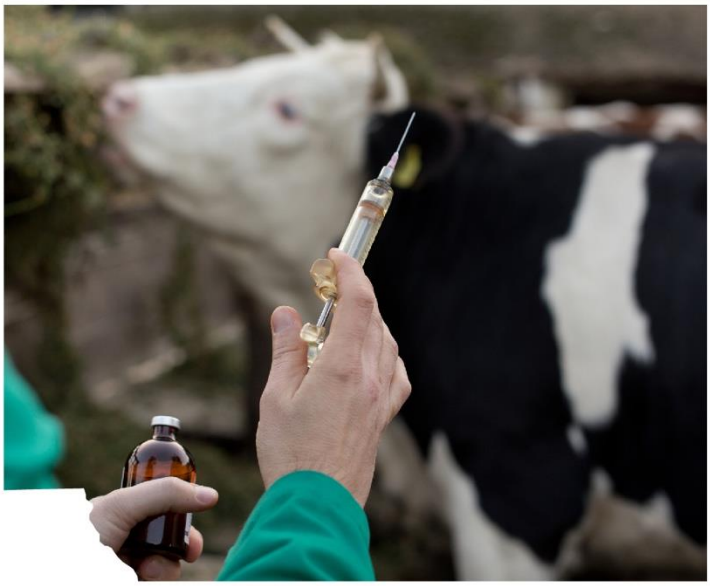

Phase I Report:

Core Competency Analysis, Platform Identification and Crosscutting Strategies for Iowa Bioscience Development

Performed for: Iowa Economic Development Authority

Performed by:TEConomy Partners, LLC

November 2017

IOWA economic development

TECONOMY PARTNERS LLC

TEConomy Partners, LLC is a global leader in research, analysis, and strategy for innovation-based economic development. Today, we're helping nations, states, regions, universities, and industries blueprint their future and translate knowledge into prosperity.

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Executive Summary

A. Introduction

Iowa benefits greatly from the bioscience sector. Biosciences overall represent an economic specialization for the state (with a location quotient of 1.36 – meaning the state has 36% more employment in biosciences than anticipated given national normative levels). Biosciences provide high-wage family sustaining jobs (with an average wage of $67,673 versus the average Iowa private sector wage of $41,964), and Iowa has been generally outperforming the nation in terms of bioscience employment growth (plus, biosciences have added jobs at a rate exceeding that of Iowa's private sector overall). Specialized, growing and paying strong, family sustaining wages – biosciences are critical to Iowa's current economic success and hold much potential for further focused development.

Because biosciences represent a fast moving and expanding area of scientific and commercial activity, it is imperative that the State of Iowa have an up-to-date understanding of its bioscience assets, core competencies and opportunities for ongoing development. The last analyses of Iowa's biosciences were performed in 2004 and updated in 2011 – conducted by the Battelle Technology Partnership Practice (TEConomy Partners forerunner organization). The analysis reported herein brings forward a current quantitative and qualitative analysis of Iowa's bioscience core competencies and prioritizes platforms that are attractive opportunities for further bioscience development in the state. In addition, the report provides a series of strategic recommendations that are cross-cutting for bioscience development in Iowa and will be followed-up by a Phase II report profiling platform specific strategies and actions.

B. Iowa's Bioscience Core Competencies

Iowa's bioscience core competencies have been identified through an in-depth process of analytics – with specialized cluster analysis performed of bioscience research output (publications) together with analysis of patents, entrepreneurial activity and business operations. These quantitative data were supplemented with a series on one-on-one and group interviews with key stakeholder organizations, companies and research teams to identify strengths, weaknesses, opportunities and threats relating to specific areas of bioscience in Iowa.

Iowa enjoys a robust base of bioscience core competencies, with these identified on Table ES-1 and provided with a numeric score pertaining to their strengths across a range of evaluated metrics (both R&D and commercial in orientation).

Table ES-1: Identified Iowa Bioscience Core Competencies and Comparative Scoring (Higher score equals a stronger core competency)

Core Competency Score	Agricultural and Associated Bioscience	Biomedical Life Sciences	Cross-cutting and Basic Sciences
>14	• Plant sciences (19) • Animal infectious diseases and veterinary medicine (18) • Biofuels and biobased chemicals (15) • Agricultural equipment (15)		• Genetic engineering and biotechnology (20) • Infectious diseases (microbiology, bacteriology, virology) (16)
10 to 14	• Animal and vegetable oils (12)	• Audiology (11) • Ophthalmology (11)	
<10	• Food products and additives/ingredients (9) • Animal nutrition (6)	• Medical imaging (9) • Orthopedics (7) • Dentistry (7) • Cancer (6) • Medical devices (6) • Cardiology (5) • Aging (4) • Diabetes (4) • Neuroscience (4) • Perinatology and neonatology (3) • Nephrology (2) • Pulmonology (2) • Cleft Disorders (1) • Obesity (1)	• Drugs and pharmaceuticals (9) • Biochemistry (9) • Biological sampling and analysis (5)

Core competencies vary greatly in their ability to promote economic development in a state, and rather than building programs around individual core competencies, best-practice is to identify "development platforms" that comprise clusters of core competencies, an existing or emerging base of relevant industry in the state, and (most importantly) a line-of-sight to substantial growth markets with good prospects for commercial growth, new job creation and wealth generation.

C. Recommended Platforms for Iowa's Bioscience Development

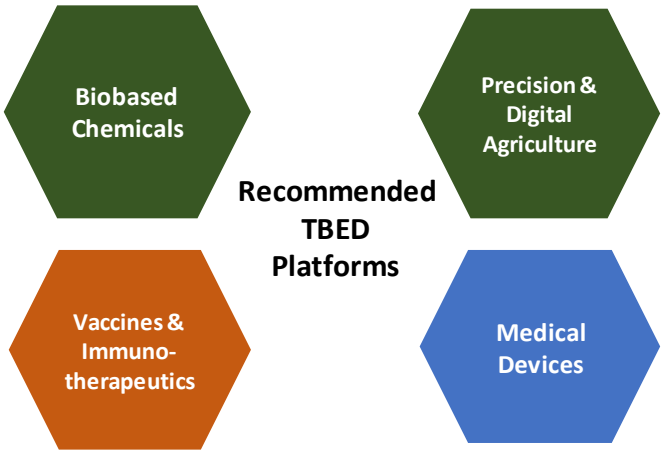
Based on the core competencies and stated parameters for bioscience platform identification a series of seven potential platforms were presented to the Iowa Innovation Council Bioscience Advisory Committee, which provided advice and feedback to the TEConomy analysis. This included discussion of:

- Platform related core competencies and the current Iowa research environment
- Innovation and corporate presence in Iowa relating to the platform
- Identified platform strengths, weaknesses, opportunities and threats
- Future projections for market size and growth trajectory.

The Advisory Committee discussion and review of the potential platforms helped to narrow the focus to those platforms holding the most promise for Iowa economic development AND most likely to benefit from state programs, industry-university partnerships and other sector stimulating activity that a strategy and action plan could positively influence. Specific attention was paid to discussion of the strengths and weaknesses of Iowa assets in these platforms, and particularly to line-of-sight to significant commercial product and market opportunities rooted in Iowa competitive advantages. Based

on the review process, the bioscience TBED Platforms for Iowa were refined and narrowed to incorporate the four platforms shown on Figure ES-1:

Figure ES-1: Recommended Iowa Bioscience Development Platforms



While these platforms do not incorporate each and every promising opportunity in the biosciences within Iowa, they do represent the focused areas where Iowa is considered (by TEConomy and the Advisory Committee) to have the greatest likelihood of achieving a differentiated leadership position based on research strengths, established or emerging industry activity, market potential, and other competitive advantage factors.

Within the main body of this report a detailed description is provided for each platform, together with an assessment of the market and narrative pertaining to the strengths, weaknesses, opportunities and threats for Iowa in each. An overall summary table for each of the platform opportunities is provided, with these summaries combined in Table ES-2 to provide a general four-platform overview:

Table ES-2: Summary Overview of Each Recommended Platform

Platform	Medical Devices	Biobased Chemicals	Precision & Digital Agriculture	Vaccines & Immunotherapeutics
Status	■ **Emerging R&D Plus** (R&D core competency and small base of industry) □ Established Growth (R&D and significant base of industry with expansion potential)	□ Emerging R&D Plus (R&D core competency and small base of industry) ■ **Established Growth** (R&D and significant base of industry with expansion potential)	■ **Emerging R&D Plus** (R&D core competency and small base of industry) □ Established Growth (R&D and significant base of industry with expansion potential)	□ Emerging R&D Plus (R&D core competency and small base of industry) ■ **Established Growth** (R&D and significant base of industry with expansion potential)
Business start-up potential	Strong potential given multiple device related clinical R&D strength areas at UI. Realizing potential depends on creating and facilitating a start-up culture with financing to advance concepts and facilities to accommodate	Strong potential given Iowa track record in starting companies in the biofuels sector and proximity to biomass and a focused suite of R&D assets in universities. Potential for specialty spin-out companies and operations from major	There could be significant start-up potential. There have been some small start-ups in Iowa in precision agriculture already, and the proximity to major agricultural equipment companies is promising for collaborations.	Evidence shows that Iowa-based R&D can lead to the development of successful start-up companies in animal vaccines. With a cluster of companies in and around Ames, other vaccine companies within the state, together with USDA and ISU related-core

	prototyping and business development.	grain and soybean processing companies.		competencies, there should be a conducive environment for innovation and commercialization. However, this optimism is tempered by interviews with sector representatives who have been unable to identify specific pathways forward.
Business expansion potential	Moderate at the present time because there is just a small base of device companies and most of these are in early business development phases.	Significant. Major agricultural processing companies are actively pursuing value-added chemical opportunities and multiple biofuels companies with potential to consider a more diversified biorefinery approach to growth. However, there is a limited base of specialty chemical companies in Iowa into which biobased products could be introduced.	Attraction of venture capital into the agricultural technologies sector is providing early-stage companies with capital access required for growth. Opportunities for acquisitions are also evident, with large companies having the resources to significantly scale-up production from emerging ventures.	Potentially strong, given positive factors influencing market growth for animal vaccines and the cluster of related companies formed in and around Ames, and more broadly across Iowa.
Business attraction potential	Challenging environment for business attraction given the much larger and more well-established device clusters in other U.S. locations.	Production industries likely to be attracted by biomass availability, biomass processing infrastructure and transportation networks. Limiting factor of lack of a workforce with specialty chemicals production experience, although Iowa community colleges have been responsive in the biofuels sector.	Organized correctly, and with the right approach to marketing, Iowa's relevant academic R&D strengths and associated workforce education attributes, combined with Iowa's substantial base of advanced manufacturing capability, may be seen as attractive to inward investors.	Potentially strong environment for business attraction given significant cluster of Iowa assets, especially in Ames. Good combination of corporate, university and government lab (USDA) operations as attractors.
Academic R&D growth potential	Good potential given funding agency priorities for translational research in biomedical sciences, but potentially restrained by current federal budget allocations.	Challenging environment for raising funds from traditional federal sources, with federal agencies facing funding cutbacks. However, agricultural commodity groups and other non-government funding sources may engage in this research area.	There is a potentially challenging environment for raising funds from traditional federal sources, with federal agencies facing funding cutbacks. However, ISU is ranked first in the nation for agricultural engineering, and has significant strengths in other disciplines, that likely support the	Challenging environment for raising funds from traditional federal sources, with federal agencies facing funding cutbacks. Potential though for "atypical" federal Homeland Security and defense-related funding applications.

			development of highly competitive proposals. Industry funding is likely to be attracted to leaders in precision agriculture R&D.	
Iowa competitive situation	Emerging only. There is an insufficient base of R&D and business development activity in Iowa in this space to be "on the radar screen" in the device industry. Major centers of gravity exist in the industry outside of Iowa that have potential to attract away successful Iowa start-ups – although the proximity of Iowa to Minnesota may mitigate this somewhat.	Iowa is very well positioned in terms of having R&D assets, robust sources of biomass and a business base that understands biofuels production and grain/oilseed processing and refining. In the biofuels sector there is only a limited presence in biorefining operations for chemicals beyond biofuels, however the big agricultural processing companies are engaged in producing value-added industrial chemical products. Competition from other regions of the U.S. to grow this sector has thinned due to short-term market constraints (fossil fuel prices and government policies), and there is thus potential to cement a position for Iowa in anticipation of a future market rebound.	This is an emerging sector, and no single state has established a robust leadership position. Iowa can be a highly competitive player in this sector if it organizes its assets appropriately and addresses identified weaknesses and gaps.	Iowa is well positioned in terms of having industry, academic and federal government R&D assets co-located in the sector – together with regulatory organizations and vaccine product manufacturing. A key will be moving to the next level by achieving another significant external investment or fast-growing start-up company to sustain growth momentum in the face of competition such as the Kansas City Animal Health Corridor.
Key barriers to overcome	• Building interest and momentum with faculty to advance innovations along a commercialization pathway. • Early stage capital availability for proof of concept and early-stage business formation and growth. • Relative lack of experienced medical device business entrepreneurs and experienced start-up management.	• Potentially constrained current environment for biorenewable project financing based on low fossil-fuel prices and de-emphasis of sustainability by current federal administration. • Building interest and momentum with faculty to advance innovations along a commercialization pathway. • Early stage capital availability for proof of concept and early-	• Highly transdisciplinary nature of precision agriculture solutions development may require investment in faculty and infrastructure in identified under-resourced fields. • Applied nature of work in this space may not hold appeal to academics across each of the disciplines required. • Building interest and momentum with faculty to advance innovations along a	• Building continued interest and momentum with faculty and federal lab personnel to advance innovations along a commercialization pathway. • Early stage capital availability for proof of concept and early-stage business formation and growth. • Development of joint industry-university-USDA research and cluster development collaborations, particularly in Ames.

		stage business formation and growth. • Coming end of NSF funding for the ISU Center for Biorenewable Chemicals. • Plant metabolic engineering pathway would require significant investment in additional faculty resources.	commercialization pathway. • Distance between the AgriTech Accelerator in Des Moines and the major academic research hub in Ames.	

D. Cross-Cutting Strategies and Actions

Each of the bioscience development platforms for Iowa are distinct-enough from one-another to require development of a series of focused strategies and actions specific to each platform. These are outlines in a separate Phase II Strategies and Actions report. There are however, several cross-cutting strategies that TEConomy's analysis preliminarily identified in Phase I for consideration relevant to bioscience development overall in the state. These are discussed in further detail within the main body of this report, but are summarized briefly as follows:

It should be noted that the strategies listed in the Phase I report herein are preliminary and have been modified and detailed more specifically in TEConomy's Phase II report titled:

"Phase II Report: Strategies and Actions for Iowa Bioscience Development. Crosscutting and Platform Specific Strategies and Actions."

Strategy One: Establish a Public/Private Iowa Bioscience Development Center

Iowa needs to establish an Iowa Bioscience Development Center as a public/private economic development initiative focused on coordinating existing assets and strategy implementation and actions to advance Iowa bioscience platforms and overall sector growth. It is recommended that this bring together existing assets in the Iowa Innovation Corporation and other related entities, rather than being a separate freestanding operation. Biosciences represent such a significant and specialized suite of sectors in Iowa that future development mandates a well-coordinated, shared approach across stakeholders to provide strategy and action plan implementation over the long-term.

Strategy Two: Increase Capital Available for Investment in Iowa Bioscience Companies

For a small state (population 3.1 million), Iowa is quite competitive in terms of performance of academic bioscience R&D and in terms of innovation (as measured using patents as proxies) – although, of course, not in the same league as major bioscience states such as California and Massachusetts. Where Iowa is far less than competitive is in venture capital to finance growth of companies based on Iowa innovations. Increasing Iowa's bioscience employment, especially in high paying technology ventures is hampered by a comparative lack of risk capital investment – particularly investment required to scale an enterprises

Note: The complexity of the capital access situation in Iowa is such that IEDA has contracted with TEConomy Partners to perform an additional focused analysis of the situation and make specific recommendations in a separate report to be completed before the end of 2017. Recommendations made in the current document, therefore, should be considered preliminary and may be subject to change.

post proof-of-concept. Specific actions are needed to increase access to risk capital (especially venture capital) in Iowa.

Strategy Three: Ensure continued legislative support for existing innovation ecosystem development programs

Investors and entrepreneurs are risk takers, but they do seek to minimize risks to the extent possible. One of the key risks that a state should have control over is the stability of its government sponsored programs and incentives (and control of a predictable and stable regulatory and tax environment for commercial enterprise). The State of Iowa needs to assure that a long-term commitment is sustained in terms of maintaining the programs and incentives in its current economic development portfolio.

Strategy Four: Improve Connectivity and Collaboration Opportunities Between Key Stakeholders in Each of the Focused Bioscience Development Platforms

Interviews and discussions held throughout the program of core competency review and platform identification provided a consistent theme of a lack of awareness and connectivity between key companies, university research teams and other key stakeholders in Iowa. This is related to the need for standing up the recommended IIC-IBDC as an organization that will coordinate activities and communication across the full bioscience spectrum – but also platform specific committees are needed that will bring together key platform stakeholders. Each of the platforms has significantly different sector foci, companies, university research teams and markets associated with it – and thus bringing these parties together to identify and coordinate actions within their specific platforms is critically important.

E. Conclusion

The overall opportunity for Iowa is significant in terms of continuing to build momentum and economic development through focused attention on the biosciences development ecosystem in the state. It is imperative that Iowa be committed to bioscience strategy and action implementation over a long-term time horizon and the time is right to stand-up a focused organizational initiative to coordinate strategic implementation of current and in-development recommendations. As shown in the successful bioscience initiatives in other regions of the country, there is significant pay-off for regional economic development accomplished through bioscience sector development pathways, but robust development within the sector takes time (often decades) and a long-term, sustained commitment of resources is required.

