2018 Evidence and Opportunity: Impact of Life Sciences in North Carolina

Prepared For: North Carolina Biotechnology Center

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Executive Summary

North Carolina has established one of the nation's leading life science industry clusters, characterized by steady, long-term growth and establishment of a diverse blend of industry, technology, and market strengths and niches. The industry employs more than 75,000 North Carolinians in jobs that pay, on average, over \$91,000 annually, or nearly twice the wages of the average state private sector.¹ The state's industry base stands out as particularly diverse—among the five major life science industry subsectors, North Carolina has a much greater employment concentration, i.e. a "specialized" employment concentration, in three of the five—drugs and pharmaceuticals; research, testing, and medical labs; and agricultural feedstock and industrial biosciences; and a fourth subsector that is highly concentrated but not yet specialized (bioscience-related distribution).

The industry's standing and top-tier position today has been hard-earned, however, in large part due to the early foresight and consistent dedication of the North Carolina Biotechnology Center (NCBiotech), with funding from the State of North Carolina, through a nearly 35-year emphasis on industry and ecosystem development programs and initiatives. Strategic investments combined with a vital role as a connector and facilitator have enhanced the innovation ecosystem for life science development. This sixth biennial edition of Evidence and Opportunity marks 10 years since the principals of TEConomy Partners, LLC (TEConomy) first began to assess and evaluate the Center's performance, impacts, and progress in achieving its vision of "North Carolina: a global life science leader."

¹ The life science industry analysis and comparisons against the U.S. and other top-tier life science states are based on TEConomy's analysis of U.S. Bureau of Labor Statistics, QCEW data from IMPLAN. These federal data allow for direct comparisons of North Carolina's industry position and performance against the nation and other states. In subsequent analyses in the report of the industry's impact on the North Carolina economy, TEConomy utilizes a separate data source—the detailed database of companies developed and maintained by the NCBiotech research team.

A Steady Growth Engine Slows its Pace though Maintains a Leading Position

The life science industry in North Carolina continues to expand, acting as a key growth driver for the state economy that consistently generates high-wage, quality jobs; however, at a slower pace in recent years.

The state has steadily grown its life science industry over several decades; and in the decade and a half through 2016, state companies have increased employment by 50 percent, or 25,000 jobs—ranking fourth among all states in its increase (Figure ES-1). The industry has been a consistent growth driver for the state, continuing to grow, or hold steady, even during recessions. The industry's 50 percent growth since 2001 compares favorably against the overall private sector, which has grown by nearly 12 percent over this same period; and has far exceeded the pace of national industry growth of nearly 19 percent. Firms in the state grew their job base by 2.5 percent from 2014 through 2016, but this pace was slower relative to national growth of 4.4 percent.



Figure ES-1: Life Science Industry Employment Trends, North Carolina and the United States, 2001–2016

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, Quarterly Census of Employment and Wages (QCEW) data; enhanced file from IMPLAN.

Two of North Carolina's industry subsectors have grown their employment base since 2014 and outpaced national job growth—research, testing, and medical labs and bioscience-related distribution; while the three remaining subsectors have experienced job losses since 2014. On balance, however, the industry in North Carolina has continued its impressive track record of job growth despite some variation in subsector performance.

The geographic footprint of the industry spans every region of North Carolina, reflecting an emphasis on statewide cluster development by NCBiotech. The diversity of North Carolina's life science industry is not only characterized by its industry subsectors but further by its geographic reach across every region of the

state. The map in Figure ES-2 pinpoints the locations of North Carolina life science firms by region, industry subsector (color), and employment level (size).



Figure ES-2: North Carolina Life Science Industry Companies, Statewide and by Region, Industry Subsector, and Employment Level, 2018

Source: NCBiotech Company Database.

North Carolina Among the Top-Tier Life Science States, Faces Stiff Competition

North Carolina's life science employment base is ninth largest among all states, but its recent growth rate is among the slowest.

Since 2014, three of the nation's largest life science states have also experienced among the fastest growth of all states—Massachusetts, which has been rapidly increasing both its employment level and its national ranking; Texas, a rapidly emerging life science player; and California, long the nation's largest life science state with leading hubs in the Bay Area, San Diego, and increasingly Los Angeles. All three of these top-performing states have ambitious and very large life science-related initiatives at work to strategically grow their life science base.





Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

Broader Economic Impacts of the Life Science Industry: A Decade of Growth

This tenth anniversary edition of Evidence and Opportunity provides a chance to look back and to assess the growth in industry impacts influenced by NCBiotech's programs and initiatives since 2008.

The life science industry has a significant and growing impact on the North Carolina economy. The total impact on state output estimated for the life science industry has increased to over \$83 billion in 2018, accounting for 9 percent of state business activity (Figure ES-4).² In terms of employment, the total economic impact from the life science industry stands at more than 240,000 jobs, accounting for more than 4 percent of total employment in the state.

- Since the 2008 economic impact report, the direct employment of the North Carolina life science industry has increased by more than 19 percent and the estimated revenues of the industry have grown even more rapidly, by 93 percent.³
- The life science industry generated nearly \$2.2 billion in state and local government revenues in 2018, up from \$1.4 billion in 2008.



Figure ES-4: The Economic Contribution of the Life Science Industry to the North Carolina Economy, 2018

Source: TEConomy Partners analysis of NCBiotech data using IMPLAN.

² The preceding industry analysis is based on federal data, which allow TEConomy to make key comparisons across all states. The data utilized here to measure the industry's impacts in North Carolina are from NCBiotech's detailed database of companies regularly maintained by the Center's research team. NCBiotech's data are available with no time lag, unlike the federal data, and therefore represent the situation for life sciences in 2018.

³ Part of this rapid growth in revenues can be attributable to changes in the underlying IMPLAN model, with the remainder being attributable to the increasing role of manufacturing and other high value-added components in the sector.

NCBiotech: Enhancing the State's Life Science Innovation Ecosystem and Catalyzing Growth for More than Three Decades

The long-term, impressive rise of North Carolina's life science industry, its broader R&D and innovation ecosystem, and its significant economic impacts can be directly tied, at least in part, to the deliberate, sustained programmatic initiatives and partnerships of NCBiotech.

For nearly 35 years, the Center has effectively designed and implemented activities and initiatives that span the range of unique elements that a complex, thriving life science ecosystem requires. NCBiotech, funded primarily through state government appropriations, has evolved its services and programming to address the key domains of industry and broader ecosystem development outlined in Figure ES-5.

Each domain addresses unique ecosystem needs both statewide and at a regional level within the state. The Center provides direct assistance to both companies and research universities through its programs, and it also acts as a facilitator and connector for companies and talented individuals to external sources of capital, job opportunities, wet-lab incubators, and professional groups. While more direct, quantifiable programs are easier to attribute and track tangible "impact," the vital role of connector and facilitator is arguably just as valuable in growing a vibrant industry cluster.



Figure ES-5: NCBiotech Center Initiative Domains and Roles Enhancing the Innovation Ecosystem

The specific programs and activities of the Center can also be assigned along the chain of activities that are necessary in the context of technology- or innovation-based economic development (TBED) ingredients that lead to thriving industry clusters. Each element of this chain and the corresponding NCBiotech programs are displayed in Figure ES-6. What stands out is the comprehensive and strategic nature of the programming to address every key element of the TBED chain.

NCBIOTECH PROGRAMS GRANTS Examples: Technology Enhancement Grant (TEG) Biotechnology Innovation Grants (BIG) **REGIONAL** & BUSINESS SERVICES GRANTS SECTOR DEVELOPMENT Examp Institutional Developm Grant (IDG) Gene Therapy Fellowship (GTF) Examples: Market Research / Competitive Intelligence Examples: RISE NC Projects; AgBiotech, Precision Health and BioDefense Initiatives BATON C Q С Q s Formatio n and Gro Business Attraction Integration into existing, expar and new cluster businesse Existing Industry Piloting & Demonstration Technology Transfer Innovation Translation Business Expansion Successful and expanding business clusters New Enterprise Development EXTERNAL FUNDING RESOURCES BIOTECHNOLOGY-INFORM & EDUCATE NCBIOTECH BUSINESS LOANS JOB SERVICES Company Inception Loan Small Business Research Loan Strategic Growth Loan Special Events Exchange Groups Life Sciences Forum Jobs Board Jobs Network Job Seeker Consulting vestor and Strateg Partnering Events • • • • • • • • Long-term, sustained commitment to development of the cluster by all parties

Figure ES-6: Technology-Based Economic Development Chain and NCBiotech Programs and Initiatives

Source: TEConomy Partners, LLC and NCBiotech

The Economic Impact of NCBiotech on the Development of the North Carolina Life Science Industry

TEConomy has estimated the economic contribution of the companies supported by NCBiotech's business loan programs since its first assessment of the economic impact of the Center in 2008 and by the companies NCBiotech has helped to recruit to the state since the 2012 report.

Targeted, early-stage loans to life science businesses help create and support business activity in the companies receiving loans, which has a long-term impact on the state's economy. As a result, NCBiotech's loan programs create a "portfolio" of businesses assisted by the Center. Since 1989, NCBiotech has made business loans to 204 companies. Of the 204 companies that have received loans, 107 are currently active in some form, employing 2,544 with estimated revenues of \$2.5 billion and accomplish the following:

- Generate \$3.8 billion in economic activity in the state;
- Create or support 10,390 jobs earning \$732 million in labor income; and
- Generate an estimated \$98.4 million in state and local tax revenues.

North Carolina receives a strong return on its investment in NCBiotech. TEConomy estimated the state government revenue portion of the estimated \$98 million in combined state and local government revenues generated by the active loan recipient companies (through direct, indirect, and induced impacts), based on U.S. Census Bureau government finances data. This analysis yields an estimated \$60.3 million in state taxes generated by these companies, an amount more than four times greater than the state's appropriation to NCBiotech of \$14.0 million for fiscal year (FY) 2018–2019.

In addition to its role in directly supporting commercialization and early-stage businesses, NCBiotech supports the broader business recruitment and expansion efforts of the North Carolina Department of Commerce and other economic development organizations. An analysis focusing on the 25 company projects in which the Center assisted its economic development partners in FY 2017 and 2018 finds the potential to create a total of

The Evolving Role and Focus of NCBiotech's Industry and Ecosystem Support: Recent Accomplishments and New Developments

With nearly 35 years of history, NCBiotech has learned that, for the industry to thrive throughout the state, its role must continually be evaluated and evolve, where appropriate, to emphasize new and emerging opportunities. Recent Center activities and new developments highlighted in the report include:

- Establishment of the Pfizer-NCBiotech Distinguished Postdoctoral Fellowship in Gene Therapy: supporting 18 postdoctoral fellows with research and professional development over 3 years.
- Crop Improvement Projects Led by the NCBiotech Crop Commercialization Program (CCP): working
 collaboratively to establish an industry base and opportunities for growing dedicated cellulosic crops for
 conversion to fuels and other high-value chemicals.
- Establishment of the North Carolina Precision Health Collaborative (NCPHC): convening partners to realize the state's potential in advancing precision health/precision medicine.
- **Establishment of the NCBiotech Clinical Research Consortium:** enhancing and advancing the state's existing strength with respect to Clinical Research Organizations (CROs) via a broad Consortium.

