas near industrial biotech feedstocks, and niche specialization is occurring in many regions. But venture capital firms do not naturally congregate in agricultural areas where the feedstock production and primary research facilities exist, so many infant clusters in industrial biotechnology rely on local angel investors, who often lack the skills and intense involvement of the venture capital arena.

Barrier 3: Long value chains asymmetrically distribute the gains from developing new products

The most expensive industrial biotech processes for making chemical products occur at the beginning of the supply chain, where extensive R&D must be accommodated, the per-unit values are lowest, and the margins are narrowest.²² The early stages also face the most direct competition from cheaply produced petroleum-based chemicals. Unfortunately, the early stage is also the period when financing is the hardest to come by, and larger profit margins are not realized until the later stages of the supply chain.

Attaining the “know-how” intellectual property for transgenic organisms (organisms with inserted DNA that originated in a different species) and production processes—used in the early stages to produce base chemicals, intermediaries, and production techniques—requires the most capital in the industrial biotech industry, and its products are in closest competition with petrochemical products. But the cost burden, research incentives, and revenue are distributed unevenly in the value chain. For example, secondary product users that turn base chemicals into more complex chemicals with broader applications do not incur the R&D costs, but they enjoy added value through performance enhancement of their production line or through the sale of their product. Then commercialization occurs through tertiary product users, such as the food and cosmetics industries, which also do not shoulder the costs of R&D and have more generous margins.²³

Meanwhile, intellectual property revenues are typically distributed to the developer for only a short time after production has commenced. Whether it is academia or a small business, the developer that originates a technology typically misses out on late-stage production revenues. This detracts from value-driven partnering and dissuades venture capital investment.²⁴

Barrier 4: Feedstock costs and energy prices are volatile

Bio-based products have less developed markets, and the volatility in oil prices creates inconsistent pricing in the feedstock of petrochemical manufacturing and increases the risk of investment. When oil prices dip, the petrochemicals industry can produce very cheaply, making investment in alternatives such as industrial biotechnology riskier and less profitable.

Oil-based chemistry is currently winning on price and scale, with biotechnology still a niche in chemical manufacturing.²⁵ Biochemicals can reduce fossil fuel inputs by up to 55 percent in potential substitution but they generally do not yet have cost advantages over petroleum-based chemistry.²⁶

The relatively low price of petroleum-based substitutes prevents bio-based plastics from taking over a larger share of the market. As of 2010, polylactic acid (PLA) was about 20 percent more expensive to produce than petroleum-based plastics, and the production cost of polyhydroxyalkanoate (PHA) was more than double that of its petroleum-based counterparts.²⁷

As a result of these higher production costs, even if the price of crude oil and biomass were at nearly a 1:1 ratio as they were in Europe last year, industrial biotech is at a disadvantage. This ratio will always depend on the country and region in which the biomass is produced, so minimizing feedstock costs may hinge on liberalizing global trade of agricultural products.

Biomass prices were once nearly as cyclical as the price of crude oil, but this apparently has improved. In 1998, mineral oil was \$17 per barrel and soybean oil was \$88 per barrel. In 2006, mineral oil was \$72 per barrel and soybean oil was \$78 per barrel.²⁸ Chemical products are extremely sensitive to feedstock costs, and the more static the price of biomass feedstocks, the lower the cost of capital for investment. Of course, as the industry grows more robust, a steadier agricultural feedstock market will develop.²⁹

In addition, some processes should be less expensive than others; for example, some processes require little or no heat, so they require less energy. But this energy savings is still subject to the price of oil and unlikely to offset the high costs of developing an entire biotechnological process chain. Furthermore, the existing infrastructure for petrochemicals cannot accommodate biotechnology without costly improvements, another benefit for the petrochemical industry.³⁰

Currently, commodity chemicals such as succinic acid are traded internationally, but there is no international trade for biomass, so expanding trade is not an option for normalizing discrepancies in the cost of biomass feedstocks between countries. On the other hand, the absence of international trade of biomass means the U.S. can prescribe its own policies to expand biomass usage without interruption from other countries.

Barrier 5: Short investment horizon does not match long gestation timeline

Capital intensity of industrial biotechnology increases sharply very early in production, and proving the technology requires sustained investment. The average period from idea to market is three to five years, partly because the capital requirements are so high that after five years the ventures cannot afford to exist.³¹ This barrier shows the conflict between the business constraints of creating a solvent biotechnology business and the technological constraints of proving physical production. The size and the cost of physical developments are prohibitive for the ventures that require full build-out, but these constraints have a lesser effect on joint ventures that may have preexisting assets. While a longer horizon from concept to commercialization would help to perfect ventures in industrial biotechnology, the costs associated with a longer time horizon are restrictively high and jeopardize businesses that cannot develop within the average three- to five-year span.