The reader of this Phase I report is specifically referred to the Phase II report for further details of recommended crosscutting and platform specific strategies and actions designed to advance Iowa's ongoing bioscience development.

I. Introduction

A. The Importance of Biosciences to Iowa's Economic Development

By any economic measure—the number of companies, economic output and exports, employment, and average wage—Iowa's biosciences industries are important to the state's continued economic growth and development. Recent state benchmarking by TEConomy for the Biotechnology Industry Organization (BIO) finds that Iowa:

- Has 1,266 biosciences business establishments;
- A high concentration of employment in the biosciences sector in comparison to the national average (with a location quotient of 1.36[1]); and
- An average wage of $67,673 compared to the Iowa private sector average of $41,964.

Moreover, as a sector that is driven by advances in scientific knowledge and research and development leading to the commercialization of new technologies, the biosciences is an industry sector that leverages the Regents universities (University of Iowa, Iowa State University, and University of Northern Iowa) for science and engineering workforce talent, research collaboration, and technology transfer.

B. About this Report and Analysis

This study builds upon previous work by the Battelle Technology Partnership Practice (TEConomy's forerunner organization) performed for Iowa. The previous work included both a 2004 strategy for Iowa's biosciences sector development, as well as a subsequent 2011 study to assess progress since 2004.

This present analysis and report seeks to answer three questions:

1. What are Iowa's existing and emerging bioscience research core competencies?
2. In which bioscience sectors is Iowa seeing translation of these research core competencies into commercial activity and competitive technology platforms?
3. What strategies can help Iowa capitalize on these opportunities for further bioscience-based economic development?

This report presents the results of R&D core competency analysis for biosciences and associated disciplines in Iowa, and works to identify technology platforms representing emerging opportunities for Iowa technology-based economic development stemming from TEConomy's analysis of the confluence of competitive research, commercial activity and line-of-sight to substantial growth markets. It then presents strategies based on identified gaps and opportunities that draw on best practices in other states. It should be noted that the bioscience advisory group of the Iowa Innovation Council directed TEConomy to focus on identification and strategies to advance emerging opportunity areas, rather than strategies to advance existing bioscience strength areas such as plant sciences or biofuels.

[1] Regional economists consider a location quotient (LQ) of >=1.20 to represent a "regional specialization". A location quotient of 1.0 represents parity with normal national levels.

II. Bioscience R&D Core Competencies in Iowa

A. Introduction to Core Competencies

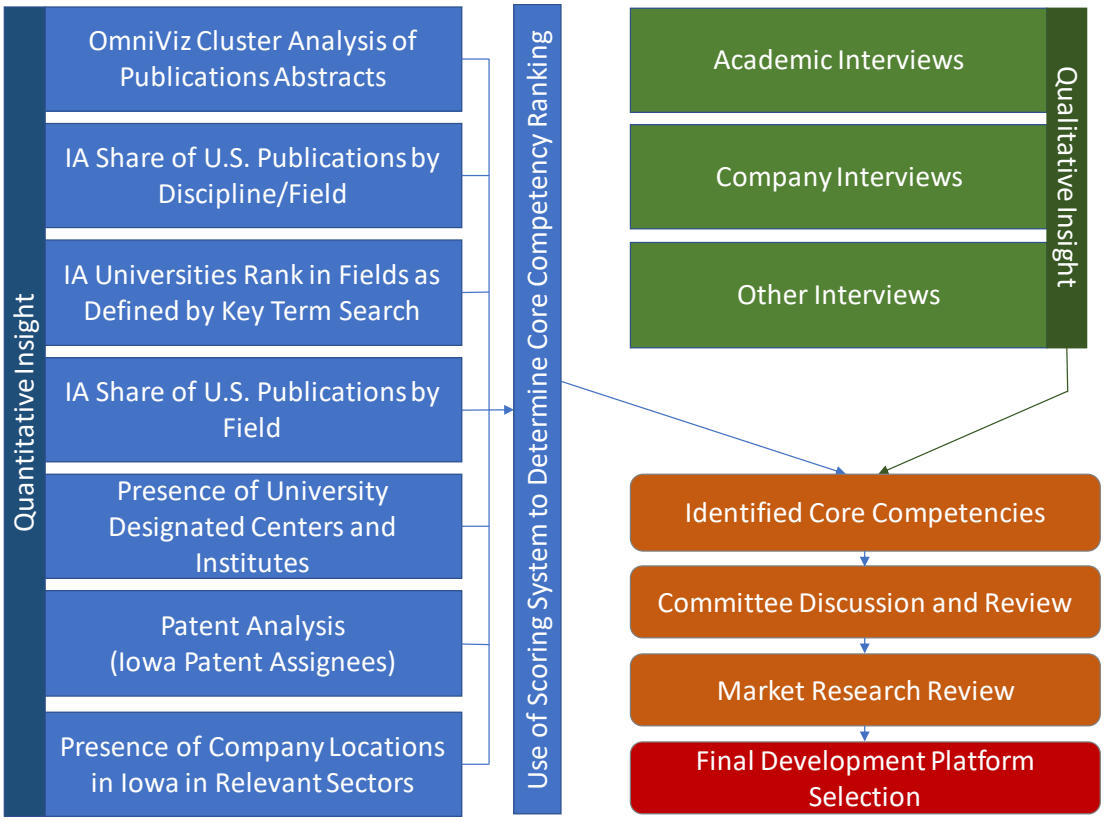
To understand the potential for bioscience development in Iowa, it is necessary to undertake a rigorous analysis of existing and emerging bioscience research core competencies found across the base of R&D performing organizations in the state (universities, national laboratories and industry). By rooting bioscience development in identified established and emerging core competencies, the Iowa Economic Development Authority and its partners in statewide economic development can leverage existing clusters of investments in research talent and infrastructure to advance associated discoveries and innovations to build high-growth technology-based sectors for the Iowa economy.

> *"Core competencies are the gateways to future opportunities. Leadership in a core competence represents a potentiality that is released when imaginative new ways of exploiting that core competence are envisioned."*
>
> Hamel and Prahalad, *Competing for the Future*

Research core competencies are those fields with an established or emerging critical mass of ongoing activity along with identifiable measures of excellence. No one single source of information is sufficient to identify research core competencies. Rather, a variety of integrated and complementary analyses are typically deployed by TEConomy to identify an institution's current or rapidly emerging position and areas of focus that may contribute or lead to Iowa's future bioscience sector growth.

Using both quantitative and qualitative methods, TEConomy has developed a rigorous approach for assessing the core competencies of research institutions (Figure 1).

Figure 1: Approach to Identification of R&D Core Competencies and Development Platforms



Quantitative assessment primarily includes examination of R&D competencies as identified via analysis of research publications (research output) and intellectual property generation (patents). The publications analysis uses records contained in the Clarivate Analytics *Web of Science* (WoS) database, with TEConomy deploying two primary analytical techniques with these data:

- 1) OmniViz™ Analysis: which uses real text cluster analysis to provide unique insight into focus areas of research activity across the 17,255 publications in the biosciences authored at institutions in Iowa (during the period 2010 through 2016). OmniViz analyzes the titles and abstracts of research papers, allowing for free association based on the use of words and phrases, rather than forcing clustering based on preselected key words. Thus, no "a priori" bias to the clusters is identified (unlike analyses of publications, research trends, and reputational rankings for which the research field categories are predetermined by the sources collecting the data). The OmniViz™ cluster analysis involves the following steps:
    - **Step 1**: **Content Development:** A data set is developed with sufficient descriptive content, in this case publication titles and full abstract text.
    - **Step 2**: **Pattern Recognition:** The analysis generates clusters where publications activity has apparent relationships and produces a series of words to describe and link these cluster areas.
    - **Step 3**: **Interpretation and Grouping by Expert Review:** The identification of key themes and groupings that result from an OmniViz™ cluster analysis requires an experienced research analyst to read through the cluster items to interpret and explain the types of technologies and specific activities that are represented.
- 2) Evaluation of Iowa universities' **rank and share of publications** in basic and applied academic fields with relevance to biosciences.

In addition, TEConomy examines the presence of **designated research centers and institutes** at Iowa's research universities – serving to identify where the institutions themselves have chosen to focus around particular research themes.

TEConomy also deployed **intellectual property analysis** using USPTO patent data for 2010 through 2016 for Iowa patent awards and patent applications. The analysis uses only patents with Iowa inventors, providing a more accurate measure of invention activity that is generated within the region rather than all patents held in Iowa (which may contain IP that companies "import" as assignees from other regions). TEConomy assesses applications as well as granted patents, since applications can be indicative of emerging innovative areas for corporate or academic innovations that have not yet made it through the lengthy USPTO approval process. The analysis of the Iowa patenting landscape included 5,565 total patent records, and demonstrates that Iowa bioscience patenting has exhibited strong growth from 2010 to 2016 with a 237% increase in number of applications and 29% growth in awarded patents.

The complete series of analyses are shown on Table 1 together with the rating system used for each analytical element.

Table 1: Measures Used in Identification and Ranking of R&D Core Competencies in Iowa Biosciences

Metric	Description	Rating System
OmniViz™ cluster analysis	Cluster analysis of 17,255 publication abstracts for 2010-2016	XXX=clusters with >500 XX=clusters with 200-500 X=clusters with 25-199
Iowa share of U.S. publications in Web of Science (WoS)	Used as criterion to decide on whether to do rank run. Used to see if a field is more or less concentrated in Iowa institutions versus all disciplines.	XXX >= 1.6% (=run rank in next metric below)
Iowa universities' rank in WoS on key terms	WoS ranking of publishing volume in key fields/terms. Identifies where each Iowa university ranks versus other U.S. universities in publishing in each set of key terms.	XXX=in top 10 XX=rank 11-25 X=rank 24-50
Patent volume	Number of patents and applications with Iowa assigned inventor(s) 2010-2016 in associated patent classes	XXX=>500 XX=200-500 X=50-199
University centers and institutes/notable programs	Identified from university web sites and on-campus interviews. The presence of a center or institute typically implies a formal system was used to determine competency in order to achieve designation.	XXX=Multiple major centers, especially those collaborating with industry XX=Multiple centers X=Single center, or department where interviews highlighted industry relationships.
Iowa company operations in this area	Identified through presence in patent analysis, interviews and other resources. Competencies are more likely to lead to in-state commercialization if there are companies present in the sector.	XXX= >10 companies XX= 5-10 companies X= 1-4 companies
Iowa university IP generation in this area	Identified in patent analysis. Identifies whether competency activity is centered in one university or multiple.	XX=2 Iowa universities with IP X=1 Iowa universities with IP

Under this core competency scoring system, each variable is weighted equally, and the maximum cumulative score that a core competency area may achieve is 20.

B. Core Competencies Identified

The analytical steps shown in Figure 1, and the scoring system shown in Table 1, resulted in the identification of 29 preliminary research core competencies. There is considerable range, however, in these core competencies in terms of overall score. They range from a high score of 20 for "genetic engineering and biotechnology" through a low of just 1 for "cleft disorders" and "obesity" respectively.

Table 2 provides an overall summary of the identified bioscience core competencies, divided into three macro categories: Agricultural and Associated Bioscience; Biomedical Life Sciences, and Crosscutting and Basic Sciences.

Table 2: Scoring of R&D Core Competencies in Iowa Biosciences

Core Competency Score	Agricultural and Associated Bioscience	Biomedical Life Sciences	Cross-cutting and Basic Sciences
>14	• Plant sciences (19) • Animal infectious diseases and veterinary medicine (18) • Biofuels and biobased chemicals (15) • Agricultural equipment (15)		• Genetic engineering and biotechnology (20) • Infectious diseases (microbiology, bacteriology, virology) (16)
10 to 14	• Animal and vegetable oils (12)	• Audiology (11) • Ophthalmology (11)	
<10	• Food products and additives/ingredients (9) • Animal nutrition (6)	• Medical imaging (9) • Orthopedics (7) • Dentistry (7) • Cancer (6) • Medical devices (6) • Cardiology (5) • Aging (4) • Diabetes (4) • Neuroscience (4) • Perinatology and neonatology (3) • Nephrology (2) • Pulmonology (2) • Cleft Disorders (1) • Obesity (1)	• Drugs and pharmaceuticals (9) • Biochemistry (9) • Biological sampling and analysis (5)

In general, it is found that the agricultural-related core competencies in Iowa tend to have strengths on both the academic and commercial sides, whereas the biomedical core competencies are more focused solely in academic R&D (primarily at the University of Iowa) and have relatively limited industry presence. As such, while medical specialties such as audiology and ophthalmology are world class in terms of academic R&D, they still score lower than most of the agricultural related competencies, which each have associated industry and academic R&D and innovations (as measured by patenting) taking place.

C. Paths to Bioscience Development: Translating Core Competencies into Technology Platforms

Iowa's core competencies in the biosciences represent foundational elements upon which the state can build its position and reputation in the global bioscience-based economy. In and of themselves they are important as areas of distinctive R&D activity, but their real utility for technology-based economic

development is to be found in the translation of these core competencies into broader Technology-Based Economic Development Platforms (TBED Platforms.)
TBED Platforms are applications-oriented, strategically chosen areas that offer the potential to realize significant gains in economic development for Iowa, against domestic and international competition. They should correspond with a line-of-sight to the potential development of technologies and commercial applications within a reasonable timeframe and be able to address substantial and growing markets. The TEConomy process roots TBED Platforms in verified existing and emerging core competencies, ideally (but not exclusively) competencies demonstrating both academic and industrial R&D presence in the state. The process helps to assure that resulting development strategies build on demonstrable existing or emerging in-state strengths and assets – as opposed to simply chasing the latest technology trend in competition with every other national or international location seeking to achieve economic development. In other words, the TEConomy approach focuses on building economies around their established and emerging scientific, technological and commercial strengths and assets in relation to expanding markets – versus simply trying to establish a position in any tech area that is temporally "hot".

A focus on core competency based TBED Platforms also allows identification of strategic actions that may be deployed to accelerate relevant technology development, foster effective collaboration and partnerships, raise awareness of the market opportunities they address, and stimulate investment in R&D and new business development. In the long term, implementation of TBED Platform-focused approaches can produce sustainable competitiveness for the state by: stimulating innovation; building upon a proven base of capabilities, and working to overcome barriers to ongoing innovation and the commercialization of innovations by new or existing Iowa enterprise.

Identification of TBED Platforms requires the consideration of several criteria:

- **Opportunities drawing upon multiple core competencies and organizations.** A technology platform should address market opportunities that directly link to, or leverage, core competencies and ideally have relevance to commercialization by in-state organizations. The goal is to develop Platforms that leverage a fertile base of R&D programs in the state and are multidisciplinary, cross-cutting, and present opportunities for collaborations, rather than just being a stand-alone, single-discipline research strength.
- **Presence of existing or emerging industry connections.** A TBED Platform should align academic and other institutional research strengths with either established or emerging local industries – creating new linkages and strengthening existing connections.
- **Opportunity for external funding.** A TBED Platform should relate to pressing issues, needs or opportunities (which helps attract ongoing external R&D funding) and have a line-of-sight to a sizeable and growing market for likely products and/or services.
- **Limited competition from other states or regions.** Ideally a TBED platform will benefit from identified competitive advantages such as geography, market base, expertise and tacit knowledge base, exclusive resources, signature infrastructure, or favorable policies. Taken together, these assets should collectively form a competitive advantage for an agglomeration of core competencies to rise to the stature of a TBED Platform.

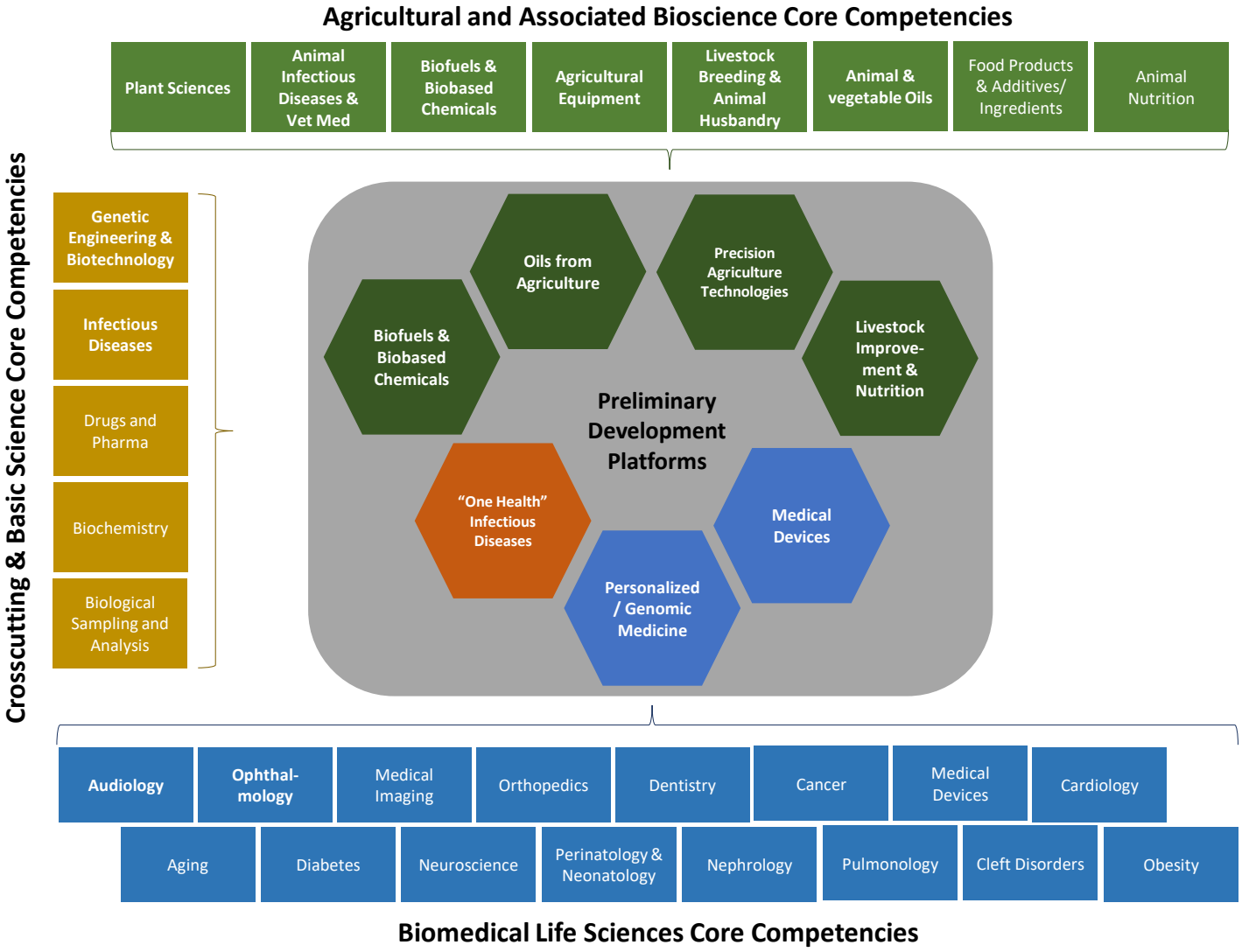
D. Translation of Core Competencies into Platforms for Consideration and Review by the Project Advisory Committee

Iowa has been focused on developing its bioscience-based economy since the early 2000's. This, in combination with the growth of the bioscience research enterprise at the University of Iowa and Iowa State – and the emphasis placed on funding of bioscience R&D at a federal level – has resulted in a

significant base of established and emerging core competencies in Iowa. As noted above, the research performed for this project identified 20 established or emerging bioscience core competencies, of varying levels of robustness, that may be considered in deliberations for potential TBED Platforms.