3,080 jobs once projects reach their projected employment levels. Once these projects reach these levels, they are expected to generate:

- \$2.1 billion in economic activity;
- Support 8,732 jobs earning \$580 million in labor income; and
- Generate \$59 million in combined state and local government revenues.

The Impact of Strategic Collaboration: Building a Biomanufacturing Sector through a First-of-its-Kind Workforce Initiative

In the early 2000s, recognizing the emergence of biomanufacturing and corresponding demands for a specialized production workforce, NCBiotech and partner organizations in North Carolina established NCBioImpact—a first-of-its-kind training program.

At the outset of the NCBioImpact initiative in 2003, North Carolina had 17 companies in biomanufacturing that employed 4,754. These figures have risen since, with companies benefitting from the education and technical training and steady supply of talent provided through the workforce initiative (Figure ES-7). In North Carolina today, at least 25 biomanufacturing companies are active, and represent an impressive breadth of biomanufactured products and industry applications that span biopharmaceuticals, including specific applications and focus in animal health, food ingredients, and broader industrial applications. Based on data from the NCBiotech Company Database, these companies employ 9,163 in 2018, a figure that has nearly doubled since 2003 (up 93 percent).





Source: NCBiotech Company Database.

Economic impacts of the biomanufacturing sector developed in North Carolina are estimated in the report for both the impact of the sector today, as well as the change in sector employment since 2003.

Just as it has throughout its more than three-decade history, NCBiotech continues to evolve and challenge itself to not only meet the demands for a thriving life sciences industry today, but also for the future. The organization's forward-looking mentality has been a hallmark of programs such as NCBioImpact, which was established ahead of a key industry and innovation inflection point and positioned the state well for the years ahead. The Center continues this tradition through its new initiatives and areas of emphasis in diverse capacities including gene therapies, precision health, clinical research, and crop commercialization, all while advancing the broader innovation ecosystem through its core programs and initiatives.



Introduction

North Carolina has established one of the nation's leading life science industry clusters, characterized by steady, long-term growth and establishment of a diverse blend of industry, technology, and market strengths and niches. The industry's standing and top-tier position today has been hard-earned, however, in large part due to the early foresight and consistent dedication of the North Carolina Biotechnology Center (NCBiotech), with funding from the State of North Carolina, through a nearly 35-year emphasis on industry and ecosystem development programs and initiatives. Strategic investments combined with a vital role as a connector and facilitator have enhanced the innovation ecosystem for life science development, with a particular focus across five domains: funds for commercializing university research and early-stage company development; talent development initiatives and career connections; industry networking; access and connections to unique spaces; and access to research and other resources.

This sixth biennial edition of *Evidence and Opportunity* marks 10 years since the principals of TEConomy Partners, LLC (TEConomy) first began to assess and evaluate the Center's performance, impacts, and progress in achieving its vision of "North Carolina: a global life science leader." As in prior reports, this edition assesses the position and performance of the life science industry in North Carolina with respect to its size, concentration, and recent as well as long-term trends, all in the context of national trends and comparisons against other top-tier life science states. The report then turns to the economic impacts and contributions of the industry, and key NCBiotech programs, to the state economy, with an emphasis on "a decade of growth." In addition, and new this year, is a final section highlighting NCBiotech's role, along with other state partners and industry, in advancing a strong biomanufacturing sector, including impacts of the sector's growth that are attributable, at least in part, to the role of NCBioImpact, a pivotal education and training initiative for training abundant talent for biomanufacturing facilities.



I. North Carolina's Life Science Industry:

A Steady Growth Engine Slows its Pace though Maintains a Leading Position

The life science industry in North Carolina continues to expand, acting as a key growth driver for the state economy that consistently generates high-wage, quality jobs; however, at a slower pace in recent years. The industry employs more than 75,000 North Carolinians in jobs that pay, on average, over \$91,000 annually, or nearly twice the wages of the average state private sector. Firms in the state grew their job base by 2.5 percent from 2014 through 2016, but this pace was slower relative to national growth of 4.4 percent.

The state has steadily grown its life science industry over several decades; and in the decade and a half through 2016, state companies have increased employment by 50 percent, or 25,000 jobs (Figure 1). The industry has been a consistent growth driver for the state, continuing to grow, or hold steady, even during recessions. The industry's 50 percent growth since 2001 compares favorably against the overall private sector, which has grown by nearly 12 percent over this same period.

NC Industry Headlines

A Large, Highly Specialized Industry

More than 75,000 jobs, 47 percent more concentrated than the national average; ranks among nation's Top 10

Diverse Strengths

Specialized concentrations in three of five major industry subsectors

Continuous Long-Term Growth

Industry has grown nearly every year; employment up 50 percent overall since 2001, average annual growth rate of 2.8 percent

Growth, However, Has Leveled Off

Industry grew 2.5 percent since 2014, below the national average of 4.4 percent

High-Wage, High-Quality Job Generator Paying wages nearly two times the state's private sector average

North Carolina has been a top performer in life science industry growth since the early 2000s. In terms of net new jobs generated, North Carolina's more than 25,000 job increase ranks fourth among all states in long-term life science industry growth (from 2001 through 2016). The state's 50 percent growth has far exceeded the pace of national industry growth of nearly 19 percent.

While North Carolina's life science employment growth has continued, in recent years the pace has slowed. Following very strong job gains in 2012 (8 percent) and 2013 (6 percent), employment growth has averaged just 1 percent during the 2014–2016 period. The primary focus of this report is 2014 through 2016 when the life science industry increased employment by 2.5 percent in North Carolina compared with 4.4 percent growth for the nation.



Figure 1: Life Science Industry Employment Trends, North Carolina and the United States, 2001–2016

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, Quarterly Census of Employment and Wages (QCEW) data; enhanced file from IMPLAN.

Life science employment in North Carolina reached 75,582 in 2016, representing 2.1 percent of all private sector jobs in the state (Table 1). This compares with 1.4 percent of all jobs nationally, meaning North Carolina has a significantly greater life science employment concentration. The ratio of these employment shares is referred to as a location quotient, or "LQ". When a state's share of industry employment matches the national average, the LQ is 1.0. When it exceeds the national average, or greatly exceeds the average (1.20 or higher), the industry is said to have a "specialized" employment concentration in that industry. North Carolina's life science industry employment is 47 percent more concentrated than the national average—representing a highly specialized state industry.

Life Sciences & Major	NC Establishments		NC Employment		U.S. Employment	NC Location	
Subsectors	Count, 2016	Change, 2014-16	Count, 2016	Change, 2014-16	Change, 2014-16	Quotient, 2016	
Total Life Sciences	3,843	16.4 %	75,582	2.5%	4.4%	1.47	
Agricultural Feedstock & Industrial Biosciences	45	-10.0%	2,331	-12.8%	-1.2%	1.16	
Bioscience-related Distribution	1,615	12.5%	15,287	4.9%	3.7%	1.10	
Drugs & Pharmaceuticals	125	5.9%	20,656	-4.6%	2.0%	2.34	
Medical Devices & Equipment	196	0.5%	8,411	-1.6%	2.9%	0.79	
Research, Testing, & Medical Laboratories	1,862	23.9%	28,896	9.9%	8.2%	1.79	

Table 1: Summary Employment Metrics, North Carolina and the United States, 2016

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

Defining the Life Science Industry

Defining the life science industry is challenging due to its diverse mix of technologies, products, research and development (R&D) focus, and companies. The industry includes companies engaged in advanced manufacturing, research activities, and technology services; and these companies have a common thread or link in their application of knowledge in the life sciences and how living organisms function. At a practical level, federal industry classifications do not provide for one over-arching industry code that encompasses the entire industry. Instead, more than two dozen detailed industries must be combined to best track the life science industry in its primary activities.

The TEConomy/Biotechnology Innovation Organization (BIO) State Initiatives 2018 report, *Investment, Innovation and Job Creation in a Growing U.S. Bioscience Industry*, has developed an evolving set of major aggregated groupings that organize the life science industry into five major subsectors shown here. For a detailed list of the North American Industry Classification System (NAICS) industry codes that define each subsector, and a discussion of recent updates to the definition, see Appendix A to this report.



The State's Life Science Subsectors—A Breadth of Diverse Strengths

North Carolina's industry base stands out as particularly diverse, with several areas of notable strengths. Among the five major life science industry subsectors,⁴ North Carolina has a specialized employment concentration (LQ of 1.2 or greater) in three of the five—drugs and pharmaceuticals; research, testing, and medical labs; and agricultural feedstock and industrial biosciences; and a fourth subsector that is highly concentrated but not yet specialized (bioscience-related distribution).

- Twenty-seven percent of the state's life science industry jobs are in drug and pharmaceutical manufacturing (20,656), with a highly specialized employment base that is 134 percent more concentrated than the nation (LQ is 2.34). North Carolina's large drug and pharmaceutical subsector ranks third among all states in its size (see subsector rankings in Figure 2). The subsector has two specialized components—biological products, representing the major element of a growing biomanufacturing specialization in the state; and pharmaceutical preparation manufacturing.
- Research, testing, and medical labs is also large and highly specialized in North Carolina, with nearly 29,000 jobs and a 79 percent greater employment concentration (1.79 LQ). The subsector ranks fifth in size among all states and includes employment in commercial life science R&D, including biotech companies and clinical research organizations (CROs), as well as more service-oriented medical laboratories. North Carolina is specialized in each of these component areas within the subsector.
- The agricultural biosciences are also a state specialization, with an LQ of 1.16 and more than 2,300 jobs primarily in agricultural chemical manufacturing.⁵ The two largest components of the subsector in North Carolina—pesticides and other agricultural chemicals manufacturing and phosphatic fertilizers—make up 85 percent of all jobs and represent areas of specialization within the subsector.
- Bioscience-related distribution exceeds 15,000 jobs and is highly concentrated in North Carolina with a 1.10 LQ in 2016. The state has specialized concentrations in drug wholesaling as well as medical, dental, and hospital equipment and supplies wholesaling.
- Medical device and equipment manufacturers employ 8,411 in North Carolina, a sizable footprint though one that is not yet at an above-average concentration of jobs (LQ is 0.79). Though no individual components yet meet the specialization threshold, surgical appliance and supplies production is highly concentrated with an LQ of 1.11 in 2016.

⁴ For a discussion on the definition of the life science industry used in this study, see the text box on the previous page. For a detailed industry definition by industry NAICS codes, see Appendix A.

⁵ The TEConomy/BIO industry definition has been updated in this report with relatively minor modifications, though this includes the removal of one life science-related NAICS code—Cellulosic Organic Fiber Manufacturing—that no longer exists and where the activity is now combined with a non-life-science-related industry and unable to be isolated. This industry in North Carolina was relatively significant, and, with the removal of this code, the agbioscience subsector is now somewhat smaller in overall size.





