Heartland BioWorks: Leading economic opportunities through a secure US biotech supply chain

With biologics widely recognized as the medicines of the future (e.g., for Alzheimer's, cancer, obesity), maintaining US dominance is critical to the health of the nation. Understanding its importance to national security, President Biden has set forth the goal of ensuring that bioproducts invented in the US are also *made* in the US.[1, 2]

Indiana's Indianapolis-Carmel-Anderson metropolitan statistical area ("the MSA") features the unmatched collection of resources and capabilities necessary to become the world-leading force that realizes the President's biomanufacturing vision. The region is home to landmark industry leaders that span the bioecosystem (e.g., global HQs of Eli Lilly, Corteva, and Elanco and North American HQ of Roche); R1 institutions focused on biotechnology and manufacturing innovations (i.e., Indiana and Purdue Universities' Indianapolis campuses, to which the State recently committed $120M[3]); coordinated state-regional-local prioritization of life sciences to advance economic opportunities[4]; a rapidly growing venture ecosystem (biotech VC investment tripled from 2019-2022[5]); and significant biotech investment momentum (i.e., 5x increase in biotech investment commitments from 2021 to 2022, resulting in 3,000 new jobs[6]). Leveraging these resources, Indianapolis has attracted more than $1.5B in biotech committed investment since 2015, while Fishers (also in the MSA) has attracted over $775M since 2020 through creative incentives and the city-led development of a 70-acre Life Science and Innovation Park.

At the state level, Indiana leads the nation in pharmaceutical exports and has the second highest concentration of life sciences jobs in the US.[7] With the highest concentration of advanced manufacturing jobs in America and a preeminent logistics infrastructure, including the second largest FedEx hub in the world, Indiana has the unique capability to both *make* and *move* life-saving medicines to support the health of the nation. Recognizing this competitive advantage, the State has made significant investments to further catalyze biotechnology and manufacturing advancements: (1) $540M investment in programs and grants for 2023-2025 that support talent and economic growth, quality of life improvements, and/or smart manufacturing and (2) $182M+ to develop the LEAP Lebanon Innovation District that comprises 10,000-acres of shovel-ready sites near Indianapolis to attract megaprojects to the region.

The region has both the *capability* and the *capacity* for accelerated growth in biomanufacturing. Central Indiana was the first place in the world to make biosynthetic insulin and the only place to make all three COVID-19 vaccines approved for use in the US. With focused investment, the EDA can capitalize on the region's significant foundation to create the global epicenter for next-generation biotechnology companies, quality job creation, and equitable workforce development and entrepreneurship.

Leading this effort, the Heartland BioWorks hub ("BioWorks") is a consortium of Indiana stakeholders concentrating their efforts and resources on key technology focus area ("KTFA") 7, "biotechnology, medical technology, genomics, and synthetic biology," leveraging technologies from KTFAs 1 and 4 to catalyze growth. BioWorks will initially focus on three integrated activities that address gaps in both the region and nation:

1. BioWorks Training Institute (BioTrain) – The nation is faced with growth-hampering bioworkforce shortages.[2] BioWorks will establish an institute to provide training and industry work experiences to prepare trainees for high-paying jobs that support the growing biomanufacturing sector. The facility will be located in a historically disadvantaged community and leverage the nation's largest singly-accredited community college system, Ivy Tech.

2. BioWorks Bioproduct Launch Network (BioLaunch) – Small biotechs and startups are often forced to offshore their production because they lack the resources and scale needed to work with

US contract development and manufacturing organizations (CDMOs) or justify development of their own production facility. BioLaunch will coordinate and implement mechanisms to access the region's contract manufacturers and distributors, addressing lab-to-launch gaps, while keeping innovations, intellectual property, and jobs in the US.

3. BioWorks Advanced Manufacturing Innovation Network (BioMake) – As noted by the White House,[1,2] the National Academies of Sciences, Engineering, and Medicine,[8] and the President's Council of Advisors on Science and Technology,[9] biopharma manufacturing must modernize to remain competitive and deliver value to patients. BioMake will provide resources, funding, and coordinated access to a partner facility dedicated to testing and demonstrating next generation biomanufacturing technologies (e.g., high-intensity processing, continuous manufacturing, advanced automation, on-line analytics, intelligent sensors, modular production, AI/ML) to improve the efficiency, capability, and cost of operations.