The initial, first-pass assessment of opportunities suggested that the following seven platforms be presented for further consideration and review by the project advisory committee (Figure 2):

Figure 2: Preliminary Development Platforms Presented to Advisory Committee



Specifically, the **preliminary** TBED Platforms comprised those shown on Table 3:

Table 3: First Round of Potential Bioscience Platforms for Iowa as Presented to Advisory Committee for Review

Potential Platform	Description	Rationale
"One Health" Infectious Diseases	The term "One Health" denotes a multi-sectoral and collaborative approach by those in human medicine, veterinary medicine and other areas of life science to improving health and well-being at the intersection of humans, animals and the environment. One Health Infectious Diseases, narrows the focus to leveraging capabilities in multi-disciplinary microbiological disciplines, animal and human infectious disease expertise, and associated skills in diagnostics, therapeutics and vaccine R&D to develop unique and holistic approaches to combatting infectious diseases.	• Large and broad clusters of R&D publishing identified for infectious diseases and associated microbiology across multiple Iowa universities. • USDA National Animal Disease Research Center located in Ames. • Existing, and recently growing, cluster of vaccine companies (particularly focused in animal health) located at ISU Research Park. • Combination of expertise at the University of Iowa in human infectious diseases, Iowa State University in veterinary infectious diseases, and at both institutions in relevant basic and applied sciences, including microbiology, genomics. • Key terms analysis shows Iowa State University ranked 1st nationally in "Animal and Infectious Diseases and Vaccines, Pharmaceuticals and Diagnostics." • Base of relevant patenting activity in Iowa.
Biofuels and Biobased Chemicals	The term "biobased" product refers to products wholly or partly derived from biomass. Using physical, chemical or biological process technologies biomass may be converted into fuels and a variety of commodity and specialty chemicals, polymers and materials. Iowa has built an early leadership position, particularly in first-generation liquid biofuels development and production. Institutions in the state also have significant intellectual and physical assets dedicated to advancing next generation biofuels and the advancement of biobased chemicals.	• An established, existing base of operating biofuels companies leveraging the intensive biomass production capabilities of Iowa agriculture. This base comprises corporate facilities producing first-generation ethanol and biodiesel fuels, together with a more limited base of investments in integrated biorefineries and advanced lignocellulosic biomass processing. • A robust base of intellectual capital and physical infrastructure invested at Iowa research universities, especially at Iowa State University. Expertise here spans multiple relevant disciplines ranging across plant transformation, bioprocess engineering, and chemical engineering using catalytic, thermal and bio-conversion technologies. • Operation of a NSF Engineering Research Center (ERC) at Iowa State focused on advanced manufacturing for sustainable biobased chemicals. The Center for Biorenewable Chemicals (CBiRC) was founded in 2008.
Oils from Agriculture	Plant oils (and to a lesser extent, animal oils) have widespread uses as food and feed ingredients and as liquid fuels and specialty chemicals.	• Publications cluster analysis showed significantly sized clusters in "soybean and other plant oils" and in the basic science of fats and lipids.

	Increasingly, they are also being investigated for further use in replacing various chemicals derived from petrochemical sources. Current and emerging technologies in plant transformation, such as metabolic engineering, present opportunities to modify the expression and characteristics of oils within plants to enable further development of the biobased economy and increase the value of oil producing agricultural crops	• Key terms analysis for Iowa State University shows the university to rank 1st in the nation in publishing in "animal and vegetable oils". • ISU has focused expertise and facilities for plant transformation work using plant transgenics, and the Crop Bioengineering Consortium at ISU is focusing work in CRISPR-CAS gene editing. • Over 80 patents are held by Iowa organizations in plant and animal oils, including patenting by industry and the Regents universities.
Precision Agriculture Technologies	Precision agriculture seeks to increase farm productivity and efficiency based on observing, measuring and responding to inter and intra-field variability in biotic and abiotic conditions and the expressed spatial variation in the growth and health of crops. It is inherently multi-disciplinary, incorporating biological sciences, physical sciences, engineering and computer and data sciences.	• Iowa contains a significant number of large, midsize and small companies engaged in the production of agricultural equipment and associated systems for which precision agriculture technologies may be applied. • Over 800 patents in Iowa were identified for "agricultural machinery and planting processes". • Iowa State University is ranked first in the nation for Agricultural Engineering publishing output. The ISU Department of Agricultural and Biosystems Engineering has two groups with focused work relevant to precision agriculture in the Advanced Machinery Engineering and Manufacturing Systems group and in Biological Systems Engineering. • Beyond agricultural engineering, multiple ISU departments, research groups and individual researchers are engaged in the development of relevant cyber-physical systems comprising, for example, on plant field sensors, field phenotyping, computer vision systems and other novel technologies. • Diverse academic capabilities in data analytics, sensors and materials science, statistical analysis, and data visualization in combination with plant science expertise and a robust network of field stations, provides ISU with opportunities to grow in this area of technological development.
Livestock Improvement and Nutrition	Livestock represent 43% of the total value of all agricultural production in the state. The scale of production is impressive with, for example, 22.4 million hogs (ranked 1st in the U.S.) 52 million layers, 11.7 million turkeys and 3.9 million cattle and calves.	• Iowa State University ranks first among U.S. universities in publishing in the area of livestock breeding, and has strong programs in animal science. • The state contains a significant cluster of industry engaged in livestock nutrition and

	Improving reproduction rates, meat yield, nutrition use efficiency, and livestock health each have important impacts on the bottom line profitability of this important component of Iowa agriculture. Modern sciences provide multiple pathways to improving livestock breeds, their rations and feed conversion efficiency – among other areas.	livestock health and animal husbandry products. • Over 150 patents held in Iowa relating to the patent class of "animal husbandry and management". • Technological capabilities highlighted for precision agriculture have potential application for livestock production processes.
Medical Devices	The term Medical Devices covers a wide range of health or medical instruments used in the treatment, mitigation, diagnosis or prevention of a disease or abnormal physical condition. In the U.S., medical devices are divided by the FDA into three classes (according to risk): • Class I devices are low risk and subject to the least regulatory control, and include products such as bandages, dental floss, examination gloves, etc. • Class II devices are subject to a higher level of regulatory control. Examples include contact lenses, diagnostic instruments (such as ultrasounds), syringes, etc. • Class III devices are subject to the highest level of control as they typically involve life sustaining devices or devices that have the ability to cause harm. Examples include replacement heart valves, pacemakers, deep brain stimulation devices, etc. Compared to pharmaceuticals, the pathway to market is typically shorter for most medical devices.	• Over 370 patents identified with Iowa inventors assigned in medical devices-related patent classes. • Small, but not insignificant, group of medical device companies located in Iowa. • Potential pathway to the development of multiple forms of medical devices (diagnostic, prosthetic, surgical or therapeutic devices) in areas of medical research and clinical excellence at the University of Iowa – for example in Audiology (ranked 3rd in the nation) Ophthalmology (ranked 9th) and Orthopedics (17th) in terms of publishing volume. • This is an emerging area of emphasis for the University of Iowa and Iowa City, with prototyping labs and associated supporting infrastructure in development. • Iowa's relative proximity to the medical device cluster in Minneapolis St. Paul may carry advantages in terms of partnerships, commercialization, talent and capital access.
Personalized/ Genomic Medicine	Personalized medicine, also termed precision medicine, incorporates medical analytics and processes that help tailor medical decisions, practices, interventions and/or products to the individual patient based on their predicted response or risk of disease.	• Approaches to cutting costs and delivering healthcare more precisely and efficiently in Iowa are economically beneficial. • The statewide scope of the University of Iowa Health System provides data and access to patients within an integrated system. The University of Iowa Health Alliance (UIHA) includes 20 hospitals and more than 1,900 physicians.

	Personalized medicine shows promise for increasing the efficacy of medical treatments and for reducing side-effects and negative impacts from medical treatment. Giving the person the right drug, at the right dose at the right time based on analysis of individual characteristics such as genome, allergies, metabolism, prior medical history, etc. has multiple advantages. Personalized medicine may also have cost control benefits, by avoiding costly trial-and-error approaches to treatment – curtailing expenses made on the wrong treatment and the personal costs involved in delayed appropriate treatment.	• The Iowa Institute of Human Genetics (IIHG) is dedicated to promoting clinical care, research and education focused on the medical and scientific significance of variation in the human genome. The IIHG is a statewide resource for understanding the extent and meaning of human DNA sequence variations. • Expertise at the U of I in biopharmaceuticals production, formulation and development has potential for application to the science of personalized drug formulations and dosing. • An expanding program in genetic counseling at U of I provides the ability to roll-out genomic medicine at scale within the state.

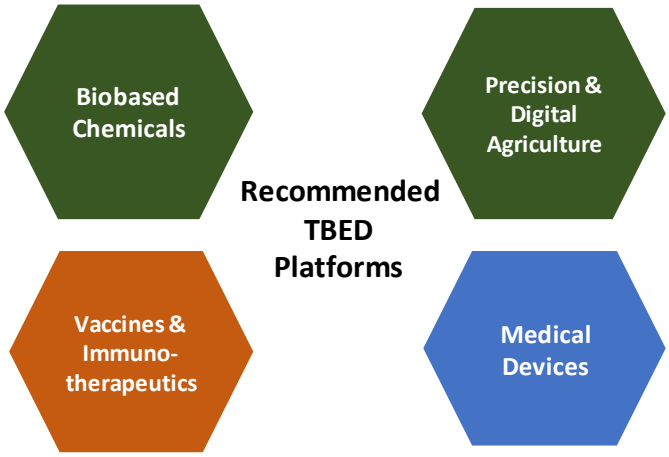
Each of these potential platforms was discussed in detail with the project Advisory Committee, comprising discussion of:

- Platform related core competencies and the current Iowa research environment
- Innovation and corporate presence in Iowa relating to the platform
- Identified platform strengths, weaknesses, opportunities and threats
- Future projections for market size and growth trajectory.

The committee discussion and review of the potential platforms **sought to narrow focus to those platforms holding the most promise for Iowa economic development AND most likely to benefit from state programs, industry-university partnerships and other sector stimulating activity that a strategy and action plan could positively influence.** Specific attention was paid to discussion of the strengths and weaknesses of Iowa assets in these platforms, and particularly to line-of-sight to significant tangible product and market opportunities rooted in Iowa competitive advantages. Consideration was also paid to the fact that advancing seven separate TBED Platforms would be too much of a heavy-lift given present resources in Iowa, and that a more refined focus on fewer platforms would enable more effective and detailed strategies and actions to be deployed on those platforms with the best chance of engendering positive economic growth in the state.

Based on this review, the bioscience TBED Platforms for Iowa were narrowed to:

- Platform 1: **MEDICAL DEVICES**
- Platform 2: **BIOBASED CHEMICALS**
- Platform 3: **PRECISION AND DIGITAL AGRICULTURE**
- Platform 4: **VACCINES AND IMMUNOTHERAPEUTICS**



While these platforms do not incorporate each and every promising opportunity in the biosciences within Iowa, they do represent the focused areas where Iowa is considered (by TEConomy and the Advisory Committee) to have the greatest likelihood of achieving a differentiated leadership position based on research strengths, established or emerging industry activity, market potential, and other competitive advantage factors.

Each of these platforms is profiled in Chapter III.

III. Recommended Bioscience Platforms for Iowa

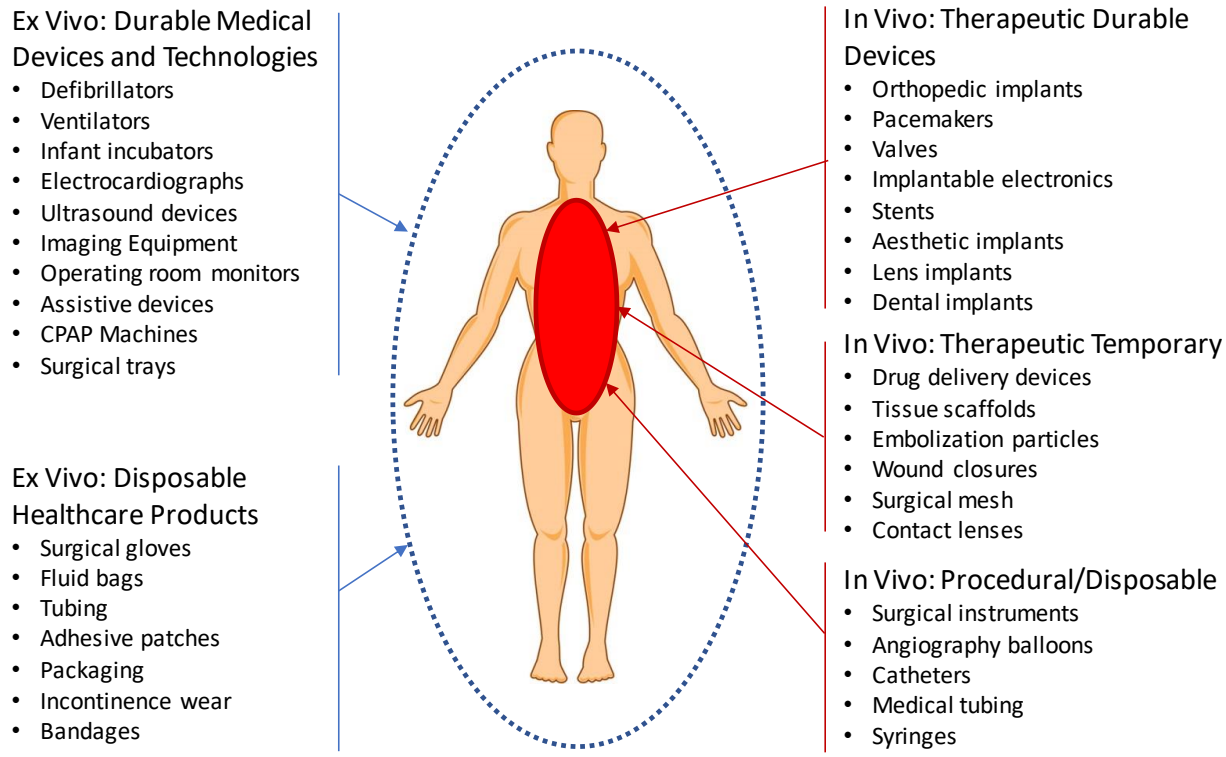
Platform 1: Medical Devices

A. Description

Healthcare currently represents 17.8 percent of the United States' GDP[2], and is a central driver for bioscience R&D and commercial activity. Within the broad healthcare segment of U.S. biosciences, medical devices represent an attractive, significant and growing market ($171.8 billion[3]), with lower barriers to entry and faster timelines to market than pharmaceuticals.

Medical devices and diagnostics encompass all software, instruments, and devices that are used in the diagnosis, prevention, treatment, and monitoring of patients. As shown in the examples on Figure 3, medical devices can include products that go inside the body (in vivo) or are used externally, or never touch the body at all (ex vivo). Medical devices can be either durable (such as an orthopedic implant or a defibrillator) or non-durable and disposable (such as temporary stents or examination gloves).