Source: Ranking analysis developed from TEConomy/BIO, Investment, Innovation and Job Creation in a Growing U.S. Bioscience Industry, 2018. The biennial report does not explicitly rank life science states.

Industry Subsector Growth—A Mixed Performance

Two of North Carolina's industry subsectors have grown their employment base since 2014 and outpaced national job growth—research, testing, and medical labs and bioscience-related distribution (Figure 3).

- Research, testing, and medical labs, the state's largest life science subsector, is showing continued competitive strength. While the overall life science industry added just over 1,800 net new jobs from 2014 through 2016, this subsector grew by more than 2,600 during this same period. Net job gains were contributed by each of the major components of research, testing, and medical labs—commercial life science R&D (a majority of the gains, just over 2,000 jobs) and medical labs.
- Similarly, bioscience-related distribution jobs have outpaced national growth and added just over 700 jobs from 2014 through 2016. Each of the major subcomponents added jobs.

The three remaining subsectors have experienced job losses since 2014.

- The modest 1.6 percent decline in medical device manufacturing meant 134 fewer device jobs over the 2-year period; and while there were job gains in electromedical devices and surgical appliance production, these were more than offset by job losses in surgical and medical instruments and in dental equipment and supplies.
- In drugs and pharmaceuticals, the net job decline was 1,000 jobs, all of which was out of the state's largest component industry—pharmaceutical preparation manufacturing—while other components saw little net change.
- The agbioscience subsector had a net decline of more than 300 jobs with job cuts coming from pesticides and other ag chemicals and from soybean processing.

On balance, the industry in North Carolina has continued its impressive track record of job growth despite some variation in subsector performance.



Figure 3: Life Science Industry Employment Trends by Major Subsector, North Carolina and the United States, 2014–2016

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

North Carolina's subsector employment size, concentration, and recent trends detailed in this section are summarized in the bubble chart below (Figure 4). The specialized concentration of three subsectors and the above-average concentration of a fourth results in four of five subsector bubbles positioned above the horizontal axis where the LQ equals 1.0. Those to the right of the vertical axis have added jobs since 2014. Subsectors that are both highly concentrated and growing—research, testing, and medical labs; and bioscience-related distribution—can be characterized as statewide "stars." Those in the upper-left quadrant—drugs and pharmaceuticals and agbiosciences—are specialized in their concentration but losing jobs in a "transitional" state that should be monitored going forward. Medical device firms have had relatively flat employment change, and the subsector is positioned closer to zero.

These status summaries are presented in Figure 5 along with the detailed components of each subsector that has a specialized concentration within the broader subsector.



Figure 4: North Carolina Life Science Industry: Employment Size, Concentration, and Change, 2014–2016

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

Figure 5: North Carolina's Life Science Subsectors, Current Status and Specialized Components

AGRICULTURAL FEEDSTOCK & INDUSTRIAL BIOSCIENCES

- Status: Transitional/Priority Retention Target (specialized, but not growing)
- Specialized NC Components: Phosphatic Fertilizers; Pesticides & Other Ag Chemicals

BIOSCIENCE-RELATED DISTRIBUTION

- Status: Emerging Strength (not specialized, growing, outpacing the United States)
- Specialized NC Components: Drugs & Druggists' Sundries Merchant Wholesalers; Medical, Dental & Hospital Equipment & Supplies Wholesalers

DRUGS & PHARMACEUTICALS

- Status: Transitional/Priority Retention Target (specialized, but not growing)
- Specialized NC Components: Biological Product Mfg.; Pharmaceutical Preparation Mfg.

MEDICAL DEVICES & EQUIPMENT

- Status: Divergent (not specialized, not growing)
- Specialized NC Components: None

RESEARCH, TESTING & MEDICAL LABS

- Status: Current Strength (specialized, growing, outpacing the United States)
- Specialized NC Components: Testing Labs; Medical Labs; Biotech and Other Commercial Life Sciences R&D

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

Average wages for the life sciences reached \$91,000 in 2016, far exceeding those for North Carolina's private sector (Table 2), an indicator of the high value-adding nature of the life sciences and the corresponding skills demanded by its firms. The premium paid to life science workers results in average annual wages more than \$44,000 greater, or 93 percent above, those for their private sector counterparts. The life sciences employ a disproportionately higher share of science and engineering professionals who most typically require at least a bachelor's degree (for lab and engineering technicians) and graduate-level degrees for professional scientists and engineers.

Life Science Industry and Subsectors	North Carolina	U.S.
Agricultural Feedstock & Industrial Biosciences	\$101,868	\$80,961
Drugs & Pharmaceuticals	\$98,800	\$113,815
Research, Testing & Medical Laboratories	\$93,432	\$106,942
Total Life Sciences	\$91,307	\$98,961
Bioscience-Related Distribution	\$91,048	\$93,677
Medical Devices & Equipment	\$63,153	\$84,746
Total Private Sector	\$47,248	\$53,354

 Table 2: Average Annual Wages in the Life Science Industry and Major Subsectors,

 North Carolina and the United States, 2016

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

In recent years, industry wage gains have increased but are just behind the pace for the private sector—3.8 percent for life sciences since 2014 versus 4.9 percent for the private sector average. Compared with national life science wage growth, the pace of average wages has slightly exceeded that for the United States since 2014—3.8 percent for the average worker in North Carolina compared with 3.1 percent for the nation. Still, at a national level, average industry wages, and those for four of the five subsectors, exceed those for North Carolina at nearly \$99,000 per worker.

A Geographic Footprint that Spans Every Region of North Carolina

The diversity of North Carolina's life science industry is not only characterized by its industry subsectors but further by its geographic reach across every region of the state. The map in Figure 6 pinpoints the locations of North Carolina life science firms by region, industry subsector (color), and employment level (size). Additional industry maps that isolate each of the state's regions are available in Appendix B.





Source: NCBiotech Company Database.

Benchmarking North Carolina against Other Top-Tier Life Science States

While national comparisons provide useful context for North Carolina's performance, the state is positioned within the top tier of life science states, and its competitive position must also be assessed against these competitor states. Its long-term job growth has propelled the industry into ninth largest among all states, maintaining this position from the assessment 2 years ago (Table 3). It is one of five states among the top 10 with a specialized employment concentration.

While in the prior assessment, North Carolina was among the fastest-growing top-tier states, its recent

Examples of Other States Making Significant Life Science Development Investments over the Last Decade

- **California:** \$3 billion funding for California Institute for Regenerative Medicine
- Maryland: \$1.1 billion funding for Bio 2020
- Massachusetts: \$1 billion funding for Massachusetts Life Sciences Initiative (2008); further funding authorized (2018)
- **Texas:** \$3 billion funding for Cancer Prevention and Research Institute

growth rate is among the slowest (Table 3 and Figure 7). Since 2014, three of the nation's largest life science states have also experienced among the fastest growth of all states—Massachusetts, which has been rapidly increasing both its employment level and its national ranking; Texas, a rapidly emerging life science player; and California, long the nation's largest life science state with leading hubs in the Bay Area, San Diego, and increasingly Los Angeles. All three of these top-performing states have ambitious and very large life science-related initiatives at work to strategically grow their life science base (see text box).

State	Establishments, 2016	Employment, 2016	Employment Change, 2014-2016	Location Quotient, 2016
California	9,924	267,844	7.0%	1.31
Massachusetts	2,567	93,912	8.9%	2.13
New Jersey	2,897	93,824	2.6%	1.94
Texas	5,578	89,746	8.6%	0.63
Florida	6,198	87,061	4.3%	0.83
Illinois	3,778	85,210	3.8%	1.16
Pennsylvania	2,517	81,035	6.1%	1.11
New York	3,514	78,872	1.4%	0.71
North Carolina	3,843	75,582	2.5%	1.47
Indiana	1,730	58,018	-0.1%	1.55

North Carolina and Comparison States, 2016

Table 3: Summary of Life Science Industry Employment Metrics,

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.





Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

Beyond its size and concentration, what further distinguishes North Carolina is its industry diversity. With three specialized component subsectors, and a fourth with a well-above-average concentration, the state has several key niche strengths. Six of the top 10 life science states, including North Carolina, have a specialized concentration in three or more subsectors (Table 4).

State	Agricultural Biosciences	Bioscience- Related Distribution	Drugs & Pharmaceu- ticals	Medical Devices & Equipment	Research, Testing & Medical Labs	Total Specialized Subsectors
New Jersey		٠	٠	٠	٠	4
Massachusetts			٠	٠	٠	3
California			٠	٠	٠	3
Indiana	٠		٠	٠		3
Illinois	•	•	٠			3
North Carolina	•		•		•	3
Pennsylvania			٠		٠	2
Florida		٠				1
New York						0
Texas						0

Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

North Carolina's growth and specialization in the life sciences position it firmly among the "stars" quadrant of the bubble chart in Figure 8; but, among a field of national stars, its relative concentration lies below Massachusetts, New Jersey, and Indiana. Its growth rate is not only behind well-established life science states such as Massachusetts, California, and Pennsylvania, but also has lagged behind rapidly emerging states such as Texas and Florida. Its size, while comparable to most of these top-tier states, is less than one-third that of California. While no other state compares with California's sheer size, it is important to acknowledge that the state still has room for advancements in its share of industry jobs and competitive position.





Source: TEConomy Partners' analysis of U.S. Bureau of Labor Statistics, QCEW data; enhanced file from IMPLAN.

North Carolina's large and specialized life science industry is generating high-wage, quality jobs for the state, which translates into significant and far-reaching economic impacts that extend well beyond its direct employment and output. The next section of this report provides estimates and further context for these contributions to the broader state economy.



II. Broader Economic Impacts of the Life Science Industry:

A Decade of Growth

This tenth anniversary edition of *Evidence and Opportunity* provides a chance to look back and to assess the growth in industry impacts influenced by NCBiotech's programs and initiatives since 2008. This section examines the impacts of the industry statewide and broken out across the major subsectors.

It is important to understand key differences between the data utilized in this section of the report and the data for the prior section. Section I is based on federal data, which allow TEConomy to make key comparisons across all states for the biennial national reports with BIO. The data utilized in this section to measure the industry's impacts in North Carolina are from NCBiotech's detailed database of companies regularly maintained by the Center's research team. NCBiotech's data are available with no time lag, unlike the federal data, and therefore represent the situation for life sciences in 2018. In addition, the two datasets define the life science industry somewhat differently—the NCBiotech database does not include a focus on distribution establishments and jobs, whereas the TEConomy/BIO concept includes this as its own major subsector. This results in relatively significant overall differences in total industry employment levels, and therefore, the industry data presented in this section feature a lower overall total.