Defined Geographic Region

The MSA (pop: 2.14M) sits at the intersection of highways I-65, I-69, I-70, and I-74, making it a critical distribution hub within a day's drive to 80% of the US population. Bioscience is a driver of the MSA economy with $13.3B in economic output and employing over 35,000 citizens with an average wage of over $85,000. While Indianapolis, an EDA Build Back Better Regional Challenge Finalist, will anchor BioWorks, the hub will reach to the adjacent MSAs of Bloomington and Lafayette. The Bloomington MSA (pop.: 161,227) is home to Indiana University and several bioscience companies (e.g., Catalent, Cook). The Lafayette MSA (pop.: 235,066) is likewise home to Purdue University and key industry members (e.g., Evonik). All three MSAs have been recently noted as having significant and diverse levels of biotech industry activity,[10] enabling BioWorks to build on a unique combination of assets that connect a larger metro area to significantly benefit two nearby smaller cities and the rural communities that lie between them.

Despite the region's economic strengths and recent growth, inequities still exist. Indianapolis' northwest area had a pre-COVID per capita income of less than $20,000 and an unemployment rate more than double that of the MSA. This, and similar inequities across the MSA, align with areas that have high percentages of people of color. Addressing inequity by locating proposed BioWorks assets in disadvantaged communities (e.g., NW Indianapolis) along with proven support services, community-building, training, and on-boarding programs for historically disenfranchised workers will enable BioWorks to create equitable outcomes for local communities.

BioWorks Partners and Collaboration

BioWorks will be led by a 501(c)(3) corporation, Applied Research Institute, Inc. (ARI). ARI serves Indiana by incubating and managing innovation ecosystems to bridge and align investments, technology development, and transition planning and commercialization. At the helm will be the BioWorks Regional Innovation Officer (RIO), John Fernandez, a first-generation American and recognized innovation expert, Fernandez was the former leader of the EDA (2009-2012), Global Chief Innovation Officer at Dentons (2012-2022), Mayor of Bloomington, IN (1996-2003).

ARI and the RIO will work closely with the region's unique assets focused on coordinating life sciences and advanced manufacturing—assets that have built a strong collaborative history among the BioWorks consortium partners. These resources include the Central Indiana Corporate Partnership (CICP), a non-profit that for nearly 25 years has brought together the region's corporations, foundations, and universities to promote economic and workforce resilience. As further described in their letter of commitment, CICP's many collaborative efforts include the incubation of key BioWorks contributors (e.g., ARI, BioCrossroads, the Indiana Biosciences Research Institute (IBRI), the 16 Tech Community Corporation (16TCC)). Working with CICP,

ARI will seek to add new voices and integrate BioWorks' core partners: Eli Lilly; Catalent; Evonik; Elanco; INCOG; IBRI; the Central Indiana Building Trades Council; Central Indiana Regional Development Authority; Purdue and Indiana Universities, Ivy Tech, the University of Notre Dame, 16TCC, Tougaloo College R&D Foundation (TCRDF), the State of Indiana/Indiana Economic Development Corporation (IEDC), and the City of Indianapolis. This team will drive collaboration and growth across the hub's full membership (see Letters of Commitment).

Equity and Diversity

To ensure inclusive and equitable outcomes, BioWorks will expand the evidence-based approaches initiated by 16TCC and EmployIndy. 16TCC was formed to develop the 50-acre 16 Tech Innovation District into a community focused on bioscience, technology, and advanced manufacturing investment. Located in a historically-distressed area of Indianapolis where 76% of the 40,000+ residents identify as people of color, 16TCC has developed expertise in cultivating grassroots, trusted, neighborhood-based connectivity. It has MOUs with seven local community-based organizations, directing neighbors to opportunities, particularly those at 16 Tech (e.g., BioTrain). Through these programs, 16TCC has created formal structures to develop and sustain social networks with diverse populations in the region.

Complementing this, EmployIndy, a Department of Labor-funded workforce development organization, has long-standing recruiting programs and wrap-around services through its network of 150+ partners to effectively support diverse community members in their career pathways. In 2022 alone, they provided nearly 23,000 career exploration experiences to K-12 students and engaged 4,677 individuals in work-based learning experiences. They also placed 1,489 individuals into good and promising jobs through Wednesdays@WorkOne and Rapid Re-Employment Response, Indianapolis' effort to re-employ dislocated workers. In total, they served over 50,000 residents of Indianapolis, and of those who self-identified, 75% were people of color.