Figure 3: Examples of In-vivo and Ex-vivo Medical Devices



[2] Sean P. Keehan, Devin A. Stone, John A. Poisal, Gigi A. Cuckler, Andrea M. Sisko, Sheila D. Smith, Andrew J. Madison, Christian J. Wolfe and Joseph M. Lizonitz. "National Health Expenditure Projections, 2016–25: Price Increases, Aging Push Sector To 20 Percent of Economy." Health Affairs. February 2017

[3] Gerald Donahoe and Guy King. "Estimates of Medical Device Spending in the United States." June 2015. Accessed online at: https://www.advamed.org/sites/default/files/resource/ 994_100515_guy_king_ report_2015_final.pdf

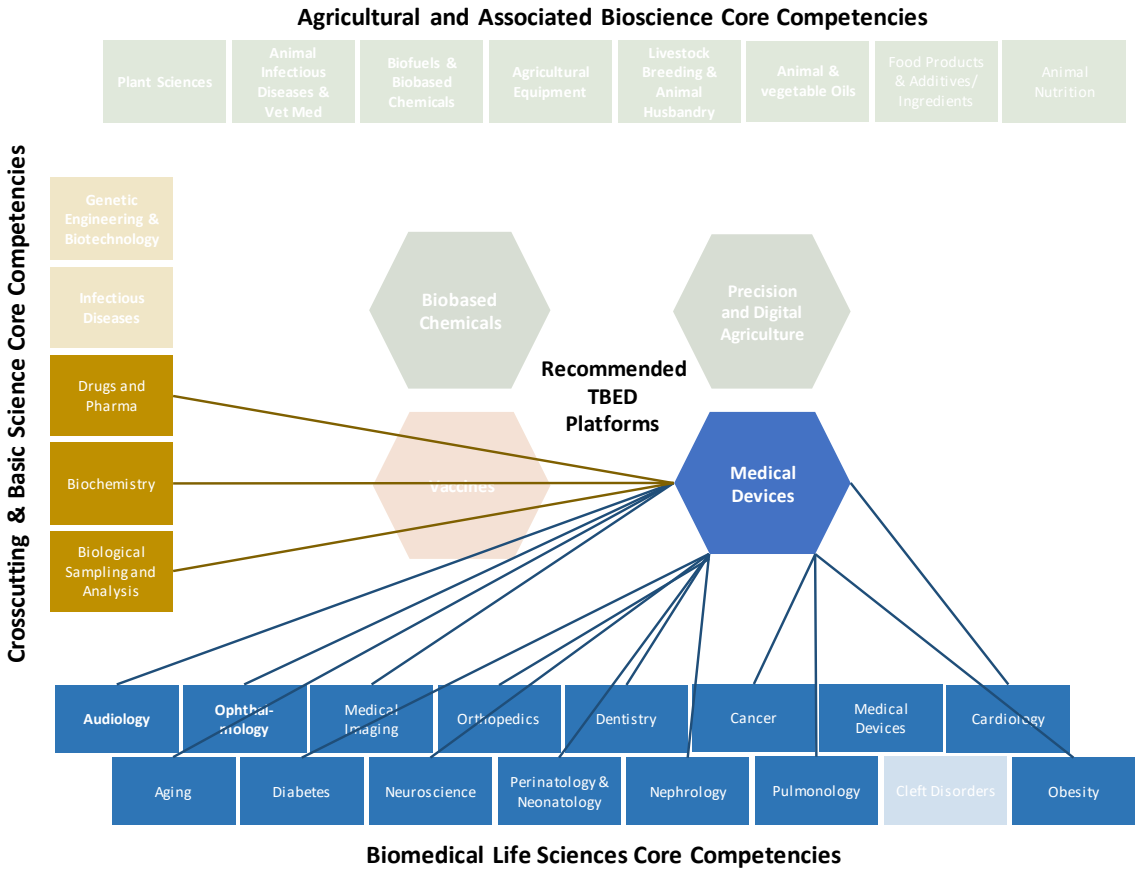
According to BCC Research, the global market for medical devices and technologies was $483.5 billion in 2016, with a robust anticipated CAGR of 5.6% to $634.5 billion by 2021. Several factors are driving strong growth, including aging populations with longer life expectancies, the need to manage chronic diseases like diabetes and cardiovascular disease, and increasing health care spending by emerging market countries (especially the Asia-Pacific [China and India], but also the Middle East, South America, and other regions with rising incomes). Because of these trends, **growth in market demand is likely to be sustained into the foreseeable future.**

Looking more narrowly at activity in med tech **startups and VC** there is continued growth in new business startups. Silicon Valley Bank (SVB) estimates 511 medical device deals attracted $3.9 billion in venture capital investment in 2016. The top subsectors of the startup market for 2016 were Neuro, Respiratory, Cardiovascular, and Orthopedic devices. According to SVB, the strongest current market demand is for cost-effective devices that are non-invasive and integrate smart technologies. These include technologies (e.g., wearable technologies) that share data with patients and hospitals, use data analytics to improve patient outcomes and reduce healthcare costs, and leverage big data to improve diagnosis. As such, these are technologies that require the integration of knowledge from multiple disciplines and technology domains to realize product development.

B. Connectivity to Iowa Core Competencies

Figure 4 illustrates the connectivity between multiple Iowa established or emerging core competencies and the Medical Devices platform:

Figure 4: Medical Devices Platform – Connectivity to Identified Core Competencies



Almost every one of the identified biomedical life sciences core competencies have the potential for research and innovation development relevant to medical devices. Table 4 shows just a partial listing of medical device examples potentially associated with individual biomedical core competencies.

Table 4: Iowa Biomedical Core Competencies and Example Types of Medical Devices Associated with the Specialty

Core Competency	Iowa Biomedical Core Competency	Selected Examples of Associated Medical Devices
Strength (11)	Audiology	Hearing Aids -- Measurement/Testing Devices – Otoscopes – Audiometers – Impedance Analyzers – Hearing Aid Analyzers – Cochlear Implants – Bone Anchored Hearing Aids (BAHA) Implants
Strength (11)	Ophthalmology	Contact Lenses – Corneal Implants – Surgical and Implantation Instruments – Surgical Lasers -- Retinal Implants – Scleral Implants -- Stents – Examination and Diagnostic Instruments – Prosthetics
Strength (9)	Medical Imaging	MRIs – CT Scanners – PET Scanners – X-ray Equipment – Ultrasound Devices – Image Processing/IT Systems – Endoscopes – Contrasts Agent Delivery Systems
Strength (7)	Orthopedics	Screws and Fixation Devices – Plates – Spacers – Surgical Instruments – Joint Replacement Systems – Bone Cement – Bone Substitutes – Soft Tissue Repair Matrices
Strength (7)	Dentistry	Dental Materials (Amalgam, Cements, etc.) – Dental Implants – Crowns and Bridges – Dentures – Surgical/Dental Instruments – Wound Dressings and Closures – Cannulae and Syringes
Strength (6)	Cancer	Focused Radiation Devices – Ultrasound Therapy Devices – Fluid Filtration Devices – Biopsy Tools – Surgical Instruments – Ablation Devices – Infusion Devices
Opportunity (5)	Cardiology	Artificial Valves – Ventricular Assist Devices – Pacemakers – Implantable Cardioverter Defibrillators – Stents – Catheters – Guidewires – Closure Devices – Wireless Monitors – Surgical Instruments
Opportunity (4)	Aging	Assistive Devices – Homecare Devices – Catheters – Adult Sanitary Products – Personal/Wireless Monitors – Wound Care Devices
Opportunity (4)	Diabetes	Insulin Pumps – Insulin Pens/Injectors – Glucose Meters – Infusion Sets – Continuous Glucose Sensors – Neuropathy Detection and Monitoring Devices
Opportunity (4)	Neuroscience	Ventricular Needles and Anvils – Neurostimulators – Aneurysm Clips – Blood Clot Retrievers – Deep Brain Stimulators – Brain Tumor Treatment Devices
Opportunity (3)	Perinatology/ Neonatology	Catheters – Surgical Instruments – Suction and Airway Clearing Devices – Incubators – Heaters – Ventilation Assist Devices – Cosmetic/Reconstructive Surgery Devices – Resuscitation Equipment
Opportunity (2)	Nephrology	Dialysis Machines – Wearable and Implantable Renal Assist Devices – Surgical Instruments – Hemofilters
Opportunity (2)	Pulmonology	Tracheobronchial and Airway Stents – Thermoplasty Systems – Pulmonary Balloon Dilators – Biopsy/Brush Cytology Tools – Aspiration Needles and Devices – Ventilators – Bronchoscopy Devices
Opportunity (1)	Obesity	Gastric Bands – Electrical Stimulation Systems – Gastric Balloon Systems – Gastric Emptying Systems

Having such a broad variety of areas with potential to engage in medical device innovation suggests that the strategy for Iowa needs to be focused on programs, activities and support mechanisms that are **flexible to supporting development across multiple technology and product types** – rather than being specific device niche focused (such as only orthopedic implants, or neurostimulation devices, etc.). That said, there are areas within the University of Iowa that are strengths and already demonstrating work in devices, including ophthalmology, medical imaging, audiology, etc. that are most likely to generate innovation inputs.

C. Strengths

In Iowa, technology development and startup activity (as one commercialization strategy[4]) is occurring around the convergence of University of Iowa biomedical research specialties and University Hospitals' clinical practice. UI's nationally recognized strengths, based upon publications in peer-reviewed scientific journals from 2010-2016, include: audiology (3rd), ophthalmology (9th), biomedical imaging of the lung (16th), dentistry (16th), and orthopedics (17th), for example, provide opportunities to leverage research and clinical excellence for the design, testing and development of novel and improved devices.

A small start-up culture around medical devices (using the broadest sense of the term) exists around the University of Iowa, with startups based on technology originally developed at UI including:

- Medical Device: **IDx** is an Iowa City-based medical device company pioneering technologies in image based computer (aided) diagnosis, particularly focused on using imaging of the eye for clinical diagnostic purposes. IDx has experienced significant success in raiding funds, already has approved products in use within Europe (and pending FDA approval for the U.S.). IDx's technological leadership has been recognized with membership in the IBM Watson Medical Imaging Collaborative, which includes 24 healthcare leaders worldwide.
- Medical Device: **IotaMotion** is a medical device company developing hearing assistive technologies based upon a robotic system for cochlear implantation that has received an SBIR Phase I award.
- Medical Device: **Voxello** is focused on assistive communications technology for hospitalized patients who cannot speak. The company has received 510(k) FDA clearance and has raised $1.3 million in grants and private equity investment. It is currently pursuing $5M VC round.
- Medical Device: **Corvida Medical** is developing closed system transfer devices for safe handling of hazardous drugs (for example, drugs used in chemotherapy).
- Medical Materials: **NanoMedtrix** is using nanoparticle technology as the basis of an engineered platform used in a variety of biomedical applications. In cancer, for example, the company is developing material designed to target solid tumors such as: bladder, colorectal and neural tumors. The materials also have applications in medical imaging as a contrast agent.
- Medical Materials: **Cartilagen**, has a platform technology called GG-Visco, which is a biomaterial for drug and cell delivery for orthopedic applications.
- Diagnostics/Imaging: **Vida Diagnostics** is a pulmonary imaging and software company which recently raised a $5 million Series B round.
- Research Tools: **Immortagen** is seeking to personalize cancer treatment through clinical decision support algorithms.

Analyzing VentureNet data for all Iowa startups it is evident that 22% are in the med tech/life sciences sector. The source of underlying intellectual property for these companies primarily comes from the Regents universities (in contrast to the ag tech and advanced manufacturing startups whose underlying

[4] Licensing to existing companies would be another commercialization strategy.

source of IP is primarily the private sector). It should be noted that not all med tech and life sciences startups in the state apply for Iowa Innovation Program funding and, therefore, are not captured by the VentureNet data.[5] For example, NewLink Genetics, a startup immuno-oncology biopharmaceutical company that went public in 2011, did not apply for Iowa Innovation Program funding (although the company did receive IEDA funding through traditional financial assistance programs).

Med tech/life sciences startup companies, interviewed by TEConomy, identified UI's Gap Funding ($50K to $75K) and tech transfer office assistance, Iowa's Innovation Funding Programs ($25K Proof of Commercial Relevance and $100K Demonstration loan), SBIR application assistance, Iowa's Angel Investor Tax Credit, and Iowa's R&D Tax Credit, as all being policies supportive of Iowa's startup ecosystem.

The University of Iowa and the Iowa City region have invested in business incubator operations suited to the development of biomedical business ventures. Three primary locations exist:

- **MERGE** is a collaboration between the University of Iowa, the John Pappajohn Entrepreneurship Center (JPEC) at UI, and Iowa City Community Area Development (ICAD). While MERGE is available to entrepreneurs and startups developing a wide range of products and services, the space specifically houses Protostudios, a biomedical and electronics prototyping hub to support small businesses and train students. MERGE opened in early 2017 and is located on the pedestrian mall in downtown Iowa City. IEDA provided a $1.5 million grant to MERGE through the Strategic Infrastructure Program to purchase 3D modeling software, hardware and electronics equipment.
- The **Translational Research Incubator** (TRI) at the University of Iowa is located on the west side medical campus. TRI is an incubator and accelerator specifically targeted toward development of innovation-based biomedical or life-science startup companies. Ventures are expected to graduate within one year.
- **The BioVentures Center** is located on the University of Iowa Research Park and facilitates the incubation of early stage life science ventures with wet lab, dry lab, office facilities and shared user facilities. Also located at the Research Park is the Technology Innovation Center which, relevant to some categories of medical devices, provides office space to engineering and technology-based ventures.

Taken together, the above represent a good base of facilities for development of start-up medical device and med tech companies. They build upon an additional asset in the UIHC "Medical Instruments Shop" which has been engaged in prototype design and build-out services for device concepts. The Medical Instruments Shop is noted by the university to lack the technical capacity to create many types of modern medical devices (e.g. those that involve non-metallic materials, have complex shapes and are miniaturized). MERGE will provide the next level of prototyping and development capabilities necessary to take the Medical Instrument Shops work to the next level.

Iowa's relative proximity to the medical device cluster in Minneapolis St. Paul may also carry advantages in terms of partnerships, commercialization, talent and capital access.

It should be noted that, particularly in Iowa City, there is a small **but** not insignificant start-up culture that has emerged around biomedical therapeutic products – in addition to medical devices. There is obviously complementarity in biopharma and medical device markets served, and a potential

[5] Iowa provides up to $25,000 for Proof of Commercial Relevance and $100,000 for Demonstration for startups that are pre-revenue. A required step in applying for Iowa Innovation Program funding is to have VentureNet meet with applicants and organize focus groups to provide technical and business feedback on the company's business plan.

intersection between the two areas in terms of drug delivery devices and materials, diagnostics technologies, and hybrid drug/device products (for example drug eluting implants). Several biopharmaceutical companies are in development at the University of Iowa Research Park, with examples including:

- **Emmyon**, which discovers and develops small molecule compounds to improve muscle mass, strength, exercise and metabolism.
- **InnoBiopharma**, which is a startup biotech company focusing on developing next generation anticancer drugs based on naturally occurring anticancer compounds.
- **KemPharm, Inc.** is an early phase biopharmaceutical company focused on the discovery and development of therapies for the treatment of Attention Deficit/Hyperactivity Disorder (ADHD), pain, and cardiovascular disease.
- **Viewpoint Molecular Targeting**, a company developing pharmaceutical drugs for therapy and diagnostic imaging of cancer, which has been awarded $4 million in SBIR funding.

D. Weaknesses

Three weaknesses represent the principle identified challenges for a medical devices platform in Iowa. First, Iowa's existing industry base for medical devices, diagnostics, therapeutics, and research tools is relatively small. From an innovation perspective, this is a challenge since it presents limitations of the number of existing startup entrepreneurs and founding teams with experience growing companies in the sector. In addition, Iowa lacks larger existing medical device and med tech companies which might serve as potential advisors, mentors, connectors, investors, customers, and exits for startup companies. As noted above, however, comparative proximity to the strong device cluster in Minnesota may help mitigate this challenge.

Secondly, there are fewer Iowa angels and VC investors investing in early-stage med tech/life sciences companies compared to IT and ag tech.[6] Iowa med tech/life sciences startups interviewed by TEConomy noted that there is a significant gap (typically in the $150K to $1 million funding range) faced by pre-revenue startups after UI Gap funding and Iowa Innovation Program funding. Most Iowa angels lack med tech/life sciences domain expertise, so are reluctant to invest. In addition, there are few Iowa seed funds or Series A or B VC funds focused on med tech/life sciences.

Thirdly, tech transfer and spin-out activity from UI and the University Hospitals is hampered by the university's relatively small biomedical engineering and computer science/bioinformatics programs. U.S. News & World Report ranks University of Iowa:

- 63rd (ISU is also tied for 63rd) for computer science
- 56th for biomedical engineering
- 65th for mechanical engineering
- 70th for computer engineering.

The small number of graduates from these programs is also a problem:

- UI produced 17 Masters and PhD-level computer science and informatics graduates (ranking 150th for number of graduates) in 2015. By contrast, the University of Illinois at Champagne-Urbana produced 167 computer science Masters and PhD-level graduates.

[6] All startups that are based upon commercializing more capital-intensive technologies, with technical/regulatory risk in addition to business risk and a longer time frame to exit, face similar capital challenges.

- UI produced 31 Masters and PhD-level bioinformatics and biostatistics graduates (ranks 25th for number of graduates). University of Minnesota, Twin Cities produced 51 Masters and PhD-level bioinformatics, biostatistics, and computation biology graduates.

E. Opportunities

Key opportunities are shaped by the existing size and projected growth in the market for medical devices and associated technologies. With the sector sized at $483.5 billion globally in 2016and anticipated to grow to $634.5 billion by 2021, even capture of a relatively minor share of the market would result in substantial economic benefits.

Iowa has generated a small number of medical device and materials start-up companies and has the potential to do more. As noted in a recent private memo from UI to the IEDA, the UI has the fundamental strengths in areas such as surgery to enable novel device development work. What it has lacked has been a culture of medical entrepreneurship and the associated support structures required for device development in terms of ideation, prototype development, testing, regulatory affairs, etc. UI notes the growth that Minnesota has experienced:

> *Beginning in the 1950's and 60's UMN surgeon-inventors, engineers and entrepreneurs drove development and commercialization of innovative medical devices that transformed patient care around the world and turned Minnesota into a global powerhouse in the Medtech field. The impact on their state's economy is massive with over 900 Med-Tech companies employing over 125,000 workers and generating > $14 Billion in annual economic activity within the State of Minnesota*.

With surgery at the root of Minnesota's success, UI justifiably sees opportunities closer to home. They note that:

> *Currently UI Healthcare surgical departments are by all objective measures higher performing units than their peer departments at the University of Minnesota. Yet, the economic development impact of our work is a fraction of 1% of that of our colleagues in Minnesota.*

There is no reason to believe that Iowa's surgeons, and others in key disciplines within the IU academic health center and across into the university at large, should be any less creative or inventive than colleagues elsewhere. What has been lacking has been a culture and associated support mechanisms to enable and encourage device innovation. This though is changing, and an opportunity is presented to build-upon nascent interest, and investment in prototyping and incubation facilities in Iowa City, to make a concerted push on sector development. With a small number of relevant start-ups underway, there now exist some entrepreneurs with experience to build-upon.