Impacts of the Life Science Industry in North Carolina

North Carolina's life science industry is one of the most vibrant in the nation, and a leading contributor to North Carolina's economic growth and prosperity. For nearly 35 years, NCBiotech has played a leading role in supporting the growth and development of this sector. TEConomy, formerly Battelle's Technology Partnership Practice, has prepared biennial analyses of the economic contribution of the state's life science industry for a decade now. Since the first economic impact assessment in 2008, the economic contribution of North Carolina's life science industry has increased with the growth and development of the sector; with key findings from the current assessment and comparisons with 2008 that include the following (Table 5):

- The total impact on state output estimated for the life science industry has increased to over \$83 billion in 2018.
- In terms of employment, the total economic impact from the life science industry stands at more than 240,000 jobs, accounting for more than 4 percent of total employment in the state.
- Since the 2008 economic impact report, the direct employment of the North Carolina life science industry has increased by more than 19 percent and the estimated revenues of the industry have grown even more rapidly, by 93 percent.⁶

⁶ Part of this rapid growth in revenues can be attributable to changes in the underlying IMPLAN model, with the remainder being attributable to the increasing role of manufacturing and other high value-added components in the sector.

• The life science industry generated nearly \$2.2 billion in state and local government revenues in 2018, up from \$1.4 billion in 2008.

Table 5: A Decade of Growth—The Economic Contribution of the Life Science Industry to the North Carolina Economy, 2008 and 2018

Economic Impact	2008	2018	Change 2008-2018	% Change 2008-2018
Direct Impact (Output \$ Millions)	\$28,691	\$55,340	\$26,649	93%
Total Impact (Output \$ Millions)	\$45,806	\$83,311	\$37,505	82%
State Impact Multiplier	1.60	1.51		
Direct Impact (Employment)	53,182	63,143	9,961	19%
Indirect Impact (Employment)	64,913	91,447	26,534	41%
Induced Impact (Employment)	61,913	85,691	23,778	38%
Total Impact (Employment)	180,007	240,281	60,274	33%
State Impact Multiplier	3.38	3.81		
State and Local Tax Revenues (\$ Millions)	\$1,436	\$2,181	\$745	52%

Source: TEConomy Partners' analysis of NCBiotech data using IMPLAN.

TEConomy's six analyses of the economic contribution of the North Carolina life science industry are all based on the NCBiotech life science company database; and based on these data, findings between 2008 and 2018 include the following (Figure 9):

- The number of life science companies increased from 475 to 718; and
- Total life science industry employment increased from 53,182 to 63,143.

Figure 9: North Carolina Life Science Companies and Employment Based on the NCBiotech Company Database



Source: TEConomy Partners' analysis of NCBiotech data.

The North Carolina life science industry makes an important contribution to the overall health and vitality of the state's economy. Figures 10 and 11 show that, in 2018, the life science companies tracked by NCBiotech had total employment of 63,143 jobs and \$55.3 billion in estimated revenues, thereby generating the following:

 \$16.5 billion in business activity and 91,447 jobs through the Indirect Impacts associated with purchases from local suppliers;

Economic Impact Approach

TEConomy's analysis of the economic contribution of the life science industry employed the IMPLAN input/output (I/O) model for North Carolina. IMPLAN is one of the most widely used and respected economic impact models in the nation.

The analysis was based on data from NCBiotech's comprehensive and unique database of life science companies operating in the state, which provides more current and specific life science employment data than that available nationally and differs from the Bureau of Labor Statistics data utilized in the previous section. The IMPLAN I/O model estimates the broader supply-chain and employee-spending impacts associated with the life science industry in order to estimate both the linkages between and the impacts of the sector on the larger state economy. These linkages are termed the "multiplier effects" of the sector and measure the sector's contribution to the overall, larger state economy.

For more on the approach and methodology utilized for this impact analysis, and for definitions of terms used here, see Appendix A to this report.

- \$11.5 billion in economic activity and 85,691 jobs through the Induced Impacts associated with the increase in household incomes associated with the jobs created by the sector; and
- A total impact of \$83.3 billion in business activity and 240,281 jobs from the combined total of direct, indirect, and induced impacts.

The life science industry has a significant and growing impact on the North Carolina economy. In total, the life science industry directly accounts for more than 1 percent of all jobs in North Carolina and, when multiplier effects are included, accounts for 4 percent of state employment. The industry's impact is even larger in terms of the level of business activity in the state, with the life sciences directly accounting for 6 percent of state output and for 9 percent when multiplier effects are included. Since the first analysis of the economic impacts of the industry in 2008, the total impacts of the sector have increased from \$45.8 billion in business activity and 180,008 jobs to current levels of \$83.3 billion and 240,281 jobs.

Figure 11: Employment Impact—2008-2018 300.000 \$90.000 \$80,000 \$11,507 250,000 \$70,000 **x** \$60,000 200,000 85.691 \$50,000 **පි** 150,000 61,913 6,896 \$40,000 \$10,219 \$30.000 100,000 \$55.340 \$20.000 50.000 \$28.691 \$10,000 63.143 53.182 \$0 2008 2018 2008 2018 Direct Indirect Induced Direct Indirect Induced

Figure 10: Output Impact—2008-2018



The economic impacts of the life science industry are also presented by major subsector in Table 6, with the following key findings:

- The drug and pharmaceutical subsector has the largest impact, generating \$56.4 billion in economic . activity and supporting 132,507 jobs earning \$9.6 billion in labor income and generating \$1.4 billion in state and local government revenues;
- The **research**, **testing**, **and medical laboratory** subsector has the second-largest impact, generating . \$13.7 billion in economic activity and supporting 75,233 jobs earning \$4.8 billion in labor income and generating \$431 million in state and local government revenues;
- The **agricultural feedstock and industrial bioscience** subsector has the third-largest impact, generating . \$7.3 billion in economic activity and supporting 14,061 jobs earning \$1.0 billion in labor income and generating \$160 million in state and local government revenues;
- . The medical devices and equipment subsector generates \$3.2 billion in economic activity and supports 11,639 jobs earning \$0.8 billion in labor income and generating \$92 million in state and local government revenues; and
- The other life science subsector, which includes life science-related distribution as well as life science . companies active in sectors not included in TEConomy's industry-based definition, generates \$2.6 billion in economic activity and supports 6,841 jobs earning \$0.4 billion in labor income and generating \$81 million in state and local government revenues.

Economic Impact	Output (\$ Millions)	Labor Income (\$ Millions)	Employment	State/Local Tax Revenue (\$ Millions)		
Total Life Science Industry						
Direct Effect	\$55,340.3	\$6,849.3	63,143	\$793.4		
Indirect Impacts	\$16,464.4	\$6,230.8	91,447	\$796.3		
Induced Impacts	\$11,506.8	\$3,600.4	85,691	\$590.9		
Total Impact	\$83,311.4	\$16,680.4	240,281	\$2,180.6		
State Impact Multiplier	1.51	2.44	3.81			
Agricultural Feedstock & Industri	al Biosciences					
Direct Effect	\$5,406.5	\$379.2	2,532	\$66.1		
Indirect Impacts	\$1,229.9	\$428.5	6,265	\$57.9		
Induced Impacts	\$706.9	\$221.2	5,264	\$36.3		
Total Impact	\$7,343.3	\$1,028.9	14,061	\$160.3		
State Impact Multiplier	1.36	2.71	5.55			
Drugs & Pharmaceuticals						
Direct Effect	\$38,688.2	\$3,270.8	25,377	\$496.2		
Indirect Impacts	\$11,035.3	\$4,283.7	57,433	\$577.4		
Induced Impacts	\$6,673.9	\$2,088.2	49,697	\$342.7		
Total Impact	\$56,397.3	\$9,642.7	132,507	\$1,416.2		
State Impact Multiplier	1.46	2.95	5.22			
Medical Devices & Equipment						
Direct Effect	\$2,061.3	\$372.7	4,211	\$33.7		
Indirect Impacts	\$637.5	\$220.6	3,579	\$31.5		
Induced Impacts	\$516.9	\$161.7	3,849	\$26.5		
Total Impact	\$3,215.7	\$755.0	11,639	\$91.7		
State Impact Multiplier	1.56	2.03	2.76			
Research, Testing & Medical Laboratories						
Direct Effect	\$7,335.1	\$2,657.9	29,106	\$155.6		
Indirect Impacts	\$3,057.7	\$1,137.4	21,376	\$104.9		
Induced Impacts	\$3,323.2	\$1,039.8	24,751	\$170.7		
Total Impact	\$13,715.9	\$4,835.1	75,233	\$431.2		
State Impact Multiplier	1.87	1.82	2.58			

Table 6: Economic Contribution of the Life Science Industry to the North Carolina Economy by Major Industry Subsector, 2018

2018 EVIDENCE AND OPPORTUNITY: IMPACT OF LIFE SCIENCES IN NORTH CAROLINA

Economic Impact	Output (\$ Millions)	Labor Income (\$ Millions)	Employment	State/Local Tax Revenue (\$ Millions)
Other Life Sciences				
Direct Effect	\$1,849.3	\$168.7	1,917	\$41.9
Indirect Impacts	\$503.9	\$160.5	2,794	\$24.6
Induced Impacts	\$286.0	\$89.5	2,130	\$14.7
Total Impact	\$2,639.2	\$418.7	6,841	\$81.2
State Impact Multiplier	1.43	2.48	3.57	

Source: TEConomy Partners' analysis of NCBiotech data using IMPLAN.

North Carolina Life Science Industry: Supply Chain Impacts

The economic activity supported by the life science industry impacts other industries across the state. The IMPLAN model used in this analysis permits the identification of the industries where the industry makes its purchases. As described above, the North Carolina life science sector generates \$16.5 billion in economic activity and 91,447 jobs through indirect impacts, or the purchases of goods and services from local suppliers. The top 20 industries impacted by the North Carolina life science industry in terms of both output (purchases) and total jobs supported are presented in Table 7. For instance, the "management of companies and enterprises" industry, which includes corporate and branch headquarters and other offices that oversee business operations, is the largest indirectly impacted industry in terms of both output and jobs, receiving \$4.2 billion in business activity and with 16,878 jobs supported by the life sciences.

NCBiotech maintains a database of identified suppliers to the life science industry. The Center's BioAssets Database contains data on 2,309 supplier companies providing goods and services to industry companies. The majority of the identified supplier companies are located in the Research Triangle Park region, 1,384 or 60 percent; still, the supply chain for the sector is distributed across the state (Figure 12). Of the 2,309 supplier companies serving the state industry, the largest number (1,019) are in professional, scientific, and technical services and provide a wide range of services from consulting to research to legal services. Other key supply chain sectors include manufacturing with 343 firms, administrative support services with 182 firms, and wholesale with 164 firms.



Figure 12: North Carolina Life Science Supplier Companies, by Region

Source: TEConomy Partners' analysis of the BioAssets Database.