Barrier 6: Cost of capital is restrictively high due to high risk premiums

Capital requirements in industrial biotechnology—and the cost of capital in this investment environment—are disproportionately high. For early-stage life sciences companies backed by venture capital, the cost of capital (20 percent or higher) is at least twice the average of all other sectors. This is due to the higher risk of failure and the time spent holding illiquid assets.³²

R&D costs are high because they demand an educated, well-paid workforce, expensive improvements, laboratory equipment, and time-consuming adherence to regulations. Wages in industrial biotechnology on average are double those in other industries. In 2008, the average wage of an employee in biosciences was \$77,595, whereas the average U.S. private-sector wage was \$45,229 per year.³³ Capital requirements for infrastructure are also particularly high for specialty chemical development, which is popular in industrial biotechnology because the applications are so broad.

High capital costs may be mitigated by incorporating advance purchase agreements with end users of bio-based chemicals. The challenge in creating purchase agreements is the fragmentation of the value chain as products are produced and transformed into other products. A potential solution is to bolster co-development activity and horizontal integration between the developers and producing companies.

Barrier 7: Lack of capital became a crisis

The recent financial crisis has affected all industries, but the industrial biotechnology industry has been especially vulnerable because of the inherent risks of a new industry and the need for large amounts of capital. The financial crisis has made funding hard to find and expensive to obtain for the smaller companies that dominate innovation in industrial biotechnology. Bank lending is down as financial industries are de-leveraging and access to the bond market is further restricted. There is not enough funding for pilot plants that are crucial to show technical proof-of-concept.

Government grants are available to some extent, but most policies require private-sector cost-sharing that cannot occur without adequate private investment.³⁴ Public-private partnerships that form at the first stages of development can shepherd ventures through the process of receiving government assistance and raising private

capital. Attracting foreign direct investment from places with more access to capital; it from countries with more stringent product sustainability standards that require bio-based inputs, is a necessary part of biotech's future. The U.S. has experienced difficulty with the issue of return on capital; it can no longer supply adequate equity and has less appetite for debt financing for such long development cycles in a new industry.

Barrier 8: Investors lack awareness, and consumer demand is undeveloped

The novelty of industrial biotechnology and the complexity of the technology are themselves barriers that result in a lack of awareness in the venture capital sphere and a lack of communication between the experts in product development and financing. Investors don't adequately understand the technologies they hope to commercialize, and the researchers and academics who develop the technologies lack a clear understanding of market demands and industrial manufacturing.³⁵

Investors prefer red (pharmaceutical) biotechnology to industrial biotech. With industrial biotech, it is harder to estimate market share, and it creates new ways to make already known chemicals instead of inventing novel new drugs. In addition, investors wrongly believe that industrial biotech is driven by big chemical companies instead of the small, underfunded ventures that are really driving the industry. In addition, investors typically are not aware of the market potential that can be accessed by replacing large swaths of the massive petrochemicals industry with bio-based competitors.³⁶

Crafting Solutions: Financial and Policy Innovations

Recommendation 1: Establish concrete, long-term government policies

Due to the low levels of investment and high costs of capital in industrial biotechnology, Lab participants identified the need for concrete, long-term policy commitments from the government. Some policies designed to help the industry have time frames that are too short for industrial biotech's long investment horizon, a shortcoming that dissuades private investment and decreases the odds of commercial success. Another weakness is that policies support some technologies over others. "We need to move toward a little more technology product neutrality in our policy going ahead," participant Brent Erickson said.

A robust and healthy business model for producing bio-based products includes having integrated biorefinery production facilities that are not restricted in what they can produce so they can make a variety of base chemicals according to demand. However, the USDA's Biorefinery Assistance Program requires biorefineries to garner 70 percent of their revenues from biofuels and restricts the opportunities for bioplastics and other products. Similarly, the Energy Independence and Security Act of 2007 and the 2008 Farm Bill have requirements for biofuels and advanced biofuels that do not allow for the production of non-fuel biochemicals. Removing the biofuels requirements to allow bio-based products would create more competition for these products and let companies capitalize on varied products as shifts in profitability occur.