Proximity to Minnesota also presents an opportunity to access the skills, experience base, capital, supporting professional services and other capabilities of the Minneapolis/St. Paul metro area to benefit Iowa.

F. Threats

Threats to Iowa's med tech/life sciences activity would come from any kind of derailment to existing state policies and programs that support research commercialization and innovation activity. For example, a recent call to cut $8 million from each Regents university on top of existing budget cuts would significantly reduce funding for tech transfer operations, commercialization grants (known as Gap Funds), and other economic development activities. Iowa's Innovation Program funding and Angel Investor Tax Credit have also come under review. These cuts, if enacted, would signal a withdrawal of

state commitment to developing Iowa's innovation economy and could slow the pace and trajectory of startup activity in the state.

Another threat relates to the long-term development horizon for regulated medical devices. While not as long as typically experienced in biopharmaceuticals, the medical device realm still requires significant patience and a stick-to-it attitude. Implementation of strategies for advancing the sector requires that a long-term perspective be adopted, which is not always in alignment with political needs to show results.

G. Platform Summary

Table 5: Medical Devices Platform Summary

Status	☐ Emerging R&D (core competency in research only, need to build industry) ■ Emerging R&D Plus (R&D core competency and small base of industry) ☐ Established Growth (R&D and significant base of industry with expansion potential)
Business start-up potential	Strong potential given multiple device related clinical R&D strength areas at UI. Realizing potential depends on creating and facilitating a start-up culture with financing to advance concepts and facilities to accommodate prototyping and business development.
Business expansion potential	Moderate at the present time because there is just a small base of device companies and most of these are in early business development phases.
Business attraction potential	Challenging environment for business attraction given the much larger and well-established device clusters in other U.S. locations.
Academic R&D growth potential	Good potential given funding agency priorities for translational research in biomedical sciences, but potentially restrained by current federal budget allocations.
Iowa competitive situation	Emerging only. There is an insufficient base of R&D and business development activity in Iowa in this space to be "on the radar screen" in the device industry. Major centers of gravity exist in the industry outside of Iowa that have potential to attract away successful Iowa start-ups – although the proximity of Iowa to Minnesota may mitigate this somewhat.
Key barriers to overcome	• Building interest and momentum with faculty to advance innovations along a commercialization pathway • Early stage capital availability for proof of concept and early-stage business formation and growth • Relative lack of experienced medical device business entrepreneurs and experienced start-up management

H. Recommendations

Primary crosscutting recommendations for bioscience cluster development in Iowa are profiled in Chapter IV. Under the recommended new Iowa Bioscience Development Center, it is recommended that each platform has an individual sub-committee focused on platform advancement. Some considerations for the Medical Device Platform would include:

- Support development of a culture of innovation within medical and associated disciplines likely to relate to medical device development at the University of Iowa. Canvas surgical and other departments across the UI Healthcare enterprise to identify physicians with an interest in innovation activity. Focus on mentoring those with interest through connectivity with existing

Iowa medical sector entrepreneurs and also through creation of linkages with Minnesota-based and Wisconsin-based medical device entrepreneurs.

- Integrate the MERGE, the UI Medical Instruments Shop and other engineering and prototyping services across IU to provide a full-serve prototyping operation to facilitate advancing innovations to the proof-of-concept phase and beyond.
- Visit and integrate best practices and learning from existing medical device focused university and related innovation centers such as: the Global Cardiovascular Innovation Center in Cleveland; the Center for Medical Innovation at the University of Utah; Medical Devices Center at the University of Minnesota, and the Stanford Byers Center for Biodesign at Stanford University.
- Use the "A New UI Medtech Economic Development Proposal" document, supplied by IU to IEDA, as a starting-point for deliberations pertaining to platform development under a platform sub-committee.

Platform 2: Biobased Chemicals

A. Description

Over the last 100 years, molecules derived from oil and gas have generated much of the innovation in the chemicals industry. The ability, however, to derive novel new chemicals from these traditional feedstocks is limited. Petrochemicals have been so well studied, and their inherent chemistry so well exploited, that there is little new to discover of commercial value.

The same is not the case with biobased feedstocks and chemistry. The future of innovation in the chemicals industry is likely to come from the discovery and exploitation of new molecules generated from biomass and also in the advanced process technologies (e.g., thermal, chemical and biological) needed to generate them. Biobased chemicals encompass an opportunity rich environment for generating both novel molecules with enhanced or novel performance characteristics and uses, as well as sustainable replacements for existing non-sustainable petroleum-based molecules.

The present reality of low oil and natural gas prices has been a limiting factor on investment in alternative chemical feedstocks and processes. Current market conditions make it uneconomic to invest in creating drop-in replacements for petrochemicals – unless they have either A) substantial price advantages (which is unlikely given how efficient the current petrochemical model has become) or B) they significantly outperform petrochemical products. In the U.S. market, there is relatively little green premium for biobased chemicals being more sustainable or environmentally benign than petrochemicals, and the present political environment means that regulatory changes or subsidies to support biobased alternatives to petrochemicals are unlikely to be a priority.

The current market, therefore, favors development and production of biobased molecules with novel performance characteristics – rather than targeted replacement of petrochemical based commodities. Longer term, as the price of fossil carbon feedstocks rises, replacement biobased chemicals will also become more competitive – but it is highly challenging to predict when that might occur given the large number of domestic and global factors that come into play.

Despite a challenged market environment, Lux Research[7] estimates that venture capitalists have invested $5.8 billion in biobased chemicals since 2010. Their research confirms much of the discussion from above:

- From 2010-2015, the investment focus was on drop-in replacements or substitutes for established petrochemicals, though the focus shifted to synthetic biology (synbio)[8] and conversion technologies in 2016. This shift is largely due to falling oil prices.
- 80% of VC investment in 2016 was on improved products (as opposed to drop-ins and substitutes) compared to only 46% from 2010-2015.
- Synbio startups received over $300 million in 2016.

A discussion of biobased chemicals, and the opportunities therein, would be incomplete without characterization of the complexity of chemicals, processes and feedstocks that can be involved.

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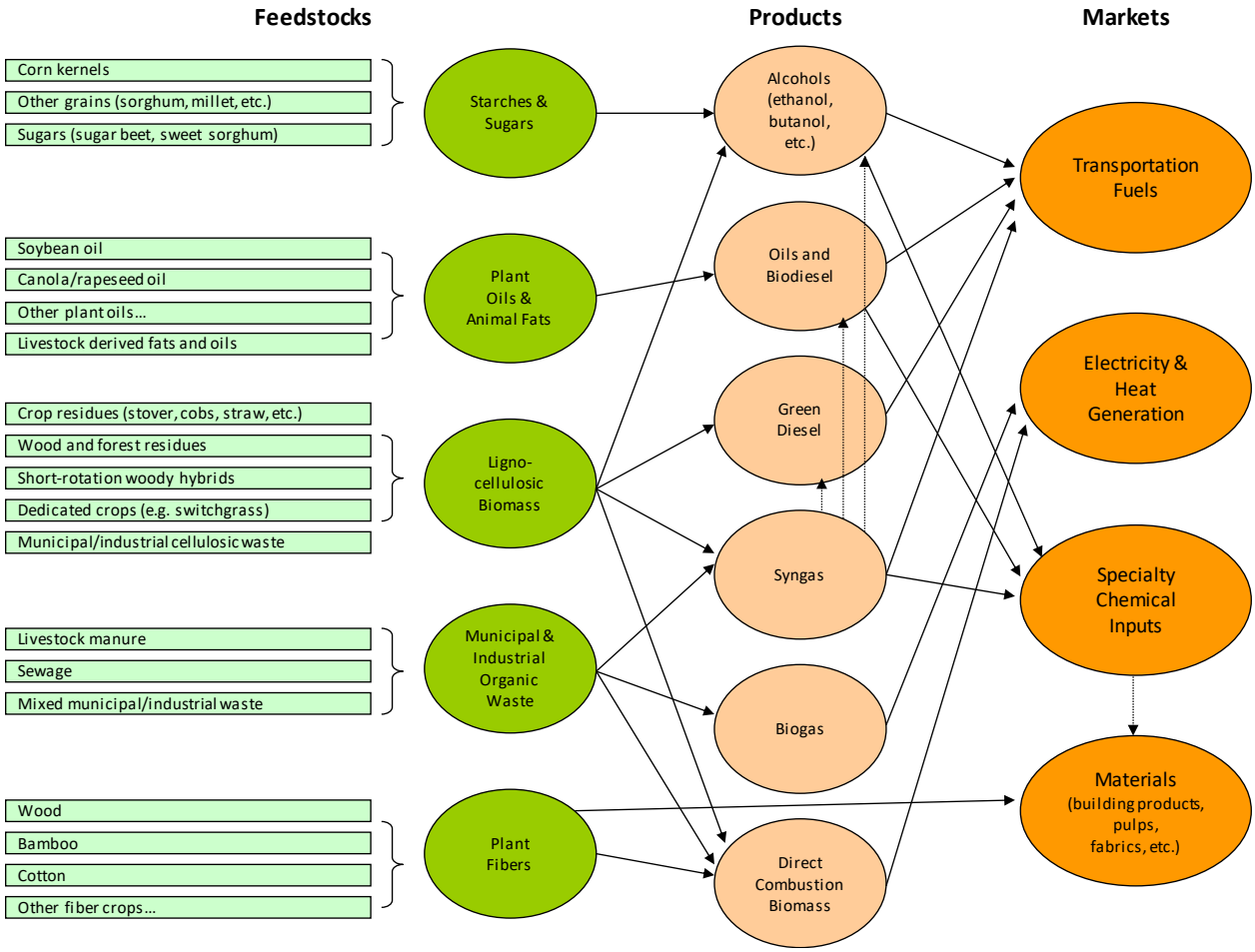
[7] Lux Research (2016). *Show Me the Money: Where Is Venture Capital Placing Bets in Biobased?* http://www.luxresearchinc.com/news-and-events/press-releases/read/vcs-invest-58-billion-biobased-chemicals-focus-shifts

[8] According to the Advanced Biofuels Association, synthetic biology is the design and fabrication of biological components and systems that do not already exist in the natural world, and the redesign and fabrication of existing biological systems.

Currently the use of plants for production of fuels, chemicals and materials may be characterized by the pathways shown on Figure 5:

Figure 5: Biobased Feedstocks, Products and Markets[9] (A Simplified Illustration)



As can be seen on Figure 5, processing of biomass via fermentation, thermal processes (such as gasification) and chemical processes can result in a variety of intermediate and end product chemicals, materials and fuels. This series of pathways to market primarily represents the use of existing types of biomass, with their known oil, starch or other chemical compositions. It is largely a process-engineering/chemical-engineering focused approach.

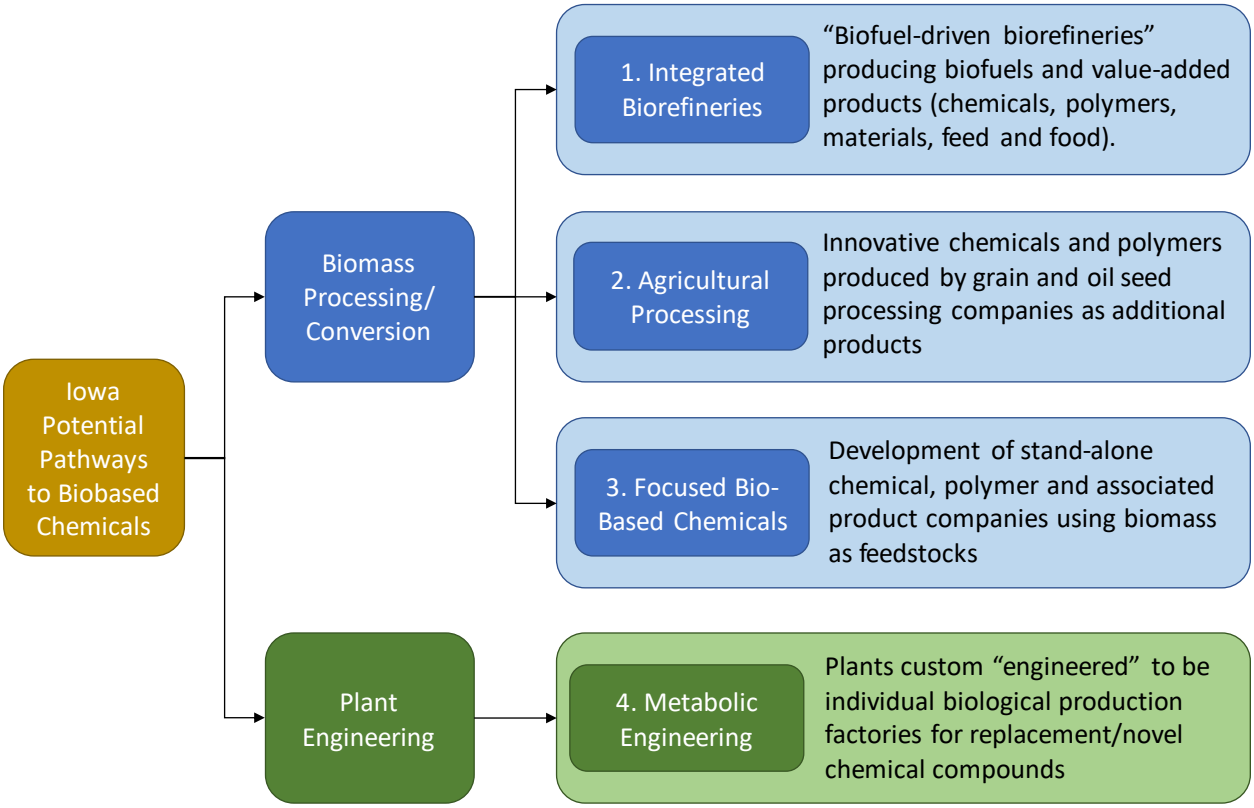
The development of biobased chemicals along these pathways may occur via add-on refining processes to an existing liquid biofuels biorefinery, additional processing of biomass into chemicals by grain or oilseed processing companies, or may involve development of stand-alone biobased chemical companies or refineries. These three potential pathways to biobased chemical production are shown on Figure 6. It is notable that all three of these pathways are currently operating in Iowa, although the third pathway is the most limited currently. Iowa (primarily at Iowa State University), as discussed further herein, has also been pioneering technologies potentially suited to these production pathways that use a novel combination of biocatalysis (using engineered microorganisms) and chemical catalysis.

[9] Simon Tripp. "Regional Strategy for Biobased Products in the Mid-South Mississippi Delta."

There is also another, quite different scientific pathway potentially driving opportunities to realize product variety and functionality from plant chemistry – that of plant metabolic engineering. Plant metabolic engineering (PME) provides a significantly different way of viewing plants in the chemical production value chain. Instead of thinking about existing plants and their oils and starches as inputs to chemical refineries (e.g. converting oil and starch into intermediate chemicals and then refining them or processing them into specialty chemical products), PME provides a pathway to using plants themselves as the chemical factories. It should be noted, however, that plant metabolic engineering as a route to novel biobased chemicals (at any kind of commercial scale) is viewed as a long-term, high-risk area of developing science and thus falls outside of the scope for Iowa's nearer-term bioscience-based economic development. Because ISU has work taking place in plant metabolic engineering, TEConomy has included some further detail in Appendix A.

In the near- to mid-term, it is biomass conversion and processing technology (rooted in catalytic processes), and its application to the conversion of Iowa-produced biomass, that is the clearest path forward for the state.

Figure 6: Iowa Potential Pathways to Biobased Chemical Industries Development



Each of the biomass processing-based pathways for biobased chemicals (integrated biorefinery operations, agricultural processing operations, and focused biobased chemicals companies) present opportunities to build upon existing assets and momentum in Iowa – including both corporate R&D and production expertise and interests and academic R&D and technology piloting (particularly at ISU). Because an R&D and asset base is already functioning within Iowa, the biomass processing pathway to biobased chemicals represents a near-term opportunity for development in this platform.

Taken together, the combination of Iowa's rich biomass production environment, initial leadership in investment in the commercial bioeconomy, biofuels and biobased chemicals, scientific expertise in plant sciences, biobased chemicals and process technology development at ISU present a robust platform for the ongoing development of a bioscience-based economy in Iowa.

Iowa's acknowledged position and leadership in process engineering for biobased products has recently been highlighted in ISU's important role in the U.S. Department of Energy's Rapid Advancement in Process Intensification Deployment (RAPID) Manufacturing Institute which represents the newest, and tenth, member of the nation's network of Manufacturing USA Institutes.

Based on the above discussion, it is evident that each of the potential pathways to biobased chemical development (illustrated on Figure 6) are open to exploitation for economic development in Iowa. The pathways, however, are not equal in terms of potential development timelines and the types of challenges faced in their development.

A key challenge facing biofuels (and therefore, the integrated biofuels-biorefinery pathway), including in Iowa, is their cost competitiveness with petroleum-derived fuels (given currently low oil prices). The market for biofuels is currently sustained largely by government regulations calling for a percentage of biofuels to be used in fuel blends. While this regulatory-based model has helped to build a market, it is effectively an artificial market and subject to the risk of regulatory change. The sustainability of biofuels producers may be improved through creating value-added biofuel-driven biorefineries that improve their profitability through the production of a diversified suite of value-added products and co-products (which may be chemicals, but may also be food products, feed products or materials). Given Iowa's existing investment in biofuel production facilities and the impact of the sector on the Iowa economy, an integrated biorefinery model is logical to pursue.

Iowa's biomass feedstocks could be processed along several biorefinery platforms, for example:

- Single carbon molecules (biogas and syngas)
- 5 and 6 carbon carbohydrates from starch or cellulose
- Mixed 5 and 6 carbon carbohydrates derived from lignin, hemicelluloses, plant oils, etc.