The networks and expertise of 16TCC and EmployIndy have been leveraged since the inception of BioWorks to ensure the inclusion of diverse voices in the planning of BioWorks strategies. We understand the value of inclusive representation and recognize the need to raise up, rather than push out, struggling local communities. Pairing these partners' efforts through BioWorks will reap multiple benefits: 1) historically underrepresented individuals will be effectively recruited and supported for high-paying biomanufacturing careers; 2) employers will have a new, diverse, job-ready talent pool to support growth; and 3) consortium members will learn strategies for inclusive outcomes through the co-production of talent and engagement with 16TCC and EmployIndy. BioWorks also includes Indiana's Predominantly Black Institution, Martin University, and TCRDF, which has committed to at least 120 interns recruited from its network of 30+ HBCUs as participants in BioTrain to further diversify the regional bioworkforce.

Composition and Capacity of the Regional Workforce

The bioscience industry provides over 43,000 good jobs across the Indianapolis, Lafayette, and Bloomington MSAs.[11] Looking ahead, there is an expected gap of at least 1,300 biomanufacturing workers per year in the region, which mirrors the national bioworkforce shortage called out by President Biden.[2] To meet this local and national challenge, BioTrain, will bring more workers into the regional economy, prepare talent for priority occupations, connect historically excluded residents with high-quality jobs, and catalyze innovation by diversifying work places and innovation spaces. BioWorks' envisioned training program is the result of several years of industry engagement by BioCrossroads (CICP's life sciences initiative), Purdue, and Ivy Tech to identify specific skill and qualification needs to address workforce shortages.

BioTrain will be a combination of classroom and hands-on training on state-of-the art

equipment. Flexible, stackable credentials coupled with industry experiences (e.g., apprenticeships, internships) will prepare participants for biomanufacturing careers (e.g., operators) and feed into existing higher credentials for technician, engineer, or scientist roles (e.g., Ivy Tech's biomanufacturing associate's degree or the advanced pharmaceuticals manufacturing BS/MS programs to be launched at Purdue-Indianapolis in 2024). Employers will also be able to upskill or reskill their current workforce. Tightly tied to Indiana's community college system, BioTrain will leverage Ivy Tech's Smart Manufacturing Lab that will also be located at 16 Tech, developed with support from Eli Lilly. Importantly, BioTrain will include industry-recognized curriculum (already used by Eli Lilly and many others) with a regionally-exclusive contract, creating a biomanufacturing workforce development hub that attracts and connects talent with regional employment. As training participants exit the program, BioWorks will leverage Ascend Indiana's unique job matching platform to connect training participants with good jobs. Since its launch in 2017, Ascend, has partnered with 700 employers; met with more than 13,000 job seekers; and connected more than 4,000 individuals to career opportunities, with approximately 50% coming from underrepresented backgrounds.

Innovative "Lab to Market" Approaches

BioWorks will leverage ARI's proven model of consortium management to rapidly accelerate the lab-to-market pipeline. ARI's model leverages its position as a neutral third party, coordinating the ideation, vetting, prioritization, IP processes, and translation of projects focused on economic and workforce development. Recently, within 60 days ARI brought together 110 members across the microelectronics innovation spectrum to generate 100 new projects designed to accelerate semiconductor commercialization across a three-state region.

This model will support BioWorks' lab-to-market framework for two critical biomanufacturing initiatives: *BioLaunch* and *BioMake*. BioLaunch will integrate the latter stages of the bioproduct value chain, moving innovations from late stage clinical development to manufacturing and distribution. Targeting small and medium biotech innovators, including start-ups, BioLaunch will coordinate the region's strong CDMO presence across both drug substances (e.g., Catalent, Evonik) and drug products (e.g., INCOG) to: (1) identify contract capacity for small-scale production, (2) connect innovators to CDMOs, (3) implement mechanisms that surmount scale/cost barriers to using this capacity; and (4) coordinate distribution with Indiana's bioproduct logistics network (e.g., Langham Logistics, Conexus). Through this networked approach, BioLaunch will catalyze regional biotech innovation, support new and existing regional companies, and accelerate the US production of innovative life-saving medicines—creating a nexus where next-generation bioproducts are quickly discovered, made, and moved.