Participants recommended establishing a tax credit at the state level for bio-based products that aligns with the BioPreferred program. The tiered program would provide a larger credit for smaller producers turning out less than 5 million pounds of product per year, and it would not apply to fuels or food products. Participants also favored government performance contracts and loan guarantees.

Government performance contracts go a step further than BioPreferred in that they guarantee a product price, while USDA loan guarantees require participating banks to enter an agreement with the applicant if the applicant is creditworthy. Both strategies have meaningful time guarantees for the five- to 10-year investment horizon, potentially attracting venture capital and particularly private equity.

Lab participants also cited uncertainty caused by the waiver authority in the federal renewable fuel standard, which requires that transportation fuels contain a minimum amount of renewable fuels each year. The waiver authority allows exceptions to the fuels mandate, resulting in uncertain demand for alternative fuels and, in turn, uncertainty among potential investors in biorefineries. The focus of Congress and political lobbying efforts has been biofuels-centric with less attention to bio-based products. The language should be changed so the policy does not put any one interest at a disadvantage and puts investors at ease.



The best way to help industrial biotech ventures is through policy and financial mechanisms that attract capital and enhance the market, said Joel Kurtzman of the Milken Institute.

Lab participants addressed two other government-related issues: fuel mandates for biorefineries and subsidies. The industrial biotechnology industry would be better off if biorefineries were allowed to produce any bio-based product instead of just fuels. It would also gain ground if the government would level the incentive playing field between oil- and bio-based products. An important step is to change the existing policy language to avoid double subsidies; the industry needs consistency.

Recommendation 2: Create prize forums to bolster early-stage innovation

The industrial biotechnology industry is young and rich in opportunity for innovative technology and processes, and prize forums are an effective way to collect expertise. Sharing pre-competitive research can increase the pace of innovation by allowing scientists, ventures, and investors to learn from each other. Prize forums are partnerships of government, academia, investors, and the participants—commercial-scale producers in the making. The award money to create a meaningful incentive for participation can come from any or all of the partners. For example, the nonprofit X-Prize Foundation awards prize money to entrepreneurial endeavors for the public interest that can produce effective change and are efficient investments. The prizes spread awareness through the publicity around the event, which attracts new research and private capital. A prize forum can help future ventures leap-frog the growing pains by sharing methods and identifying failures.

Unlike the X-Prize, which encourages innovation in a broad discipline, this prize forum should focus on developing industrial biotechnology and bio-based products. One example is the California Innovation Center, formed with the assistance of numerous state and federal agencies. A focused affiliation of researchers from academia, the private sector, and the Department of Defense, the Center works toward developments in computer modeling and nanotechnology with the goal of moving technology innovations into the public and private spheres. Despite plans for four research locations at \$100 million apiece, the model has been unsuccessful due to insufficient funds and inadequate participation from the government. For the purpose of the Lab, this model helps identify not only the pitfalls of unreliable government assistance but also the potential to assemble experts who can create ways to improve an entire industry.

Recommendation 3: Create partnerships to share development costs (and disseminate knowledge of the sector)

■ Incubating technologies by sharing development costs

The costs of scaling up to commercial production can escalate prohibitively quickly. The industry needs to find mutual interests with government and academia in order to share development costs. A more specific framework than the innovation incentives mentioned in Recommendation 2 is that of public-private partnerships that emphasize connecting multiple private-sector partners, similar to a consortium or joint venture. Once success has been realized, the government has the ability to step out of the program. The partnerships would still allow for sharing. For example, participants in the Semiconductor Manufacturing Technology (SEMATECH) research consortium contribute their existing intellectual property or help develop new intellectual property with the other members. Originally designed to be overseen by the government with private-sector and government participants, SEMATECH received

\$500 million through the Defense Advanced Research Projects Agency (DARPA), the R&D office of the Department of Defense, but contributions also came from consortium members. This allowed for cooperation, sharing, and incubating intellectual property and product development with minimal risk. Once SEMATECH flourished, international organizations and foreign companies formed International SEMATECH. The U.S. government left the program at that point, but the success continues with nearly half of the companies being from outside the U.S.

An example closer to the industrial biotechnology industry is BIOFAB: International Open Facility Advancing Biotechnology, which focuses on synthetic biology. Another consortium of public and private investors, BIOFAB includes the University of California, Stanford University, the Department of Energy, and the National Science Foundation. With about \$3 million in its investment pool, the consortium is an open technology platform that shares biological component developments for academic and commercial use. These developments are useful to industrial biotechnology processes and can help industrial biotechnology ventures scale up to commercialization more easily and avoid the funding gaps that often occur between stages of development.