These biorefinery platforms can be further refined to produce value-added products using thermal, biological and chemical processes and combinations thereof.

The second pathway leverages the substantial investment in Iowa of major agricultural processing companies (such as GPC, ADM, Cargill, etc.) in large-scale grain and oilseed processing infrastructure. These companies are already engaged in the production of multiple chemicals (beyond the food and feed products that primarily drive their business). GPC, for example, uses expertise in carbohydrate chemistry to produce binder chemicals (starch based sealers and adhesives) and powered starch products with absorbency characteristics used in personal care products. ADM similarly produces starch-based binding agents, and specialty vegetable-based lipids and natural anti-oxidant chemicals from soybean ingredients. They are also active in biobased polymers and a broad range of products as acidulants, solvents, industrial oils, surfactants and wetting agents. Cargill is similarly engaged in producing a broad range of industrial chemical products from biomass feedstocks.

The third pathway is also logical, building on the significant R&D assets (especially at ISU) in terms of the development of new biobased chemicals, novel processes, or combinations thereof for application in stand-alone specialty chemical businesses.

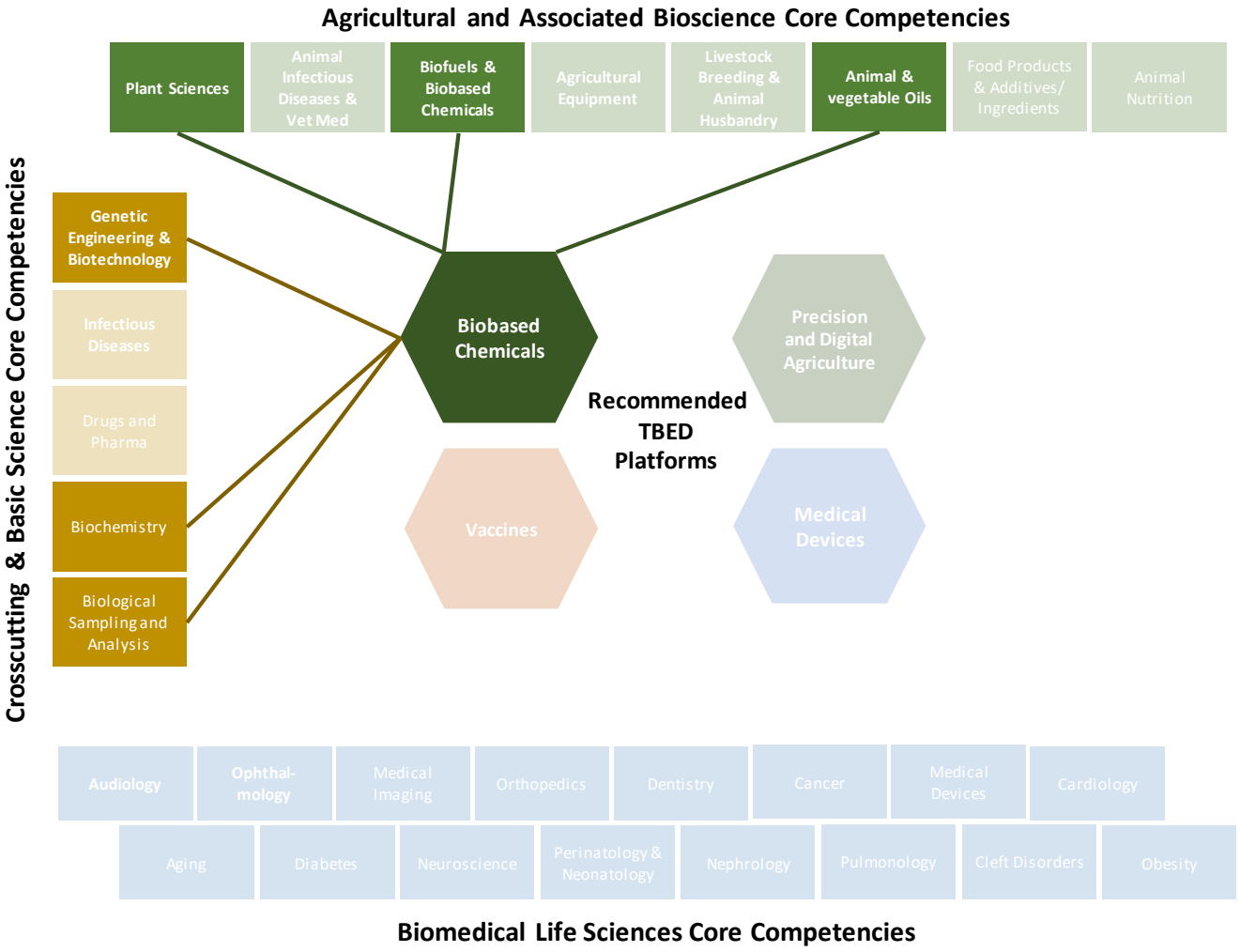
The fourth option of metabolic engineering, is fascinating as an alternative model, but has a significantly longer-term development horizon rooted in building scientific capabilities in Iowa, particularly within the

universities (most notably ISU) to advance capacity to perform R&D in plant metabolic engineering – particularly focus on plants suited to growth in the Iowa agricultural production environment.

B. Connectivity to Iowa Core Competencies

Figure 7 illustrates the connectivity between multiple core competencies and the Biobased Chemicals platform, illustrating how multiple Iowa R&D core competencies may be leveraged to drive transdisciplinary work on the platform.

Figure 7: Biobased Chemicals Platform – Connectivity to Identified Core Competencies



C. Strengths

As noted previously, Iowa already has developed a significant base of assets for biobased chemical platform advancement. First, Iowa already has many companies engaged in manufacturing intermediate biobased chemical products: ethanol and biodiesel. There is also a base of Iowa companies engaged in R&D related to the use of different feedstocks as biofuels and process-related technologies for conversion of these feedstocks. Iowa presently has 43 ethanol production facilities producing over 27% of the U.S. ethanol output, and has 12 biodiesel refineries producing 16% of U.S. output.[10] And, the state is home to several early-stage companies focused in the biobased chemicals technology market, including for example:

- **SusTerea Biorenewables LLC** is a startup company focused on developing and commercializing the manufacture of an array or aromatic chemical products from biomass feedstocks. (An affiliate of the ISU Research Park).
- **Swamp Fox Chemical, LLC** is located at the ISU Research Park and is a chemical technology company focused on using biobased and synthetic raw materials to develop chemical solutions for industrial markets.
- **VariFAS Biorenewables LLC** is cofounded by a team of researchers from Iowa State University focused on sustainable, biobased technologies. VariFAS has been the recipient of Iowa State i6-green award and NSF Phase I SBIR award for its research and business development. VariFAS is developing biomass-derived mono-unsaturated fatty acids of various chain lengths. As VariFAS notes: the technology "can be used to make variety of fatty acid derivatives and other bi-functional specialty chemicals for the application in surfactants, lubricants, and polymers. Our vision is to produce biorenewable chemicals economically, help our partners create environment-friendly products, and contribute our effort to build a biobased sustainable chemical industry."

Iowa was also successful in attracting a major facility of **Valent BioSciences Corporation** which constructed a $150 million biorational manufacturing facility in Osage, Iowa. Valent performs fermentation using Iowa- grown raw materials (corn and soybeans) to produce value-added chemical and microbial products, primarily serving agricultural markets. Valent is a subsidiary of Japanese chemical company Sumitomo.

In addition to the above chemical companies, Iowa has a robust base of major agricultural processing companies:

- **Cargill** has multiple processing plants in Iowa, performing soybean and corn processing operations. Examples include major production facilities in Fort Dodge, Cedar Rapids, Eddyville, Sioux City and Iowa Falls.
- **Grain Processing Corporation** (part of Kent Corporation) has large processing facilities and HQ operations in Muscatine
- **ADM** has major production operations in Cedar Rapids and Des Moines.
- **Bunge**, with oilseed crushing operations in Council Bluffs
- **Ag Processing Inc.** with 6 crusher locations in Iowa and refining operations in Cedar Grove
- **American Natural Soy Processors** in Cherokee.

[10] Iowa Economic Development Authority.
https://www.iowaeconomicdevelopment.com/userdocs/programs/FS_RenewChemTaxCredit.pdf

As noted above, grain and oilseed processing companies are presently engaged in the production of a broad-range of industrial chemicals –primarily using corn and soybean feedstocks in Iowa.

The presence and operations of multiple plant science/seed companies in Iowa is also a related strength in terms of potential partners for work on increasing functional chemical expression in crops – whether that be via traditional breeding and transgenics/gene-editing work or via plant metabolic pathway engineering. Companies present, include, for example:

- **DuPont Pioneer**, headquartered in Johnson Iowa, is a leading global developer and supplier of advanced plant genetics providing seeds to farmers around the world. Pioneer develops and sells corn, soybeans, sorghum, sunflower, alfalfa, canola, wheat, rice, cotton, pearl millet and mustard seed, as well as forage additives and a variety of services and expertise. Pioneer uses conventional plant breeding and is the preeminent company in Iowa with respect to traditional breeding, plant gene editing and plant metabolic engineering.
- **Monsanto** has multiple locations in Iowa, including R&D (incorporating corn research at their facility in Ames).
- **Syngenta** has a major R&D facility in Slater Iowa which is a hub for Syngenta R&D in corn and soybean breeding.
- **BASF Plant Sciences LLC**, has operations at the ISU Research Park (although the company has downsized its R&D).
- **NuTech Seed,** at the ISU Research Park, uses plant hybrid and variety selection processes to bring to market high yielding, disease tolerant crop products. NuTech seed is subsidiary of DuPont Pioneer.
- **Stine Seed Company** has a biotechnology facility in Ames.
- **Data2Bio LLC**, which is an ISU Research Park Affiliate, provides sequencing services for breeding programs that rely on genomic selection.

Additional strengths are provided in the private sector with company operations in Iowa including:

- **Novozymes**, an international biotech company with a strong focus on enzyme production.
- **Kemin Industries**, a privately held global nutritional ingredient company headquartered in Des Moines. Kemin has a diversified range of products using biological ingredients to enhance human and livestock nutrition, and for industrial applications such as biofuels and biopharmaceutical ingredients.

In addition to industry activity, a second core strength for Iowa is in academic R&D in biobased chemicals and associated research. Iowa has a prestigious NSF-funded Engineering Research Center (ERC) focused on biobased chemicals for nearly 10 years: the Center for Biorenewable Chemicals (CBiRC) at Iowa State University. ERCs are highly competitive, nationally awarded research centers that seek to advance interdisciplinary discovery and innovation through research collaboration among academic researchers, small innovative firms, and larger industrial partners. CBiRC represents a 10-year, $33 million investment in biorenewable chemicals research in Iowa. Approximately 60 ISU faculty and graduate students are involved with the center, and Iowa industry partners include Cargill, DuPont, Renewable Energy Group (REG), Archers Daniels Midland (ADM), and Grain Processing Corporation (GPC). There are also industry partners from outside the state. While there have been no new biochemical molecules commercialized out of CBiRC to date, there are a number in the pipeline that are currently undergoing testing. The commercialization vehicle for many of these molecules is licensing to startup companies that have spun out of CBiRC.

Iowa has multiple R&D center assets to build-upon in biobased chemicals, including for example:

- Center for Biorenewable Chemicals (ISU)
- Center for Metabolic Biology (ISU)
- Biocentury Research Farm (ISU)
- Center for Crop Utilization Research (ISU)
- Center for Bioprocessing and Biocatalysis (UI)
- BioEconomy Institute (ISU)
- Biobased Industry Center (ISU)
- Center for Bioplastics and Biocomposites (ISU)
- Plant Sciences Institute (ISU)
- Ames National Laboratory

CBiRC as a Foundational Iowa Asset for Platform Development

Engendering a shift from a petroleum based resources economy to a biorenewable resources economy is clearly no small task. The chemicals industry has more than a century of experience in developing highly efficient processes for petrochemical conversion into value-added products, and has a huge sunk investment in the infrastructure required for such processing. The marketplace can only pivot to biobased chemicals if they can offer enhanced economic returns or provide significant novel or enhanced performance characteristics.

Like any frontier area of science and innovation, success in building a new biobased chemicals economy cannot occur overnight, but rather derives from a long-term, sustained commitment to building a program of R&D supported by investment in specialized R&D infrastructure and highly skilled, expert scientific talent. The development of a base of talent and infrastructure has been greatly facilitated in Iowa through the federal investment in CBiRC which has focused on advancing fundamental knowledge and technology in biobased chemicals and the academic and industrial partnerships needed to advance a renewable resource-based industry. The overarching goal of CBiRC has been to:

> *Enable the transformation of the chemical industry through the optimized coupling of two catalyst types such that a biocatalyst will convert glucose to an intermediate chemical that can be readily converted by a chemical catalyst to the desired chemical product.*

The Center has drawn together a substantial multidisciplinary team of researchers, with R&D focused along specific research "thrusts":

- Thrust 1: Biocatalysis of fatty acid or polyketide biosynthetic pathways
- Thrust 2: Enhanced microbial production through highly targeted biotechnologies

- Thrust 3: Combining Biocatalysis and chemicals catalysis to produce fatty acid or polyketide-based platform chemicals (examples include carboxylic acids, dienes, pyrones, branched and ring structures, ethers and esters, bi-functionals and multi-functional chemicals).

Advancing the mission of CBiRC has required both fundamental and applied research focused not only on advancing and testing novel biocatalysis and chemical catalysis technologies but also consideration of market, environmental and other factors. This mission is certainly a "heavy lift" but it has potential for development of multiple novel biobased chemicals that can be used as precursor chemicals for an array of biobased products and materials.

The approaches used by CBiRC have borne fruit in terms of innovations and spurring the development of new start-up enterprise to advance the commercialization of these innovations, including for example: Glucan Biorenewables; OmegaChea Biorenewables; Pareto Biotechnologies; Pure Oleochemicals; SusTerea Biorenewables; WebChemi; Technology Holding; VariFAS Biorenewables; Sumatra Biorenewables, and WE Complement.

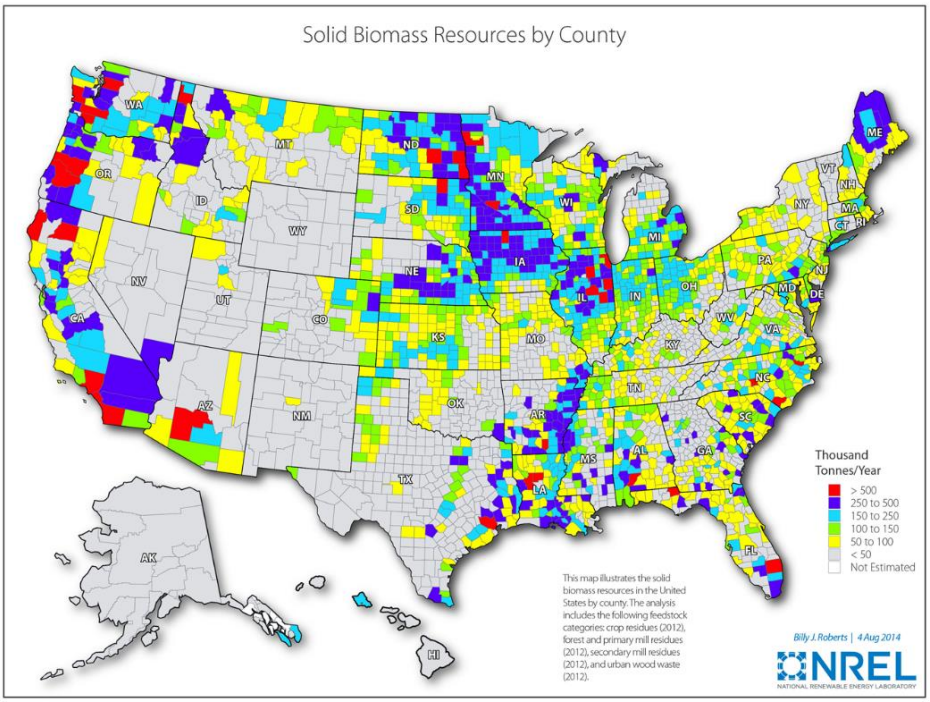
As the ten-year NSF funding for CBiRC comes to an end in 2018, it is imperative that means be found in Iowa for the Center to continue its mission. The capabilities at ISU within CBiRC, and other complementary research programs and centers, represents an investment that should be further built-upon. In a complex and challenging technology and market space, CBiRC has started to yield success for the state in terms of invention disclosures and new business enterprise formation. It does not have a true peer in other universities, and represents a unique signature for Iowa in advancing a biobased chemicals industry. In terms of strategies and actions for the Biobased Chemicals platform, figuring out how to sustain CBiRC upon the close-out of NSF funding, should be a priority.

A third core strength of Iowa is that, in 2016, the State of Iowa passed a Renewable Chemicals Production Tax Credit which incentivizes production of 30 high-value chemicals derived from biomass feedstocks.[11] The tax credit offers $.05 per pound, up to $1 million for startups and $500,000 for established companies. It is the first tax credit of its kind in the U.S. demonstrating a commitment by Iowa to be a leader in developing the biobased chemicals economy.

Fourth, Iowa is one of the richest environments in the United States for the production of biomass (Figure 8). As reported by the Iowa Economic Development Authority, the state has the second largest supply of biomass in the nation – with the ability to harvest 14.4 million dry tons of biomass per year (including total cellulosic and crop biomass). Developing a biobased chemicals industry for Iowa, therefore holds promise not only in the development of new or expanding companies in the development and production of novel biobased chemical production technologies, or metabolically engineered plants, but also in high productivity agronomy in producing biomass for chemical production and the further development of the biorefinery cluster in the state to process biomass into valuable chemicals, plastics and other products.