BioMake will further advance these industries through support (e.g., seed funding) of biomanufacturing innovations that dramatically improve processes—lowering costs, improving speed of production and preparing manufacturers to make next-generation medicines (e.g. precision therapeutics). BioMake will help coordinate the Purdue Advanced Pharmaceutical Manufacturing Technology Incubator, a 10,000 sq. ft. suite at the Indiana Manufacturing Institute. The incubator will provide flexible space for pilot scale manufacturing research for both industry and academic groups, and will be supported by an adjacent analytical lab. With industry-led selection and prioritization of incubator projects, innovations are expected to span automation, AI/ML, process analytical tools, flexible manufacturing, real-time release, etc. BioMake will integrate Purdue's NIST Manufacturing Extension Partnership to support commercialization and adoption of these advancements, enabling the region to spearhead biomanufacturing innovation.

Opportunities for Accelerated Growth

The region has a long history of strategically prioritizing KTFA 7, with initiatives such as the 2002 creation of BioCrossroads and the 2013 founding of the IBRI, the country's first industry-led life sciences research institute. Ultimately, Indiana is positioned to greatly outperform national biotech growth trends. Already, Eli Lilly is developing a $3.7B R&D and manufacturing campus at LEAP (the company's largest manufacturing investment at a single site *ever*), which leaves 90% of the district ready for new tenants and creates a potential investment pipeline of $56B. IEDC is exploring other sites, such as a long-closed GM plant near the BioTrain facility, for its next such project, aiming for more equitable growth across the region.

BioWorks has conducted significant research and industry outreach over the past two years (e.g., six workshops, three industry surveys, and 150+ interviews) to identify the specific gaps that need to be addressed to effectively capitalize on the region's resources to become the global leader in biomanufacturing. Addressing these gaps through EDA and additional investment will enable the region to capture a greater share of the $2.4 trillion in global economic impact expected annually from the sector in the near future.[12] The biotech jobs in the MSA represent one of the nation's most concentrated and diverse bioscience industry sectors.[7] Through BioWorks, we will build on Central Indiana's biotech growth trends to beat national projections, resulting in the creation of nearly 13,000 new bioscience jobs in the region over the next 10 years, with an economic labor impact of nearly $30B. These new jobs will be filled through the pipeline of diverse participants that gain relevant skills at BioTrain, which has been designed to meet this expected demand. This influx of workers to the bioscience industry should also prompt new business starts. Between recently launched State initiatives to support entrepreneurship and the bio-specific capacity made available through BioLaunch, BioWorks expects the launch of 65 new bioscience businesses.[13]

Given the region's per capita income of $40,912 compared to its average wage of $158,002 in pharma and biosciences,[14] BioWorks will catalyze massive economic benefit and lift a significant number of families out of poverty. To measure the ongoing impact of BioWorks, we will work with the Purdue Center for Regional Development (an EDA University Center) to develop a robust evaluation framework and identify and track additional metrics (e.g., those from Justice 40, Opportunity Insights, and Indianapolis's framework for inclusive growth[15]).

Impact on Economic and National Security of the Entire United States

BioWorks directly addresses national security concerns related to the health of the American people.[1,16] Ensuring the US is able to drive new innovations in biotechnology and keep them here through advancements in biomanufacturing capabilities and capacity will help secure the health of the nation, strengthen our economy, and provide new laneways to achieve White House goals around equity, rapid innovation, and supply chain security. As the pandemic demonstrated America's unmatched capabilities in biotechnology innovation, Indiana rose to the challenge as the only state to manufacture all three of the leading COVID-19 vaccines—doing so in record time through a collaborative government-industry approach. Beyond this, with partners like Eli Lilly, Elanco, and Corteva Agriscience and the region's unique capabilities in agbiosciences, BioWorks can leverage innovation and workforce synergies between the human, animal, and ag sectors—addressing the full spectrum of the bioeconomy for the nation.[2] By coordinating our growing resources and creating key assets and networks that equitably address commercialization and workforce gaps, BioWorks will rapidly accelerate the region's economy, advance equitable economic mobility, and secure the US's global leadership in bioproducts.

Note: Tech-based potential of the region; Role of the private sector detailed throughout

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