■ **Developing and sharing intellectual property to attract private investment**

In an industry where finding start-up capital is a challenge, a successful example is In-Q-Tel, a public-private partnership in which the government relinquishes control over investments, and intellectual property returns are divided by the intelligence and investment communities. It is an independent nonprofit strategic investor started by the CIA that now has \$100 million dedicated to this research. In-Q-Tel essentially provides start-ups with a business partner in the form of the government. A structure like this makes start-ups more attractive to investors from the early stages through private equity investment and commercial production. On average, the venture capital industry invests \$9 for every dollar that In-Q-Tel invests. The California Life Sciences Fund is a similar program that has proven successful at attracting private-sector investment up to four times that of government investment. Funds operating at a state level may have an advantage in galvanizing regional participation that national funds may not have.

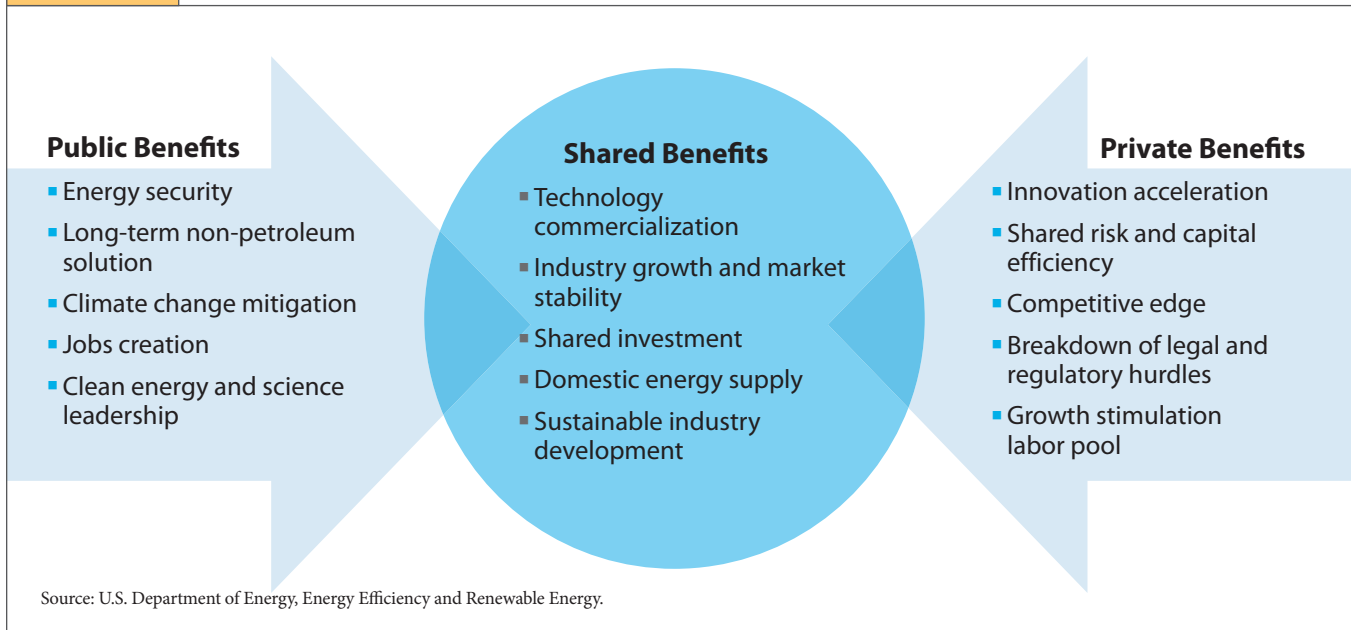
State and federal governments and their agencies have limited capacity to effect big developments in industrial biotechnology R&D, but they can play an integral role in connecting the appropriate partners to combine their complementary strengths. Most importantly, governments and their agencies provide the facility and credibility to attract private investment, which strengthens the industry.



Ally LaTourelle represented BioAmber Inc. at the Lab. BioAmber's core product is bio-based succinic acid, a chemical building block that can be used to produce diverse products.

FIGURE
7

Benefits of algal biofuels public-private partnerships



Recommendation 4: Utilize established resources to lower costs, accelerate development, and reduce risk

Beyond strategic partnerships, the industrial biotechnology industry can take advantage of existing pilot plants and encourage the development of more pilot and demonstration plants to test (and thus de-risk) technology and reduce the capital expenditures the industry would have incurred to upgrade physical assets on its own.