[11] https://www.iowaeconomicdevelopment.com/Business/RenewableChem

Figure 8: Iowa is Among the Leading State in Solid Biomass Resources



D. Weaknesses

While Iowa has a considerable base of agricultural processing companies and biofuel production facilities, these are located in the state predominantly because of access to their raw feedstock – primarily corn. Further refining of platform chemicals into downstream value-added products, however, is not guaranteed to occur at the same locations – and may be pulled toward major existing chemical company infrastructure and end user facilities (which are primarily outside of Iowa).

While metabolic engineering is a new area, the main pathway engineering companies (including those that would make a biological intermediate and then conduct traditional chemistry) are not in Iowa. Rather, they are particularly concentrated in California (e.g. Amyris, Zymergen, BP, DuPont Industrial Biosciences).

The currently low price of oil has made petrochemicals and plastic less expensive, which act a disincentive for corporate investment in biobased chemicals and bioplastics development in the short term. In addition, the change in environmental regulatory policy in the U.S. will also negatively impact demand for biobased chemicals. While the chemicals industry appears to be pivoting to specialty biobased chemicals with enhanced performance properties, innovation is this area is still challenging due to the process innovations that are also required to get these biochemicals to market.

While Iowa State University has a strong base of assets in multiple areas relating to biobased chemicals, there is a need to bring them together under a more coordinated approach to development of this sector. Combining the capabilities of ISU in plant sciences and plant transformation, plant metabolic engineering, biobased chemical processing and refining, etc. holds promise for forming a uniquely capable and holistic platform unmatched in other locations.

E. Opportunities

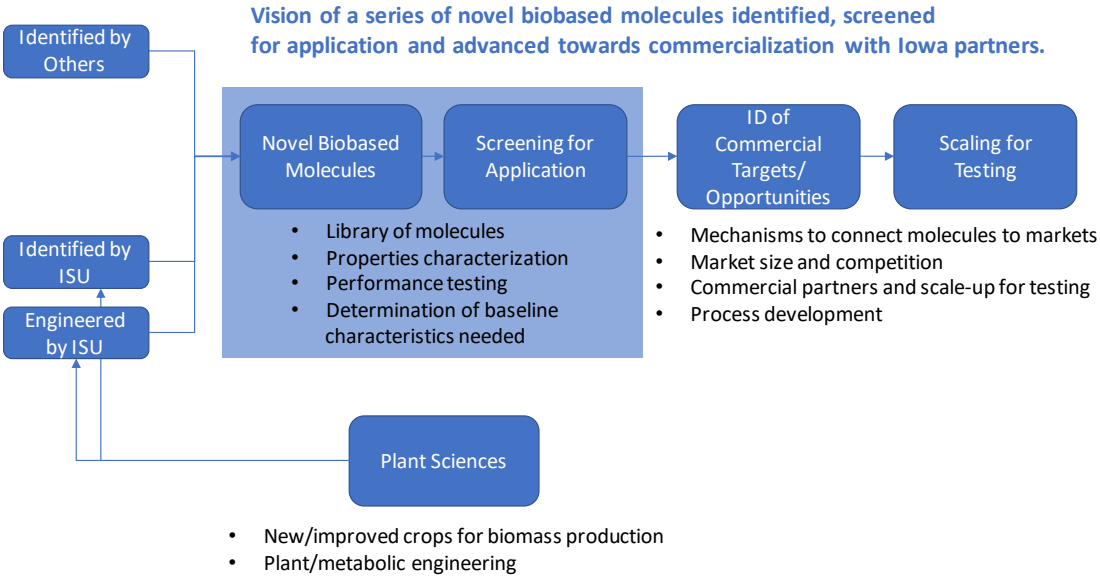
Despite the currently low price of oil today, the price of oil is unlikely to stay this low over the next 10-15 years. An important value proposition for biobased chemicals is the fact that molecules with enhanced performance properties are unlikely to come from the petrochemical industry in the future, in addition to their improved cost competitiveness when the price of oil rises.

Second, as the *Biobased Chemicals: The Iowa Opportunity*[12] report points out, in the same way that the petrochemical industry grew out of where the refinery infrastructure was located, biobased chemicals will also likely cluster around the biomass production and biomanufacturing infrastructure. Iowa has significant biomanufacturing infrastructure that can be leveraged for biochemicals—e.g., corn wet mills, soybean processing facilities, wood mills, corn dry mills, biodiesel plants, and ethanol plants.

Third, Iowa has research talent and technology commercialization infrastructure for biobased chemicals. The number of faculty and graduate students focused on biobased chemicals research and existing research infrastructure at CBiRC, and other centers (shown in the sidebar on page 28), represent an important competitive asset that can be further leveraged. The state commitment to the sector, embodied partly in the innovative new state tax credit, is also an advantage.

The Office of the Vice President for Research at Iowa State University arranged for TEConomy to participate in a focus group/brainstorming session with leaders of major biobased R&D programs at ISU. During the meeting, a potential vision for Iowa was expressed for the state to cement a leadership position in discovery of novel biobased molecules that are screened for commercial application and tested for efficacy, functionality and other characteristics. The vision would combine a series of what were described as strong but "currently fragmented" ISU assets to create an integrated pathway to identifying, screening and testing novel biobased molecules for application to value-added biobased chemical production in Iowa. Figure 9 depicts a draft structure for the concept based on conceptualization of the idea during the meeting.

Figure 9: ISU Potential Vision for an Integrated Novel Biobased Molecule Development Structure



[12] Hayes, D.; Shanks, B.; and J. Euken (2016). *Biobased Chemicals: The Iowa Opportunity*. Commissioned by Iowa's Innovation Corridor with support from the Iowa Biotechnology Association.

Engaging existing Iowa industry in the further development of this model and in potentially forming a joint university and industry R&D collaborative would be a preferred mechanism for organizing around this opportunity.

F. Threats

Other universities with strong chemistry departments are also focused on biobased chemicals, and NSF ERC funding for CBiRC will end in 2019. An example of a regional competitor is the Center for Sustainable Biopolymers at the University of Minnesota, Twin Cities, which was awarded a five-year, $12 million NSF Center for Chemical Innovation in 2014 to develop next-generation plastics. The University of Minnesota's Chemical Engineering program is ranked 5th by U.S. News & World Report. ISU's ranks 33rd. There are also competitor regions with historically strong chemicals industries and chemical engineering programs like Delaware, California, Michigan, Pennsylvania, Texas, etc., which are also turning their attention to biobased chemicals.

A key challenge is to maintain interest and investment in biobased chemicals research and innovation in Iowa despite the weakness in short-term demand caused by the low price of oil and downgrading of environmental and sustainability policy. A current wild card is also how federal research funding, especially for sustainable and renewables technology research, will be affected. It is likely that policies promoted by the current federal administration will have a chilling effect on investment in domestic green technologies that sell based-on a sustainability marketing strategy – but this does not mean that unique biobased chemicals having novel properties and functional characteristics would be so market constrained.

G. Platform Summary

Table 6: Biobased Chemicals Platform Summary

Status	☐ Emerging R&D (core competency in research only, need to build industry) ☐ Emerging R&D Plus (R&D core competency and small base of industry) ■ Established Growth (R&D and significant base of industry with expansion potential)
Business start-up potential	Strong potential given Iowa track record in starting companies in the biofuels sector and proximity to biomass and a focused suite of R&D assets in universities. Potential for specialty spin-out companies and operations from major grain and soybean processing companies.
Business expansion potential	Significant. Major agricultural processing companies are actively pursuing value-added chemical opportunities and multiple biofuels companies have potential to consider a more diversified biorefinery approach to growth. However, there is a limited base of specialty chemical companies in Iowa into which biobased products could be introduced.
Business attraction potential	Production industries likely to be attracted by biomass availability, biomass processing infrastructure and transportation networks. Limiting factor of lack of a workforce with specialty chemicals production experience, although Iowa community colleges have been responsive in the biofuels sector.
Academic R&D growth potential	Challenging environment for raising funds from traditional federal sources, with federal agencies facing funding cutbacks.
Iowa competitive situation	Iowa is very well positioned in terms of having R&D assets, robust sources of biomass and a business base that understands biofuels production and grain/oilseed processing and refining. In the biofuels sector there is only a limited presence in biorefining operations for chemicals beyond biofuels, however the big agricultural processing

	companies are engaged in producing value-added industrial chemical products. Competition from other regions of the U.S. to grow this sector has thinned due to short-term market constraints (fossil fuel prices and government policies), and there is thus potential to cement a position for Iowa in anticipation of a future market rebound.
Key barriers to overcome	• Potentially constrained current environment for biorenewable project financing based on low fossil-fuel prices and de-emphasis of sustainability by current federal administration. • Building interest and momentum with faculty to advance innovations along a commercialization pathway. • Early stage capital availability for proof of concept and early-stage business formation and growth. • Coming end of NSF funding for the ISU Center for Biorenewable Chemicals • Plant metabolic engineering pathway would require significant investment in additional faculty resources.

H. Recommendations

Iowa has made impressive strides in building a grain and oil seed processing industry and a biofuels industry, but the development of these industries in Iowa have been more a result of biomass availability (corn and soybeans primarily) than of novel R&D development and technology commercialization stemming from Iowa-performed research. Recognizing the promise of a biobased economy, however, universities (especially ISU) have invested in developing a deep base of infrastructural and intellectual assets applied to bioeconomy R&D and development opportunities. While the market for biobased products is somewhat challenged at present, the long-term future of the sector is likely such that doubling-down on biobased chemicals and associated products is a valid strategy for Iowa. This is an area where Iowa has established definite R&D leadership that deserves to be sustained, better coordinated and further built-upon.

Primary crosscutting recommendations for bioscience cluster development in Iowa are profiled in Chapter IV. Under the recommended new Iowa Bioscience Development Center, it is recommended that each platform has an individual sub-committee focused on platform advancement. Some considerations for the Biobased Chemicals Platform would include:

- Significantly increasing awareness and coordination of respective research interests and assets between academe and industry.
- Increasing awareness of the Iowa Renewable Chemicals Production Tax Credit among the investment community and across the biobased products industry nationally.
- Attracting venture investment firms with interests in agricultural and biobased products to consider Iowa investment opportunities.
- Assessing the interest of the existing biofuels industry to move into more integrated biorefinery operations and diversified biobased product portfolios
- Screening international technology markets for new technologies potentially suited for application to processing of Iowa biomass types.
- Evaluation of the history of CBiRC, and other university centers, to determine what barriers and challenges need to be addressed to create a flow of novel commercializable biobased chemicals that may be piloted.
- Examining opportunities to build long-term leadership in plant metabolic engineering and associated plant transformation.

- Reinforcing the existing investment in CBiRC and other ISU assets and expertise to sustain Iowa as a leading center for biobased chemicals R&D. With NSF funding closing out for the Center, and CBiRC now generating spin-out commercial enterprise and promising innovations, there is a clear need for a state strategy to maintain and build-upon the asset base and intellectual capacity within ISU.

Platform 3: Precision and Digital Agriculture Technology

A. Description

Agriculture faces a huge challenge in meeting the food demand generated by the world's expanding population. The world can seek to meet the challenge in two ways: one positive and one negative. On the negative side is the destruction of forests and other fragile habitats to press fragile land into an unsustainable agricultural production model. On the positive side is the use of R&D to enhance productivity (yield) from the agronomic land we already have. Clearly it is in the interest of the world and future generations to take this latter path. Doing so, however, requires the development and application of a broad range of technologies and advanced agricultural practices.

Much of the focus on increasing yield in agriculture has been via improvement to the varieties and cultivars of crops grown. Producing crops resistant to diseases or pests, or resistant to herbicides so weeds can be better controlled, has led to significant yield improvements. While new areas of technology application in plant improvement (such as gene editing and plant metabolic engineering discussed in the previous section) will remain a focus for seed companies and plant researchers, there is also a second important area of technology that is increasingly being brought to bear with the joint goals of enhancing yield and more efficiently using scarce inputs to agricultural production – precision agriculture technology.

Precision agriculture is primarily, but not exclusively, an agricultural engineering-based approach to improving yield that focuses on the fact that conditions in the field are not spatially uniform – and, therefore, a one-size-fits-all approach to fertilization, pesticide application, irrigation etc. is inefficient. In crop agriculture, precision agriculture systems use highly precise global positioning systems in concert with advanced sensors, and data analysis technologies to provide the tools and information farmers need to optimize and customize the timing, amount, and placement of seed, fertilizer, pesticides, irrigation, and other inputs – all towards the goal of producing maximum yield at the lowest cost. As noted by TEConomy in a report for AgriNovus in Indiana:

"Digital Agriculture"

An alternative title for this platform, suggested in a focus group work session at ISU comprising both university and industry representatives, is "DIGITAL AGRICULTURE". This recognizes the centrality of data collection and data analytics to realizing the promise of precision agriculture and overall improvement in agricultural production systems.

> *Precision agriculture is the next evolution in production systems, embracing an emerging set of technologies in sensing and data analytics to gather, track, and analyze agricultural data, usually in conjunction with other systems such as harvesting, planting, or field-inputs application machinery. Integrating multiple hardware and software technologies, precision agriculture includes not only traditional agricultural equipment manufacturers, but also includes companies engaged in information- or computer-oriented technologies, including agricultural decision support software, sensors and monitoring systems, GPS and mapping systems, predictive modeling technologies, and unmanned aerial surveillance (UAS) and imaging technologies.*

Precision agriculture for crop production promises to provide a multifaceted set of benefits:

- Improved yield through providing plants with "prescription" doses of nutrients, crop protection chemicals, water, etc. on an as-needed basis
- Reduced input costs, through using only the amount of inputs required in precise doses.
- Reduced run-off of agricultural chemicals.

Several different types of technologies are converging to realize the full promise of precision crop agriculture:

- Real-time sensing technologies providing rapid sensing of field conditions (such as soil moisture content, soil chemistry, etc.), physiological condition of crops and individual plants, and the presence of emergent weeds, pathogens, or other pests.
- High precision location-fixing technologies using GPS and correctional augmentation technologies such as Wide Area Augmentation System (WAAS) technology and Real Time Kinematic (RTK) technology. Combined with mapping software and tied into steering systems, this technology can guide equipment and the application of agricultural inputs down to the centimeter level of precision.
- Data analytics using data analysis and statistical algorithms and AI decision support software to guide precision actions in real-time. Plus wireless technologies connecting agricultural equipment to online/cloud decision support systems, specialist analytical services, weather data, etc.
- Variable rate application systems. Current applicators of irrigation water and agricultural inputs such as fertilizer, growth stimulant biologics and crop protection chemicals typically distribute the input at a fixed rate. The real promise of precision agriculture is realized when the technologies noted above are combined with applicators that are able to vary their rate of input application based on sensor-data and decision support software.

Because of the required integration of both cyber and physical systems, advancing the development of precision agriculture technologies is an inherently transdisciplinary endeavor. Developing data capturing hardware, guidance systems, precision metering technology, sensors – together with the software and data management components – requires expertise in mechanical engineering, electrical and electronic engineering, signal processing, software engineering, and information technology, together with a range of agricultural science disciplines (plant science, soil science, agronomy, agricultural economics, animal science, etc.).

As the reference to Animal Science above implies, opportunities for deployment of precision agriculture technologies are not confined to field crops. Precision livestock systems are also a focus of R&D in precision agriculture. The application of technology to precision livestock management presents opportunities across a range of technologies, such as:

- On-animal sensors and monitoring systems recording livestock vitals, health status, location, stress levels, etc.
- Precision feeding systems delivering customized metered rations to individual animals
- Disease and disease vector monitoring and reporting systems
- Environmental monitoring of livestock housing conditions
- Estrous monitoring.

As noted by the National Institute of Food and Agriculture (NIFA):

> *Current technologies allow producers to monitor individual animal feed consumption, feedlot movement, temperature, lameness, milk production, meat composition and quality, and weight gain—often without any human intervention or presence.*[13]

[13] NIFA "Precision Agriculture in Animal Production." https://nifa.usda.gov/precision-agriculture-animal-production

It should also be noted that sensors, data analytics and the types of cyber-physical systems that may be deployed in precision production agriculture also have application in the scientific research and R&D phase of crop development. What started as the development of automated phenotyping using various imaging and other sensing modalities in greenhouse research environments has now started to migrate to the field. Iowa State University has been coordinating research across a range of disciplines, such as agronomy, computer engineering, statistics to develop on-plant sensors, machine vision systems and cyber-physical systems to enable in-the-field phenotyping to occur. Understanding how improved crop varieties and cultivars perform outside of a controlled greenhouse setting is crucial to realizing the true promise of crop improvement efforts and to testing precision agriculture technologies themselves (such as metered doses of irrigation water, fertilizers, pesticides or other inputs). Similarly, precision technologies applied in animal/livestock science can enable enhanced research in livestock breeding, nutrition, animal housing and health.

The development of the precision agriculture sector will engage companies that have been traditionally engaged in agriculture as well as companies that have not. Traditional agricultural equipment manufacturers (such as Deere & Company) are actively engaged in integrating precision technologies into their product lines, but this is also a space attracting the attention and presenting opportunities for:

- Agricultural inputs manufacturers, such as seed and crop chemical agbioscience companies
- Software and information technology companies
- Aerial systems producers
- Companies producing imaging, sensing and precision instrumentation solutions
- Robotics manufacturers.

Despite currently depressed agricultural commodity prices, startup activity and investment in agricultural technology, including precision agriculture technology is growing. AgFunder, an equity crowdfunding site focused on agricultural and food technology, estimates that venture capital (VC) investment in ag tech grew from $0.4 billion in 2010 to $3.2 billion in 2016 (a CAGR of 41.4%). Within the ag tech space, AgFunder notes the following statistics for precision agriculture technologies:

- Farm Management Software, Sensing, and IOT (internet of things): $363 million in 117 deals
- Supply Chain Technologies: $180 million in 69 deals
- Robotics, Mechanization & Other Farm Equipment: $109 million in 19 deals.