Table 7: Top 20 Supplier Industries to the North Carolina Life Science industry in Terms of Output and Jobs, 2018

Top 20 Indirect Impact Industries	\$ Millions
Management of companies and enterprises	\$4,200.5
Wholesale trade	\$2,706.9
Real estate	\$979.1
Management consulting services	\$823.0
Employment services	\$352.3
Advertising, public relations, and related services	\$345.8
Monetary authorities and depository credit intermediation	\$324.6
Legal services	\$319.0
Electric power transmission and distribution	\$289.8
Truck transportation	\$258.1
Maintenance and repair construction of nonresidential structures	\$246.6
Architectural, engineering, and related services	\$215.8
Wireless telecommunications carriers (except satellite)	\$206.3
Lessors of nonfinancial intangible assets	\$200.4
Marketing research and all other miscellaneous professional, scientific, and technical services	\$193.7
Scientific research and development services	\$171.0
Data processing, hosting, and related services	\$168.5
Wired telecommunications carriers	\$151.1
Accounting, tax preparation, bookkeeping, and payroll services	\$151.0
Waste management and remediation services	\$137.7

Top 20 Indirect Impact Industries	Jobs
Management of companies and enterprises	16,878
Wholesale trade	11,959
Management consulting services	6,856
Real estate	5,079
Employment services	4,434
Services to buildings	2,792
Marketing research and all other miscellaneous professional, scientific, and technical services	2,745
Legal services	1,970
Maintenance and repair construction of nonresidential structures	1,764
Truck transportation	1,617
Business support services	1,609
Advertising, public relations, and related services	1,536
Office administrative services	1,501
Accounting, tax preparation, bookkeeping, and payroll services	1,493
Architectural, engineering, and related services	1,349
Warehousing and storage	1,220
Full-service restaurants	1,135
Landscape and horticultural services	1,10
Computer systems design services	1,07
Environmental and other technical consulting services	879

Source: TEConomy Partners' analysis of NCBiotech data using IMPLAN.

III. NCBiotech:

Enhancing the State's Life Science Innovation Ecosystem and Catalyzing Growth for More than Three Decades

The long-term, impressive rise of North Carolina's life science industry, its broader R&D and innovation ecosystem, and its significant economic impacts can be directly tied, at least in part, to the deliberate, sustained programmatic initiatives and partnerships of NCBiotech. For nearly 35 years, the Center has effectively designed and implemented activities and initiatives that span the range of unique elements that a complex, thriving life science ecosystem requires. The Center's early beginnings and activities created opportunity for statewide economic development in the life sciences, and today, its activities represent a best-in-class example of a world-class life science development organization.

NCBiotech, funded primarily through state government appropriations, has evolved its services and programming to address the key domains of industry and broader ecosystem development outlined in Figure 13. Each domain addresses unique ecosystem needs both statewide and at a regional level within the state. The Center provides direct assistance to both companies and research universities through its own programs, such as university grant funding to advance commercially viable life science research, and loan funding to early-stage companies through targeted programs; and it also acts as a facilitator and connector for companies and talented individuals to external sources of capital, job opportunities, wet-lab incubators, and professional groups, to name some examples. Each of these roles is important in ensuring a high-functioning ecosystem. While more direct, quantifiable programs are easier to attribute and track tangible "impact," the vital role of connector and facilitator is arguably just as valuable in growing a vibrant industry cluster, though it is not appropriate nor feasible to assign tangible dollar or job values to these activities.



Figure 13: NCBiotech Center Initiative Domains and Roles Enhancing the Innovation Ecosystem

The specific programs and activities of the Center can also be assigned along the chain of activities that are necessary in the context of technology- or innovation-based economic development (TBED) ingredients that lead to thriving industry clusters. Each element of this chain and the corresponding NCBiotech programs are displayed in Figure 14. What stands out is the comprehensive and strategic nature of the programming to address every key element of the TBED chain that extends out from basic scientific research to applied R&D, addressing the ecosystem for investment capital and workforce, and on through to support for business formation, attraction, and retention.





Source: TEConomy Partners, LLC and NCBiotech

This section of the report assesses economic and other ecosystem impacts generated by NCBiotech through specific funding and recruitment and expansion activities where formal impacts are measured. It also highlights new programs implemented by the Center since the prior edition of Evidence and Opportunity.

Measuring the Economic Impact of NCBiotech on the Development of the North Carolina Life Science Industry

In addition to NCBiotech's broad strategic impact on the industry through its role as connector and facilitator, the Center has directly supported the growth and development of the life science industry in North Carolina in two principal areas:

- 1. NCBiotech directly supports the growth and development of the industry through its Emerging Company Development program, through which the Center invests in promising, emerging life science companies across the state; and
- 2. NCBiotech also supports industry growth and development via retention, expansion, and recruitment activities, largely by providing its specialized bioscience capabilities, knowledge, and relationships to the North Carolina Department of Commerce, regional economic development organizations, and city and county economic development departments.

TEConomy has estimated the economic contribution of the companies supported by NCBiotech's business loan programs since its first assessment of the economic impact of the Center in 2008 and by the companies NCBiotech has helped to recruit to the state since the 2012 report.

NCBiotech's Business Loan Programs

Targeted, early-stage loans to life science businesses help create and support business activity in the companies receiving loans, which has a long-term impact on the state's economy. As a result, NCBiotech's loan programs create a "portfolio" of businesses assisted by the Center, and the operations of these businesses created or assisted represent the economic development impacts associated with NCBiotech. This analysis focuses on the impact of the total portfolio of all of the companies who have received funding since 1989 and are still in operation.

Since 1989, NCBiotech has made business loans to 204 companies. Of the 204 companies that have received loans, 107 are currently active in some form and these companies employ 2,544 workers.⁷ NCBiotech's business loan programs have invested in an expanding portfolio of companies that account for a growing share of life science employment in the state. The growth in employment in the portfolio of companies supported by the NCBiotech business loan programs is presented in Figure 15.

⁷ Some of these companies may have been acquired by other companies or have changed their names and, thus, may be active in some form. In cases where a company was known to be acquired, the acquiring company was included.



Figure 15: Number of Active Companies that Received NCBiotech Business Loans and Associated Employment

TEConomy has estimated the economic impacts of these 107 active, loan-recipient companies. As presented in Table 8, these 107 companies had total employment of 2,544 and estimated revenues of \$2.5 billion and accomplish the following:

- Generate \$3.8 billion in economic activity in the state;
- Create or support 10,390 jobs earning \$732 million in labor income; and
- Generate an estimated \$98.4 million in state and local tax revenues.

The economic impacts associated with the portfolio of life science companies assisted by NCBiotech's business loan programs have grown rapidly over the past decade, increasing from 64 companies generating \$1.1 billion in economic activity and supporting 4,700 jobs as noted in TEConomy's 2008 report to 107 companies supporting \$3.8 billion in economic activity and 10,390 jobs today.

Source: NCBiotech data.

Table 8: The Economic Contribution to the North Carolina Economy of the 107 Currently Active Companies that Received NCBiotech Business Loans

Economic Impact	Output (\$ Millions)	Labor Income (\$ Millions)	Employment	State/Local Tax Revenue (\$ Millions)
Total Life Science Industry				
Direct Effect	\$55,340	\$6,849.3	63,143	\$793.4
Indirect Impacts	\$16,464	\$6,230.8	91,447	\$796.3
Induced Impacts	\$11,507	\$3,600.4	85,691	\$590.9
Total Impact	\$83,311	\$16,680.4	240,281	\$2,180.6

Impact of the 107 Currently Active Companies that Received Economic Development Loans				
Direct Effect	\$2,499	\$287.8	2,544	\$35.0
Indirect Impacts	\$746	\$286.0	4,080	\$37.4
Induced Impacts	\$506	\$158.2	3,766	\$26.0
Total Impact	\$3,751	\$732.0	10,390	\$98.4

Share of Total Industry Impact				
Direct Effect	4.5%	4.2%	4.0%	4.4%
Indirect Impacts	4.5%	4.6%	4.5%	4.7%
Induced Impacts	4.4%	4.4%	4.4%	4.4%
Total Impact	4.5%	4.4%	4.3%	4.5%

Source: TEConomy Partners' analysis of NCBiotech data using IMPLAN.

North Carolina receives a strong return on its investment in NCBiotech. TEConomy estimated the state government revenue portion of the estimated \$98 million in combined state and local government revenues generated by the active loan recipient companies (through direct, indirect, and induced impacts), based on U.S. Census Bureau government finances data. This analysis yields an estimated \$60.3 million in state taxes generated by these companies, an amount more than four times greater than the state's appropriation to NCBiotech of \$14.0 million for fiscal year (FY) 2018–2019. Companies that have received business loans from the Center now account for almost 5 percent of the economic activity associated with the entire life science industry.

NCBiotech's Support for State, Regional, and Local Economic Development Efforts

NCBiotech plays multiple roles in supporting the development of the life science sector in the state. In addition to its role in directly supporting commercialization and business growth through its Emerging Company Development program, NCBiotech supports the broader business recruitment and expansion efforts of the North Carolina Department of Commerce and other economic development organizations. With offices across the state, NCBiotech's team provides expert knowledge of the industry to support state and regional life-science business attraction, expansion, and retention efforts.

In the 2012 report, TEConomy began tracking the economic contribution made by companies recruited to or expanding in North Carolina, when the Center supported the recruitment. Since 2008, the Center has assisted in the effort to attract or retain 77 major life science employers, including Argos, Fresenius Kabi, INC Research (now Syneos Health), Merck, Novartis, and Novo Nordisk. This analysis focuses on the economic impact of the 25 company projects in which the Center assisted its economic development partners in FY 2017 and 2018. Based on data provided by the Center, these 25 companies have the potential to create a total of 3,080 jobs once they reach their projected employment levels.

North Carolina's Recruitment and Expansion Highlights from FY 2017-18

- INC Research (now Syneos Health) will move its corporate headquarters and 1,000 workers from Raleigh to Morrisville and add 550 jobs over the next 5 years as part of a \$37.9 million investment.
- German pharmaceutical company **Fresenius Kabi** will expand its drug manufacturing operations in Wilson, potentially bringing at least 445 new jobs over 5 years and \$100 million in investment.
- Corning Incorporated selected North Carolina for a two-location expansion and announced a \$189 million, 317-job project in Durham County and an \$86 million, 111-job project in Edgecombe County.
- AveXis, an Illinois-based clinical-stage company developing gene therapies for neurological genetic diseases, is investing \$55 million in a new Durham manufacturing facility that will create 200 jobs.
- bluebird bio, a Massachusetts-based, clinical-stage company committed to developing potentially transformative gene and cell therapies, has purchased a 125,000-square-foot manufacturing site in Durham County that will create an estimated 50 jobs.

Table 9 presents the results of TEConomy's analysis, indicating that, once the companies involved in these 25 projects attain their full projected level of employment, they will generate \$2.1 billion in economic activity and support 8,732 jobs earning \$580 million in labor income and generate \$59 million in combined state and local government revenues.