The nonprofit Michigan Biotechnology Institute (MBI), which partners with government, university, industry, and private investors, helped PLA technology succeed by providing the facilities and equipment for initial proof of production. New technologies can be scaled up to establish commercial viability at modest cost to the developer and greatly accelerate time frames at nonprofit development facilities such as MBI. Bringi of MBI said government funding for accelerated de-risking and scale-up could help advance promising technologies to market by making them better investment propositions. Further, the intellectual property and know-how developed during de-risking could be bundled with the base intellectual property to facilitate commercial implementation and more equitable profit-sharing among the stakeholders. Corinne Young of Myriant Technologies said a demonstration grant from the Department of Energy enabled Myriant to set up business in the U.S.; previously it operated solely in other countries that offered the company more favorable conditions.

Another way to reduce capital expenditures through the demonstration project strategy is to utilize the infrastructure of existing companies or bankrupt corn-based ethanol facilities. Companies that are just beginning to test production of their technologies can rent from companies that have the physical assets like Archer Daniels Midland or Cargill.

A tolling arrangement whereby products are sold based on their input costs plus a predetermined profit margin can guarantee that some profit will return to the demonstration plant or rented facility.

With numerous bankrupt ethanol fermentation facilities, new ventures may be able to make arrangements with the owners of these fallow assets and retrofit a facility far more cheaply than building a new multi-purpose biorefinery. The assessed value of the facility must take retrofitting into account, but the benefit is that it is already permitted, which is half the logistical battle. Such facilities also contain valuable assets: centrifuges, cooling towers, large-scale electrical systems, pipes, storage tanks, loading docks, etc.

These options are even more desirable if they are part of a program rather than individual arrangements made on a per venture basis. Agency involvement through the state or through an industry group could perpetually connect start-ups with demonstration plants or with private equity companies looking to use their bankrupt assets. The consistency of a program gives the industry desperately needed stability and certainty.

Recommendation 5: Upgrade Infrastructure

Like biofuels, industrial biotechnology would benefit from greater retail demand, with consumers at the wholesale and retail levels having a choice between traditional petroleum-based products and bio-based products. Roger Conway of Growth Energy presented his organization's Fueling Freedom Plan as an example. Under the plan, flexible fuel vehicle standards would be required for all new cars. Blender pumps, ethanol pipelines, storage tanks, and other infrastructure would be funded by the current ethanol tax program, which would phase out over time. Once the infrastructure for higher ethanol blend levels is in place, further federal help would be unnecessary. A similar infrastructure plan could be developed for industrial biotechnology.

Recommendation 6: Create innovative securitization and de-risk equity investment

Start-ups that have already developed intellectual property can obtain financing by bundling their idea for the purpose of portfolio valuation and patent securitization. Investors can buy into bundled intellectual property once it is put up as collateral. If the financing is non-recourse, the risk of receiving royalty payments from a licensee is transferred to the investor, as are the risks of patent infringement and obsolescence of the technology. This approach also assuages much of the debt burden of venture capital's very high interest rates. The lump-sum payments for intellectual property can be put toward the start-up's capital expenses and allow it to produce and create more intellectual property.

Another innovation is to create a valued reserve of long-term crop contracts. It is a way to bundle multiple years of feedstock crop yields to normalize feedstock prices. This removes market fluctuations and crop production fluctuations from the bio-based products industry, and it helps ease the competition bio-based products face from petroleum-based products. This also opens the door to developing long-term forward markets (i.e., an informal futures market) for the base chemicals produced at biorefineries. Having long-term purchasing agreements insulates ventures from dips in demand and attracts investment.

To remove some risk for equity investors and lower the cost of capital, participants considered efficacy of technology insurance, which would follow Germany's dry hole insurance model, put in place to de-risk geothermal drilling and partially backed by the government. Also recommended was a best practices standard of risk

assessment in the entire industrial chemicals industry to account for social and environmental costs of petroleum-based products and the benefits of bio-based products. Many of these costs do not present themselves in the marketplace, and the benefits of using domestically supplied biomass rarely decrease the costs of producing bio-based products. Applying this kind of standard may shift demand and have the desired effect of making bio-based products the more affordable option. Mechanisms such as a cap-and-trade system for fossil fuel use or a tax on carbon could also balance out these externalities.

Recommendation 7: Innovate financial instruments with government-backed investment options

In addition to the vast amounts of capital required to prove technology and scale up to commercialization, a great barrier for ventures in this industry is the cost of capital that rapidly becomes unserviceable. This prevents equity investors from investing in infrastructure like biorefineries. Alan Boyce of Adecoagro estimated that nearly 50 percent equity is required for companies to handle the debt service coverage ratios and secure feedstocks. This is a risky proposition for investors in early-stage technologies with known logistical complications.

Leveraging private investment with public funds is one path to attracting capital. The most direct way to do this is to create a bond structure that works as a green finance facility for bio-based industrial technologies. Similar to how Clean Water Act projects were financed by state money matched by federal funds, a state revolving fund could be created for industrial biotechnology. The contributions become equity in the capital markets, and private investment follows.

In addition, a transparent and liquid secondary market can also help reduce the cost of debt financing for industrial biotechnology firms. One example is a covered bond model, in which banks are required to match loans with the issuance of bonds and keep the loans on their balance sheets.³⁷ Boyce said financing with covered bonds can be supported in a similar manner to the Danish mortgage market. By providing a standardized, transparent bond market solution, the Danes have lowered interest rates and extended the maturity of financing for renewable energy.



A covered bond model helped Denmark extend the maturity of financing for renewable energy, according to Alan Boyce of Adecoagro, left. With him are Glenn Yago of the Milken Institute, center, and Ronald Stolz of Sandia National Laboratories.

This model is a primary reason Denmark has become a world leader in rate-sensitive wind farms. Denmark's wind farms garnered interest rates of about 4 percent. If that can be replicated in the U.S. industrial biotechnology sector, it can greatly reduce the barrier of the huge up-front capital costs required to get a biorefinery running.

Finally, to minimize the ventures' credit risk, defeasance pools can act as financial collateral to secure payment obligations. Setting U.S. Treasury notes, T-bonds, and TIPS to mature at specific dates along the timeline of a biorefinery's development ensures a matching payment schedule and abates the risk of non-payment, as long as the nominal interest rates are high enough. Although this provides a strategy to mitigate credit risk, the challenge for start-up companies in industrial biotechnology will be to obtain the collateral in the first place. Ideally, the solutions discussed above will make investment more attractive.

Moving Forward: Future Policy Considerations

Citing the intent of the USDA's BioPreferred procurement program, Lab participants agreed that government efforts to push supply and pull demand could be the most effective market support for the industry and ventures in the early stages. Having government agencies as customers is a huge boon to the industry, and since BioPreferred has existed for only a short time, and preferred procurement does not include space exploration or combat materials, the program has the potential to mature and expand. More—and more reliable—government assistance programs were widely accepted policy enhancement solutions among Lab participants. Government guarantees and long-term purchasing contracts could also benefit bio-based products.

To assuage the austerity measures that have hit many government programs, another accepted solution was more public-private partnerships in the form of shared research and product-testing facilities, which are some of the biggest financial barriers in the industry. Solutions also included exploiting the unrealized value of intellectual

property to leverage financing, creating technology efficacy insurance to de-risk new ventures, and using standardized, transparent bond market solutions, similar to those found in Denmark.

Various forms of public-private partnerships drew the most interest of the proposed solutions because participants believed that hands-on government assistance is paramount, but that participation and risk must be shared with private-sector participants. These public-private partnerships should have a project infrastructure investment model, a highly targeted model with private and public investment. The suggested models are those designed to increase intellectual property development with government assistance, such as the Energy Frontier Research Centers (EFRC), which partners with the U.S. Department of Energy; the SEMATECH industry consortium that formed with the help of the U.S. government to

For Further Study

The Lab raised several issues for policymakers that will require further study.

- How can state and local governments invest in research that involves academia and private investment to develop incubator facilities?
- How can bio-based materials be separated from the existing recycling stream?
 - The U.S. lacks sufficient industrial compost facilities.
 - Bioplastics melt at lower temperatures and pollute recycling feedstock chains.
 - For recycling purposes, most plastics are identified by numbers denoting the type of plastic that makes up the container, but codes don't exist for bioplastics.
- How can the proper information regarding bio-based products be disseminated to counter misleading product claims?
- How can governments help reallocate assets from bankrupt ethanol refineries to emerging biotechnology companies?

share intellectual property and improve industry infrastructure; and BIOFAB, funded by the National Science Foundation, the Lawrence Berkeley National Laboratory, and several universities, that standardizes and shares DNA sequences to make innovation easier.

In the broadest terms, the best way to help industrial biotech ventures thrive is through policy and financial mechanisms that attract capital and enhance the market, said Joel Kurtzman of the Milken Institute.

APPENDIX

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