Economic Impact	Output (\$ Millions)	Labor Income (\$ Millions)	Employment	State/Local Tax Revenue (\$ Millions)
Direct Effect	\$1,235.4	\$302.1	3,080	\$21.1
Indirect Impacts	\$420.3	\$153.4	2,678	\$17.1
Induced Impacts	\$399.2	\$124.9	2,973	\$20.5
Total Impact	\$2,054.9	\$580.4	8,732	\$58.6
State Impact Multiplier	1.66	1.92	2.83	

 Table 9: Economic Contribution of the 25 Life Science Companies Assisted by NCBiotech in State Recruitment/

 Expansion Efforts in FY 2017 and 2018 to the North Carolina Economy

Source: TEConomy Partners' analysis of NCBiotech data using IMPLAN.

The Evolving Role and Focus of NCBiotech's Industry and Ecosystem Support— Recent Accomplishments and New Developments

With nearly 35 years of history, NCBiotech has learned that, for the industry to thrive throughout the state, its role must continually be evaluated and evolve, where appropriate, to emphasize new and emerging opportunities. Recent Center activities and new developments are profiled here.

Establishment of the Pfizer-NCBiotech Distinguished Postdoctoral Fellowship in Gene Therapy

Pfizer's growing presence in North Carolina now extends beyond its Sanford manufacturing facility to include the Chapel Hill-based gene therapy design and production capability following its recent acquisition of Bamboo Therapeutics. Bamboo was founded based on the work of Professor R. Jude Samulski, the director of the Gene Therapy Center at the University of North Carolina. (Samulski was recruited to UNC with the help of funding from NCBiotech.) Bamboo's, and now Pfizer's, technology focus is in Adeno-Associated Virus (AAV) vectors, which requires top scientific talent with extensive education and training and specific skill sets and scientific background.

To develop and expand this expertise in AAV gene therapy, Pfizer provided NCBiotech with a \$4 million gift to fund a postdoctoral fellowship program for early-career gene therapy researchers. The fellowship was established in 2017 and is designed to fund a total of 18 fellows spread across three classes, with the first six awarded in fall 2017. Pfizer-NCBiotech fellows conduct projects related to AAV gene therapy under the mentorship of gene therapy faculty researchers associated with any of North Carolina's research universities. In addition to the laboratory project, the training features nontechnical professional development as a distinguishing feature; this track consists of day-long modules that are organized by NCBiotech and cover key topics such as leadership and communication, project management, U.S. Food and Drug Administration (FDA) regulations, intellectual property, and the downstream manufacture of gene therapy products, all of which represent industry-relevant skills and knowledge that are typically not part of the academic training of life scientists.

The fellowship adds to the Center's suite of programming and support for initiatives related to workforce and talent as well as further rooting leading-edge research activities at the state's universities.

Crop Improvement Projects Led by the NCBiotech Crop Commercialization Program (CCP)

The Center's CCP group provides project management and coordination of research for several crop improvement projects focused on boosting viability of higher-profit cropping systems for North Carolina growers and for attracting new or enhancing existing state agribusiness. CCP leverages an industry-academic collaborative model to yield crop improvements with examples that include the following:

- Grain sorghum to support state swine and poultry producers;
- Stevia to support U.S. Stevia, LLC and to attract PureCircle, Ltd. to the state;
- Winter wheat and winter oilseeds to support livestock and to diversify winter cropping system opportunities; and
- Black carrots to assess production diversification for food ingredient companies.

Recently, the CCP engaged in addressing a long-term interest in attracting an industry base and opportunities for growing dedicated cellulosic crops for conversion to fuels and other high-value chemicals. State entities, as well as global renewable energy companies Biochemtex and Abengoa, have explored and promoted crops for bioenergy production in North Carolina. Biomass sorghum has been identified as the appropriate purpose-grown crop to provide the feedstock necessary for this endeavor, and the CCP has led a team of six researchers at North Carolina State University (NCSU) and Virginia Polytechnic Institute and State University (Virginia Tech) in a collaborative effort to optimize production.

The CCP and its research team were awarded one of just seven awards from the Biomass Research and Development Initiative (BRDI) of the U.S. Department of Agriculture (USDA) in 2016 to support research on the optimization of biomass sorghum production. The 3-year award totaled \$2.35 million, which was the largest among all awards. The North Carolina proposal was the only award with a non-university lead principal investigator, a major accomplishment for the Center in this coordinating role.

Establishment of the North Carolina Precision Health Collaborative (NCPHC)

North Carolina's multidimensional strengths that span its healthcare institutions, biomedical R&D capabilities, and information technology companies and competencies form the capacity to become a leading player in advancing precision health/precision medicine. NCBiotech has convened a leading group of partners across these areas to establish the NCPHC to foster innovation, create new companies, and grow jobs, while improving health outcomes for North Carolinians.

NCPHC is piloting a project to screen state residents for preventable or "highly actionable" conditions such as hereditary breast and ovarian cancer and Lynch Syndrome. In addition, NCPHC is participating in an update to the state's genetic plan and creating programming to educate healthcare professionals about precision health, including its value and opportunities for the state. The Center and NCPHC are also hosting or partnering around precision health conferences in 2019.

The work of NCPHC is currently focused on the following areas:

- Population-based genetic screening
- Pharmacogenomics
- Education/Policy
- Data infrastructure/governance/analytics.

Establishment of the NCBiotech Clinical Research Consortium

North Carolina is a world leader in contract research organizations (CROs) that provide analytical services, preclinical and clinical research and clinical trial management for pharmaceutical, biotechnology, and medical device companies and research institutions across the world. NCBiotech has organized a consortium of representatives from the CRO sector, academic institutions with clinical education programs, and representatives of the major state medical centers' clinical site programs to support and increase CRO investment and employment in the state.

The Consortiums' goals are to: 1) improve and expand clinical-based workforce development in North Carolina via curriculum enhancement and development; 2) develop and broaden the availability of CRO internships; and 3) increase awareness of CRO industry trends and career opportunities across the state.



IV. The Impact of Strategic Collaboration: Building a Biomanufacturing Sector through a First-of-its-Kind Workforce Initiative

In the mid- to late-1990s, recognizing that biopharmaceutical manufacturing was on the cusp of expansion, NCBiotech conducted an assessment of the workforce needs of manufacturers. The Center published the first in what would be an ongoing series known as *Window on the Workplace*, and then with the North Carolina Biosciences Organization (NCBIO), convened industry and postsecondary educators to discuss the unique requirements for workers in this evolving life science segment. The assessment found strong demand for process technicians, the largest occupational group in the burgeoning biomanufacturing sector. However, companies were facing several challenges in filling these positions, not the least of which was a misalignment of existing graduates with biotech associate degrees, who were trained in laboratory, not production, techniques. The then-current scale of educational programming was insufficient as well—the industry needed more qualified graduates with the right training for manufacturing.

Resulting from the needs assessment, NCBiotech and NCBIO collaborated with industry and the state's community college system to pilot an introductory course for technicians, BioWork. The course was modeled after Novozymes' training program with Vance-Granville Community College. At that point, companies began to realize that their workers needed the same knowledge and skills, despite the companies' different products and production processes. The aggregation of demand helped the workforce training program scale, leading to a breakthrough in biomanufacturing training. The Center and others began to distribute the course materials for both classroom and incumbent worker training, seeding the growth of bioscience and pharmaceutical manufacturing jobs in North Carolina.

In the early 2000s, building on the momentum of the BioWork course and continued growth of the biomanufacturing workforce, state industry leaders and NCBIO again came together around workforce needs and NCBiotech's next assessment in the *Windows* series. The collaborations, along with support from state government leaders, resulted in the formation of a consortium later named NCBioImpact, a first-of-its-kind industry-academic partnership described in the 2012 *Window on the Workplace* report as:

"This internationally recognized, first-of-its-kind training program combines the resources of the life-science industry, NCBIO and NCBiotech with the University of North Carolina System and the North Carolina Community College System (NCCCS)."⁸

NCBioImpact's training partners were funded with more than \$70 million from North Carolina's Golden LEAF Foundation, which administers tobacco settlement funds and invests them to advance economic development

⁸ Window on the workplace 2012: North Carolina's biomanufacturing and pharmaceutical-manufacturing workforce, North Carolina Biotechnology Center, page 9.

in the state, as well as a combination of in-kind corporate donations and equipment, and state funding for operating expenses. The new capability took form around the following assets and nodes across North Carolina:

- Golden LEAF Biomanufacturing Training and Education Center (BTEC) at NCSU's Centennial Campus—BTEC operates two facilities, the 82,500 square-foot main building and 5,000-square-foot annex, utilizing \$12.5 million of industry-standard equipment and a simulated cGMP (current Good Manufacturing Practice) pilot plant production facility. BTEC provides hands-on, industry-relevant training for undergraduates, graduate students, and working professionals within the life science industry and offers undergraduate minors or certificates in biomanufacturing; postbaccalaureate certificates to nondegree students; two Professional Science Master's degrees; a graduate minor; and two graduate-level certificates.
 - BTEC Impacts: Programs have enrolled more than 7,000 students since 2008 with steadily rising numbers of graduates; placement rates in industry reach 95 percent for undergraduates and 98 percent for graduate-level through FY 2018; BTEC master's graduates have been hired by 25 different biomanufacturing/biotech companies. Nearly 2,900 individuals have been trained in professional development programs.⁹
- NC BioNetwork—It leverages the state's network of 58 community colleges to deliver courses, certificates, workshops, and company-specific skill development in biomanufacturing, pharmaceuticals, food and beverages, and natural products. The Capstone Center, at NCSU's Centennial Campus, has a certified cleanroom and industry-standard equipment to simulate a real biomanufacturing production environment for education and training.

What is Biomanufacturing?

Biomanufacturing uses living cells and biological systems to make commercial products, or to extract and utilize a particular molecule via the bioprocessing of tissues or cells. These products or biological molecules are used across a varied set of applications and markets for medicines and vaccines; food and beverage ingredients and processing; and other industrial applications. Biomanufactured products can be harvested from animal or plant cells, from blood, or from microbes.

Biomanufacturing has come to play a critical role in the pharmaceutical and biological products manufacturing industry and represents an ongoing paradigm shift from traditional small-molecule therapeutic product manufacturing to products based on biomaterials and biomolecules. The role of this key segment of the biotech manufacturing industry is expected to continue growing to meet the needs of new generations of biobased products, ranging from medical products like immunotherapeutics to food and beverage applications in enzymes to industrial uses in plastics and other commercial products.

North Carolina represents a major hub of biomanufacturing activity and expertise. More than two dozen companies are part of this multidimensional sector of the life sciences (see details on the North Carolina context that follows).

⁹ Golden LEAF Biomanufacturing Training and Education Center Annual Report 2018.

- **BioNetwork Impacts:** It has served 90 companies; delivered 137 customized training courses; and trained 1,252 teachers and nearly 2,300 individuals overall.¹⁰ In 2017–2018 alone, 67 life science companies received training and support through the BioNetwork.
- Biomanufacturing Research Institute and Technology Enterprise (BRITE) at North Carolina Central University—BRITE features a 52,000-square-foot, state-of-the-art facility for hands-on learning for bachelor's and master's degree programs in pharmaceutical sciences as well as professional development short courses. BRITE has complementary research focus areas in drug discovery and manufacturing technology.
 - BRITE Impacts: In 2018, enrollment in the BRITE programs totaled 107 undergraduates in Pharmaceutical Sciences and 16 graduate students. Twenty of its undergraduates participated in a summer internship in 2018, spanning both research and industry work experiences. Nearly 90 percent of recent graduates have been placed in either industry, academia, or research positions. Since its inception in 2008, BRITE's Outreach Program has served 14,334 K-12 students and 743 teachers from 86 North Carolina counties.¹¹

While the *Window on the Workplace* series, and the institutions themselves, have compiled and published impacts of their efforts, some of which are summarized above, this section of the report focuses on the biomanfacturing sector that the NCBiotech and its partners in the NCBioImpact initiative have helped to build and support across the state and the impacts it is realizing.

NCBioImpact Presentation, accessed at: https://chambermaster.blob.core.windows.net/userfiles/UserFiles/Chambers/9295/CMS/Legislative_Life_Science_Caucus_ Files/Presentation---BioNetwork.pdf.

¹¹ North Carolina Central University, Biomanufacturing Research Institute and Technology Enterprise (BRITE).

Growth and Economic Impact of the North Carolina Biomanufacturing Sector Since 2003

At the outset of the NCBioImpact initiative in 2003, North Carolina had 17 companies in biomanufacturing that employed 4,754. These figures have risen since, with companies benefitting from the education and technical training and steady supply of talent provided through the workforce initiative (Figure 16). In North Carolina today, at least 25 biomanufacturing companies are active, and represent an impressive breadth of biomanufactured products and industry applications that span biopharmaceuticals, including specific applications and focus in animal health, food ingredients, and broader industrial applications as highlighted in Figure 17. Based on data from the NCBiotech Company Database, these companies employ 9,163 in 2018, a figure that has nearly doubled since 2003 (up 93 percent).





Source: NCBiotech Company Database

Continued attention to this area has translated into a highly specialized concentration for North Carolina in biological products manufacturing within the broader drug and pharmaceutical subsector—the state is nearly 400 percent more concentrated than the national average with an LQ of 4.71. North Carolina has developed a particularly strong concentration in vaccine development and manufacturing, with a group of companies recently emerging in developing and manufacturing gene therapies.



Biopharma	Animal Health	Food-related	Broader Industrial
 Gene therapies Immunotherapies Vaccines Biologics 	Enzymes for gut healthVaccines	 Botanical extraction products Citric acid Yeast mannan for animal feed 	 Industrial enzymes, microorganisms
Example Companies: Bluebird Bio, Biogen, Medicago, Merck, Pfizer, Xellia	Example Companies: Huvepharma, Zoetis	Example Companies: ADM, Avoca, White Labs	Example Companies: Novozymes

Economic impacts of the biomanufacturing sector developed in North Carolina can be estimated for both of the following:

- 1. The impact of the sector today, for the 25 companies active in the sector and their 2018 employment of 9,163; and
- 2. The change in sector employment since 2003 with the inception of the NCBioImpact education and training initiative.

As presented in Table 10, the 25 active biomanufacturing companies had estimated revenues of \$9.9 billion and generate nearly \$14.2 billion in economic activity in North Carolina while supporting 36,187 jobs earning an estimated \$2.7 billion in labor income. The firms generate an estimated \$368 million in state and local government revenues. The companies account for approximately 17 percent of the business activity related to the total life science sector.

Table 10: Economic Contribution of the 25 Currently Active Biomanufacturing Companies on the North CarolinaEconomy, 2018

Economic Impact	Output (\$ Millions)	Labor Income (\$ Millions)	Employment	State/Local Tax Revenue (\$ Millions)
Total Life Science Industr	у			
Direct Effect	\$55,340	\$6,849.3	63,143	\$793.4
Indirect Impacts	\$16,464	\$6,230.8	91,447	\$796.3
Induced Impacts	\$11,507	\$3,600.4	85,691	\$590.9
Total Impact	\$83,311	\$16,680.4	240,281	\$2,180.6

Impact of the 25 Biomanufacturing Companies Assisted by NCBioImpact				
Direct Effect	\$9,850	\$1,187.6	9,163	\$136.9
Indirect Impacts	\$2,485	\$904.4	13,251	\$136.2
Induced Impacts	\$1,850	\$578.7	13,773	\$95.2
Total Impact	\$14,185	\$2,670.7	36,187	\$368.3

Share of Total Industry Impact				
Direct Effect	17.8%	17.3%	14.5%	17.3%
Indirect Impacts	15.1%	14.5%	14.5%	17.1%
Induced Impacts	16.1%	16.1%	16.1%	16.1%
Total Impact	17.0%	16.0 %	15.1%	16.9%

Source: TEConomy Partners' analysis of NCBiotech data using IMPLAN.

Since 2003, employment in the companies served by NCBioImpact programs has nearly doubled, with a net increase of 4,409 jobs. NCBioImpact supported this growth by providing training and other workforce development support services. TEConomy estimated the economic contribution of the 4,409 jobs added by companies using NCBioImpact training since 2003. As presented in Table 11, these jobs generate nearly \$6.5 billion in economic activity in North Carolina, support 16,615 jobs earning an estimated \$1.3 billion in labor income, and generate \$166.4 million in state and local government revenues.

Table 11: Economic Contribution of the Growth in Employment in Biomanufacturing Companies since 2003 on the North Carolina Economy

Economic Impact	Output (\$ Millions)	Labor Income (\$ Millions)	Employment	State/Local Tax Revenue (\$ Millions)
Direct Effect	\$4,506	\$582.1	4,409	\$60.7
Indirect Impacts	\$1,082	\$399.3	5,735	\$60.9
Induced Impacts	\$869	\$271.9	6,471	\$44.7
Total Impact	\$6,457	\$1,253.2	16,615	\$166.4

Source: TEConomy Partners' analysis of NCBiotech data using IMPLAN.

It is important to recognize that in addition to supporting biomanufacturing, the NCBioImpact initiative has played a major role in meeting the workforce and talent needs of the even larger traditional pharmaceutical manufacturing subsector.

The Changing Landscape of Biomanufacturing: Considerations for Meeting Future Needs

While the advent of modern biomanufacturing itself represents a shift from traditional pharmaceutical manufacturing processes, the landscape of biomanufacturing is also continuing to evolve in real time as new cell-based and bioengineered product pipelines mature and increasing numbers of emerging therapies in this space are awarded FDA approval. The National Cell Manufacturing Consortium's 2016 technology roadmap notes that, even for cell-based products alone, "though this relatively new industry has been growing significantly—with annual U.S. revenue above \$1 billion—its potential is still far from being fully realized."¹² Now, market forces shaping the demand for biomanufactured products are converging with novel technologies coming online. This creates a changing landscape that requires ongoing innovative development to manufacture new therapeutic products, which has implications for the sector's workforce.

In many ways the ongoing evolution of the biomanufacturing industry mirrors broader technology and innovation trends across a number of other manufacturing industries, which all seek to remain competitive in the face of consumer demands for increased efficiency and customizability. This constraint is especially acute for biomanufacturers facing emerging product markets in cell-based and gene therapies (a growing concentration and focus in North Carolina), where a critical shortage of supply to advance into clinical

¹² Achieving Large-Scale, Cost-Effective, Reproducible Manufacturing of High-Quality Cells: A Technology Roadmap to 2025, National Cell Manufacturing Consortium, February 2016, page 1.

pipelines remains. Several related overarching trends shaping the adoption and advancement of new technologies in the biomanufacturing space include the following:

- Ongoing demand for refinements in production efficiency, particularly around the adoption of single-use systems, development of enabling technologies for continuous bioprocessing (CBP), and addressing downstream processing choke points;
- Broader shift toward "flexible" and "on demand" manufacturing operations that are optimized for smaller product batch sizes and to meet consumer demand for highly customized products that display highly specific biological properties and compositions;
- Increasing regulatory approvals for novel biobased therapeutics and the need to scale operations in the short term to meet demand from new patient populations;
- Increasingly competitive landscape with the emergence of broader portfolios of biosimilar and biogeneric
 options as well as fast-growing international competition in biomanufacturing operations; and
- Spillover effects from a number of other emerging technology areas being integrated in biomanufacturing and biotech business operations, including next-generation bioinformatics driven by machine learning advances; digitization and automation of manufacturing and industrial processes; Internet of Things (IoT)-enabled devices and equipment for continuous monitoring; and need for new data management, quality control, and "virtualization" technologies for synthetic biology processes.

The cumulative effect of these trends has caused biomanufacturers to begin to adopt the next generation of enabling technologies and will continue to push the industry to embrace more adaptable and affordable production models.

Technology Trends Enabling Next-Generation Biomanufacturing

Biomanufacturing has traditionally relied on batch processing of large-molecule compounds using limitedcapacity bioreactor runs in open facilities with relatively fixed-use facilities and operations models required to achieve scalability. As a result, biologically derived products and therapeutics have typically had costs that are orders of magnitude higher than chemical-based small-molecule products that have been able to better leverage overall advancements in industrial and manufacturing automation. This issue has spurred investment in the development of a first wave of biomanufacturing technology platforms over the past decade that are geared primarily toward improving cost efficiency and product quality in the manufacturing process itself. The aim of this group of technologies is to increase capacity while lowering operational costs required to support development pipelines, and many are only now reaching the technological maturity levels needed for companies to deploy them at scale. These technologies are being incrementally improved in an ongoing cycle as they are more effectively implemented by various biomanufacturing industry segments, but have begun to take root as the key pillars of the next-generation operations model needed to meet increasing demand. These production and processing-related technologies include the following:

 Production-scale bioreactor systems and high volume cell-processing advances: Driven by increasing demand for biobased compounds from end consumers, industry has begun incorporating technologies that have the potential to dramatically increase processing capacities. Advances in bioreactor process modeling and equipment have allowed new bioreactor systems to develop to meet production-scale needs while maintaining quality relative to bench-scale systems. Additionally, advancements in screening technologies, novel high-yield culture media alternatives, and parallel processing of varied cell lines continue to advance cell-based products.

- Continuous and closed-system bioprocessing: Processing and purification have historically created a bottleneck for biomanufacturers in meeting demand, with new advancements representing a paradigm shift from the traditional open-facility batch-processing model. Continuous bioprocessing technologies, which allow for continuous movement of compounds between processing steps similarly to traditional manufacturing, have been of particular interest to industry in improving capacity issues, but have been slow to be adopted due to complexity and regulatory concerns. New technologies have begun to come online that enable companies to more easily integrate continuous processing into their existing operations, such as perfusion and continuous chromatography systems, with adoption expected to accelerate as new types of systems are introduced. Similarly, a closed-system production flow, where compounds are never exposed to room environments during manufacturing, presents advantages to biomanufacturers in terms of reduced risk of contamination and reduced process times. New technologies are making these approaches more feasible, particularly connected instrumentation and sensors that are able to monitor product purity in real time as well as industrial automation equipment used to maintain process flow without human intervention.
- Single-use systems: Complementary to continuous and closed-system bioprocessing systems, these involve the increasing adoption of novel single-use systems characterized by disposable components replaced after each use in the manufacturing process. In addition to cost savings from cleaning and reconfiguration of operations between production runs, these technologies are the primary enablers of more modular biomanufacturing facilities that are at the initial stages of transitioning to the flexible, multiproduct manufacturing "cell" operations models that are being adopted by other types of manufacturing industries. A wide variety of single-use technologies are already in use and being actively prototyped by industry, ranging from disposable tubing and filtration to single-use bioreactors and diagnostic arrays. These technologies have proved to be invaluable to bridging the gap to smaller batch and more highly customized production runs for the biomanufacturing industry and are likely to see continued use and improvement for some time. Due to emerging concerns about managing waste from single-use operations, new hybrid approaches are beginning to combine disposable components with continuous processing systems for even greater efficiency gains.

While continued adoption of processing technologies and new manufacturing models takes hold and impacts both primary biomanufacturers and their supply chains, a further follow-on wave of new technologies has begun to emerge that are geared toward supporting new types of biobased therapeutics and bioengineered products. These technologies are enabling in nature and allow biomanufacturers to meet demand for novel immuno- and "-omics"-based therapeutics as well as highly tailored food and industrial biotechnology products. Several key emerging technologies representing new developments that biomanufacturing operations will need to integrate as these trends continue to unfold include the following:

 Next-generation DNA synthesis and sequencing technologies: While the costs for DNA synthesis and sequencing have declined exponentially over the past decade, a key driver for next-generation product development will be the ability to cost effectively incorporate upstream DNA "stock" and delivery vector manufacturing into existing processes to accommodate development of new genetically engineered products and ensure consistent high-purity yields. Novel microfluidics and microarray technologies are expected to be the primary enabling technologies for scalable production of DNA-based synthetic biology applications, with next-gen sequencing required for quality control.

- Scalable genetic editing toolkits: Another critical component of the success of next-generation bioproducts will be the ability to accurately target genetic sequences for modification at scale. Many current technologies utilize guide RNA approaches, but next-generation biomanufacturers will need to incorporate new iterations of gene editors that reduce off-target activity and incorporate increased delivery efficiency into processing of bioproducts. Similarly to DNA synthesis and sequencing, subsequent advancements in technology are expected to drive integration of genetic editing technologies into the manufacturing processes for downstream products in order to take advantage of efficiencies of scale. Biomanufacturers may become the primary managers of gene drives for large-scale production of certain types of genetically modified organisms to maintain quality control within the supply chain and will need to be positioned to rapidly respond to end-user needs in enabled downstream products.
- Novel synthetic biology components: Advancements in synthetic biology will continue to yield novel components that will need to be manufactured at scale for use in therapeutics, consumer products, and downstream manufacturing. These synthetic biocomponents can include upstream DNA constructs (also sometimes called BioBricks) that form building blocks for protein engineering and other functions, genetic delivery vectors, and other synthetic genes. They also include downstream synthetic systems such as cellular "factories," synthetic chromosomes and genomes, and synthetic microorganisms and tissues. Next-generation synthetic biology components will need to be highly modular and customized to individual consumer needs, necessitating flexible and efficient manufacturing approaches.
- Integrated bioinformatics: Advancements in high-performance computing technology and accessibility
 to machine learning tools will continue to drive computing closer to the point of use where it can have
 the greatest impact. This is particularly true of biomanufacturing, where advancements in bioinformatics
 have enabled biomanufacturing operations to make detailed on-site refinements to bioproducts
 in virtual production settings before implementing them. Advancements in comparative genomics
 and gene design technologies allow for optimized synthesis of downstream proteins and organisms,
 while continuous monitoring and high-throughput diagnostics software applications will continue
 to become integrated into production operations for enabling real-time product purity assessments.
 Biomanufacturers will need to attract and integrate a new bioinformatics workforce as well as IoTenabled infrastructure into traditional operations to fully realize the potential of this technology area.

The intersection of these two groups of technologies has the potential to produce revolutionary advances for the biomanufacturing industry. Short-term industry concerns tend to reflect the need for cost-effective solutions to meet demand, in large part due to the lag experienced by biomanufacturers in developing new technologies and production models relative to both the pace of innovation in broader manufacturing industries as well as the pace of development of potential breakthrough therapeutics and novel biological engineering techniques. This perspective is reflected in industry stakeholder survey results from an annual survey of biopharmaceutical capacity and production shown in Figure 18, indicating a prioritization of operations and processing technology integration. However, it is important for biomanufacturers to keep in mind the enabling technologies when planning for future capacity as their long-term impacts potentially have amplifying effects on other systems employed to address production costs and efficiency.



Figure 18: Requirements Expected by End Users in Future Biomanufacturing Systems

Source: 14th Annual Report and Survey of Biopharmaceutical Capacity and Production: A Study of Biotherapeutic Developers and Contract Manufacturing Organizations, BioPlan Associates Inc., April 2017.

As NCBiotech and its state partners have done in the past, the industry challenges and technology trends highlighted here should be monitored, and the vital dialogue they have facilitated with the industry must continue to ensure that the workforce, talent, and broader ecosystem needs of this vibrant and highly competitive sector are met into the future. To this end, NCBiotech sponsors a Biomanufacturing and Process Development Exchange Group composed of industry and academic biomanufacturing professionals. This group meets regularly to track bioprocessing issues, learn from presentations by various experts, and discuss solutions to the future needs of this sector.

Appendix A: Data and Methodology

Defining the Life Science Industry

The following presents the industry definition utilized in Section 1 of this report based on the detailed North American Industry Classification System (NAICS) codes that make up the five major subsectors of the life science industry.

Table A-1: NAICS-based Definition of the Life Science Industry

Life Science Subsector	NAICS Code	NAICS Description
Agricultural Feedstock & Industri	al Biosciences	
	311221	Wet Corn Milling
	311224	Soybean and Other Oilseed Processing
	325193	Ethyl Alcohol Manufacturing
	325311	Nitrogenous Fertilizer Manufacturing
	325312	Phosphatic Fertilizer Manufacturing
	325314	Fertilizer (Mixing Only) Manufacturing
	325320	Pesticide and Other Agricultural Chemical Manufacturing
Drugs & Pharmaceuticals		
	325411	Medicinal and Botanical Manufacturing
	325412	Pharmaceutical Preparation Manufacturing
	325413	In-Vitro Diagnostic Substance Manufacturing
	325414	Biological Product (except Diagnostic) Manufacturing
Medical Devices & Equipment		
	334510	Electromedical and Electrotherapeutic Apparatus Manufacturing
	334516	Analytical Laboratory Instrument Manufacturing
	334517	Irradiation Apparatus Manufacturing
	339112	Surgical and Medical Instrument Manufacturing
	339113	Surgical Appliance and Supplies Manufacturing
	339114	Dental Equipment and Supplies Manufacturing
Research, Testing, & Medical Lab	oratories	
	541380*	Testing Laboratories
	541711	Research and Development in Biotechnology
	541712*	Research and Development in the Physical, Engineering, and Life Sciences (except Biotechnology)

Life Science Subsector	NAICS Code	NAICS Description
	621511	Medical Laboratories
Bioscience-Related Distribution		
	423450	Medical, Dental, and Hospital Equipment and Supplies Merchant Wholesalers
	424210*	Drugs and Druggists' Sundries Merchant Wholesalers
	424910*	Farm Supplies Merchant Wholesalers

*Includes only the portion of these industries engaged in relevant life science activities.

Economic Impact Approach and Methodology

Using the information on the size and composition of the North Carolina life science industry provided by the North Carolina Biotechnology Center (NCBiotech), TEConomy Partners. LLC prepared an analysis of the economic impact of the industry on the State of North Carolina's economy using the IMPLAN input/output model.¹³ IMPLAN, one of the most widely used models in the nation, can be used to analyze the impacts of companies, projects, or entire industries. An input/output (I/O) analysis examines the relationships among businesses and among businesses and final consumers. I/O analysis is based on the use of multipliers, which describe the response of an economy to a change in demand or production. Multipliers measure the effects on an economy from a source of economic activity, in this case, the jobs and activities of companies in the life science industry in North Carolina.

The economic activity generated in a state is greater than the simple total of spending associated with the event or activity being studied. As money is earned, it is, in turn, spent, earned, and re-spent by other businesses and workers in the regional economy through successive cycles of spending, earning, and spending. However, the spending in each successive cycle is less than in the preceding cycle because a certain portion of spending "leaks" out of the economy in each round of spending. Leakages occur though purchases of goods or services from outside of the region and federal taxation. The IMPLAN multipliers used in this analysis capture the effects of these multiple rounds of spending.

This report measures the economic impact of the life science industry by focusing on four measures of economic impact:

- Employment. The total number of full- and part-time jobs in all industries;
- **Output.** The total value of production or sales in all industries;
- **Labor Income.** Total labor income including wages and salaries, benefits, and self-reported income earned by the workers holding the jobs created;¹⁴ and

¹³ See www.implan.com for a description of the model.

¹⁴ The earlier 2008 and 2010 reports used Employee Compensation as a measure of economic impact. Beginning in the 2012 report and continuing in this report, in order to be comparable with other research done in this area, the broader Labor Income measure, which includes self-reported and proprietor income, was used.

• **State and Local Government Revenues.** The fiscal benefits accruing to both state and local governments in North Carolina as a result of the direct and multiplier impacts associated with the North Carolina life science sector, and the portfolio of companies assisted by NCBiotech.

Four measures of the economic activity and impact of the jobs supported by the life science industry are included as follows:

- Direct effects. The change in economic activity being analyzed—in this case, the business activities
 of the life science industry, including life science companies, life science research, and the Center's
 portfolio of assisted businesses. For this analysis, TEConomy used the employment data from the
 NCBiotech Company Database and the IMPLAN model to estimate business activity based on these
 activities;
- **Indirect effects.** The changes in inter-industry purchases, for example, the purchase of raw materials by a life science manufacturer, in response to the change in demand from the directly affected industries;
- **Induced effects.** The changes in spending from households as income and population increase due to changes in production; and
- Total effects. The combined total of direct, indirect, and induced effects.



Appendix B: Regional Life Science Industry Maps

The following maps present the location of North Carolina's life science industry companies by region, by industry subsector (color), and employment level (size) for 2018. Information for each map is generated from the NCBiotech Company Database.

Figure B-1: Charlotte Region



Figure B-2: Eastern Region





Figure B-3: Southeastern Region

Figure B-4: Piedmont Triad Region





Figure B-5: Research Triangle Region

Figure B-6: Western Region