The most recent report on the precision farming sector by BCC Research projects very strong growth rates for the sector, summarizes the market as follows:

- The global market for precision farming technologies totaled nearly $3.3 billion in 2016, and should total $5.9 billion in 2021, a five-year compound annual growth rate (CAGR) of 12.4%, through 2021.
- Hardware as a segment totaled $2.1 billion in 2016 and should total nearly $3.6 billion by 2021, a CAGR of 10.8% through 2021.
- Software as a segment totaled $1.1 billion in 2016 and should total $2.3 billion by 2021, a CAGR of 15.2% through 2021.[14]

Representing a fast-growing market, with multiple opportunities open for innovative technologies and integrated technology solutions, the precision agriculture space is clearly attractive as a technology-based economic development target.

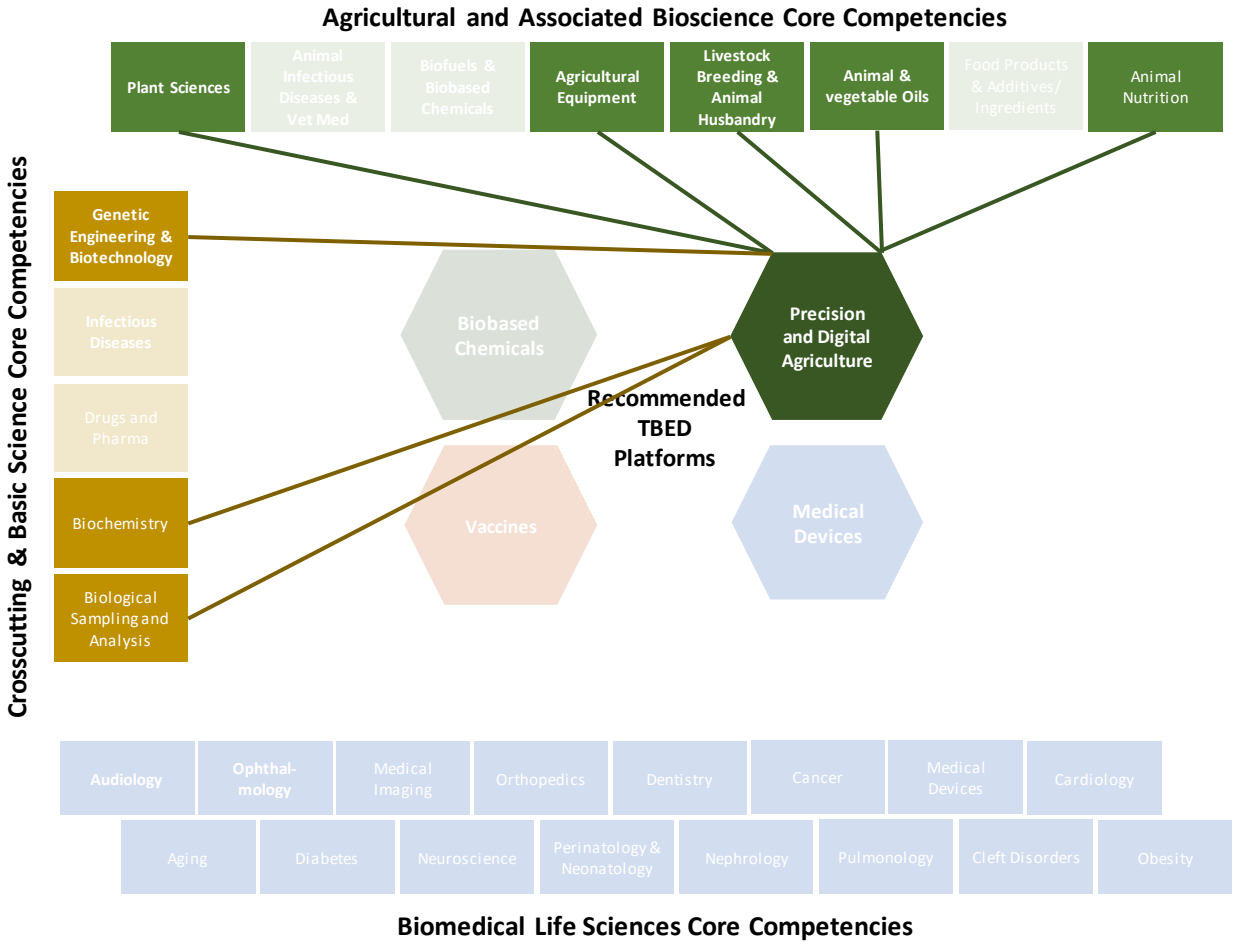
[14] BCC Research. 2017. “Precision Farming Technologies and Global Markets.”

B. Connectivity to Core Competencies

A precision and digital agriculture platform would connect to several identified Iowa core competencies, including particularly those in agricultural engineering, plant sciences, livestock operations, and biological sampling and analysis.

Figure 10 illustrates the connectivity between multiple identified Iowa core competencies and the Precision Agriculture Technologies platform:

Figure 10: Precision and Digital Agriculture Platform – Connectivity to Identified Core Competencies



C. Strengths

Iowa has several strengths it can leverage for precision and digital agriculture platform development and associated economic development. First, Iowa has an existing agricultural machinery cluster engaged in research and commercialization activities, in addition to manufacturing. The top Iowa industry innovators in agricultural machinery, as measured by total number of patents awarded from 2010-2016 include:

- John Deere (285 patents)[15]

[15] Deere & Company has opened a strategic technology office in the Iowa State University Research Park, growing its on-campus presence in recognition of the research, education, and talent development capabilities at Iowa State.

- CNH Industrial (42)
- DuPont (21)
- Kinze (20)
- Vermeer (18)
- Kooima (7)
- Ag Leader Technology (5).

Second, Iowa has significant agricultural and livestock production occurring across the state, together with ISU research stations, which provides opportunities for the pilot testing of new technologies. Iowa farmers and livestock producers represent potential early-stage investors and customers for these technologies.

Third, Iowa State University has the top-ranked graduate agricultural engineering program in the country (ranked #1 by U.S. News & World Report in 2017), and there is strong existing university-industry research collaboration and innovation occurring already.

On the innovation side, there is more early-stage risk capital available in Iowa for agricultural technology startups compared to other sectors like med tech. There is also a new industry-led ag tech accelerator, which has support from DuPont Pioneer, Farmers Mutual Hail Insurance Company, Grinnell Mutual, Kent Corporation, John Deere, Peoples Company, and Sukup Manufacturing. Based in Des Moines, the **Iowa AgriTech Accelerator** is a mentor-led accelerator focused on

A Growing Start-up Culture in Iowa in Precision Ag at ISU

IntelinAir, Inc., located on the ISU Research Par, is an aerial imagery analytics company focused on the agricultural production market, with "a goal to deliver actionable intelligence to help farmers make data-driven decisions to improve operational efficiency, yields, and ultimately their profitability."

Farmers Edge uses proven Variable Rate Technology to power precision agronomy – optimizing inputs and resources and directing their application where they will count most.

Smart Ag, also located at ISU, is developing software and hardware which will enable farms to "use and benefit from internet connected machinery, supervised and fully autonomous equipment, data to machine integration and advanced path planning."

DecisionPx, at the ISU Research Park, develops vision-based phenotyping solutions. Their data analysis pipelines are designed to provide real time data that enable growers to make crop management decisions. DecisionPx also provides image analysis services to assist plant breeders with the development improved crop varieties.

Source: ISU Research Park Directory.

AG LEADER TECHNOLOGY INC.

An Iowa Based Company on the Frontier of Precision Agriculture.

Located in Ames, Ag Leader Technology provides a wide range of precision farming technology solutions. The company sells its products through dealers in the United States, as well as through regional sales representatives in both its home market and Canada. Key products and solutions include:

- Displays: InCommand 1200, InCommand 800, and Compass Display.
- Guidance and steering systems: GPS receiver systems (GPS 6000, GPS 6500, GPS 6500 base station, Relay), SteerCommand, OnTrac3, and L160 Lightbar.
- SeedCommand: Advanced Seed Monitoring, Sectional Control, Hydraulic Down Force, Air Seeder Cart Support, and SureDrive.
- DirectCommand: An application rate control product with features such as total liquid control with variable rate application, chemical injection, AutoSwath; spreader control; strip-till applicator; OptRx Crop Sensors (for measuring crop health and providing application rate recommendations in real

AgTech innovations. These private sector-led activities build upon Iowa's Angel Investor Tax Credit, Iowa's Innovation Funding Programs, Iowa's R&D Tax Credit, and tech transfer and commercialization activities supported by ISU through its tech transfer office, Startup Factory, and Research Park.

It should also be noted that it was hypothesized in a project advisory committee that California is the likely hub for precision agriculture industry growth given its confluence of hardware and software companies, large agricultural sector, and available risk capital. However, a review of the companies listed as active in precision agriculture in the major 2017 market research report produced by BCC Research shows this not to be the case. Indeed, the report profiles 32 U.S. companies active in the precision ag market, with 15 located in midwestern U.S. states (47%). California only listed four, and after the Midwest the largest number were in the southern region of the country, with five.

D. Weaknesses

The two sides of the precision agriculture coin are hardware and software – with both factoring similarly in importance to the cyber-physical systems at the heart of precision agricultural technology. While Iowa State University ranks first in the nation in agricultural engineering, ISU ranks 63rd for computer science and graduated 39 undergraduates and 30 graduate level students in 2015. While these are obviously not the only disciplines relevant to such a transdisciplinary area of technology-development as precision agriculture, they are indicative of the degree of variability across universities of various disciplinary elements that will need to be integrated to advance in cyber-physical systems for precision agriculture.

While companies on the market with technologies and products in precision agriculture are most likely to be based in the Midwest (based on BCC Research) the more active startup markets in agricultural technology, according to AgFunder data, are in California, New York, and Massachusetts – which together accounted for nearly three-quarters of the startups as ranked by venture capital investment in 2016. Illinois though ranked fourth. These are all states (except Massachusetts) that have a strong agricultural industry base coupled with a significant information technology workforce and Top 15 university computer science departments—MIT, Stanford University, and UC Berkeley (tied for 1st), University of Illinois—Urbana-Champagne (5th), Cornell University (6th), California Institute of Technology (11th), UCLA (13th), Columbia University and UC San Diego (tied for 15th).

In Iowa, it will be important for platform development that the comparative strengths of individual contributing disciplines and research fields be evaluated. Weaknesses and gaps must be identified that need further investment in talent and infrastructure to assure balanced transdisciplinary strengths are developed that enable robust cyber-physical systems development.

E. Opportunities

Unlike many other technology sectors, precision agricultural technology is still in the early stages of development with a lot of seed stage deals. AgFunder estimates that **seed stage** deals accounted for 57% of all agricultural technology VC deals in 2016. This is a technology sector that is still quite open for new entrants, and in which Iowa's universities and existing industry base can be leveraged to catalyze more innovation and startup activity. Existing companies can serve as potential advisors, mentors, connectors, investors, customers, and provide a pathway to liquidity exits that remain in Iowa. Iowa's startup ecosystem is already responding to this market opportunity by creating the AgriTech Accelerator and through the launch of seed funds focused on agricultural technology.

TEConomy sees an opportunity to invest today in targeted computer science and associated discipline faculty hires at Iowa State University to expand programming, data analytics, data visualization capabilities and the development of decision support systems. These will enhance university research capacity, precision agriculture technology development, and dovetail with efforts to address the excess

demand for information technology workers in the state. Capabilities in big data analytics will also be highly useful across the other recommended platforms also.

A precision agriculture platform for Iowa presents opportunities for R&D expansion and business development across a broad range of technologies. Examples may include:

- Field-research phenotyping systems for evaluating plant physiology, gene expression and other factors important in plant variety development.
- Sensors for detecting soil conditions and soil chemistry
- Sensors for assessing the physiological and growth status of individual plants, and the presence of pests or disease-causing pathogens.
- Software systems for decision making based on sensor-inputs that also provide positional guidance of equipment and variable rate control of inputs applicators.
- Guidance systems and precision autosteer systems.
- Unmanned aerial and terrestrial remote sensing systems and sensor platforms. Imagery collection from aerial and satellite platforms, including multi-spectral imaging.
- High-precision variable rate agricultural input applicators for seed, crop protection chemicals, biologics, fertilizer, manure spreading, irrigation water, etc.
- Variable rate livestock feeding and watering systems.
- Sensors and systems for monitoring livestock health, stress levels and other factors influencing yield.
- Systems for monitoring and handling waste streams and emissions from livestock operations.
- In-cab/on-equipment control interface and real-time decision support information for operators.
- Cloud and remote services for data storage, current and historic data analytics and decision support, and data sharing.

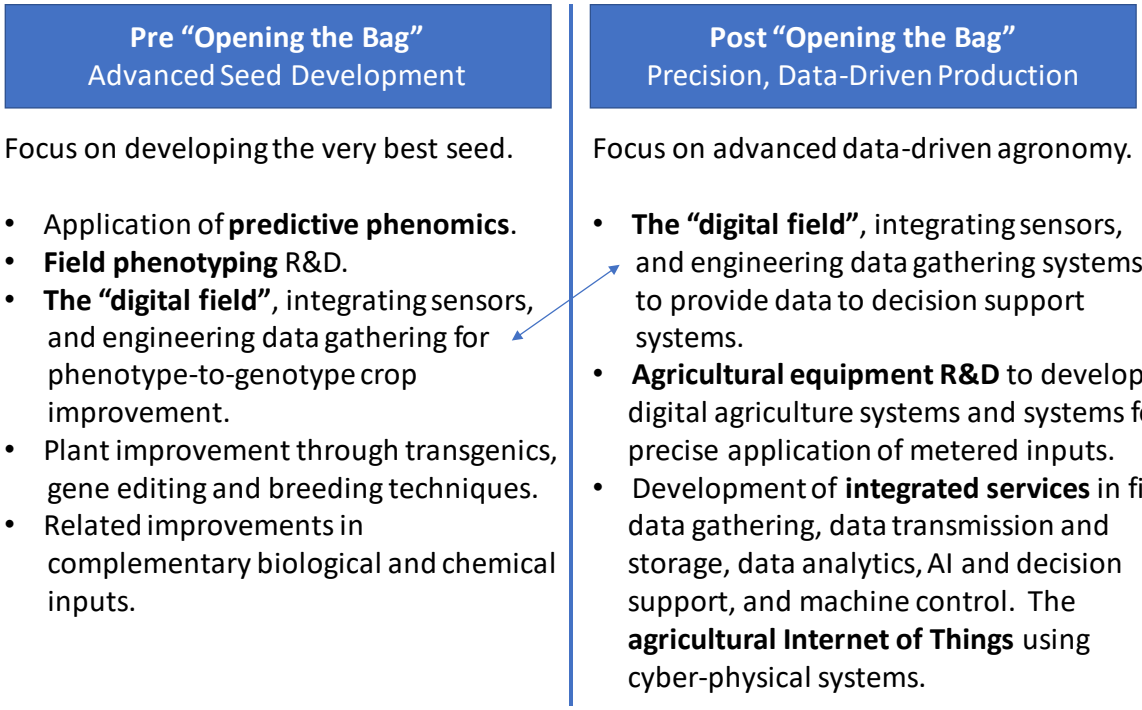
The precision agriculture sector is presenting opportunities for significant start-up business enterprise formation. While still in the relatively early stages of market growth, the opportunity to attract significant private equity capital is being enhanced by the fact that there have already been several significant acquisitions by major corporations of entrepreneurial business ventures. Seeing such "exit liquidity events" occurring in a sector is critically important for building further venture capital and angel investor interest. Some notable examples acquisitions occurring in precision agriculture include:

- AgJunction, Inc. purchased by Hemispheres GPS for more than $10 million.
- Climate Corporation, purchased by Monsanto for $1.1 billion.
- Ezee-On acquired by Buhler Industries.
- Geosys, acquired by Land 'O Lakes.
- Precision Planting Inc., purchased by Monsanto for more than $200 million.
- Rainwave LLC, Hydro-engineering Solutions LLC, Farm Works Software, and Nitech Solutions acquired by Trimble Navigation.
- Ranchview acquired by Raven Industries.
- RDS technologies acquired by Digi-Star LLC.
- Spratronics acquired by Nozzleworks Inc.

In the focus group held with industry and university representatives at Iowa State University participants noted that this platform should be considered a "must do" for Iowa. In particular it was noted that "Digital Agriculture" represents an area where Iowa could have a very real chance to dominate, leveraging the very strong intellectual assets and infrastructure in agricultural engineering, other engineering disciplines, data sciences (including robust capabilities in statistics and I data visualization).

Participants also noted that this "Digital Agriculture" opportunity presents opportunities for Iowa development along two distinct paths which can be termed "pre-" and "post-opening the bag" (Figure 11).

Figure 11: Dual Pathways for Digital Crop Development and Digital Agronomy



A definite recommendation of the focus group was for Iowa to focus on the development of integrated service solutions for digital agriculture – whereby solutions would be offered that integrate field data collection, data transmission and storage services, data analytics and the provision of decision support services based on the data.

F. Threats

As with any fast-growing technology sector, there is a threat of disruptive technology that may negatively impact existing agricultural equipment companies in Iowa if they do not participate and adapt.

Another threat is that the intense cyber-physical systems/internet-of-things aspects of precision agriculture technology and applications development will penalize any state trying to develop in the sector that has insufficient R&D capabilities in information technology, communications systems, data analytics, sensors and instrumentation, and the multiple other specialized areas required to produce integrated precision agricultural systems.

There are also uncertainties for future growth attached to how much precision agriculture will penetrate the market beyond the largest agribusinesses, and whether smaller farmers will be slow to adopt the technologies involved (and possibly reluctant to have precision agriculture companies have access to data about their farms). This is still very much an emerging technology space, and it remains to be seen how new technologies will be absorbed and adopted by the farming communities in each state.

There are also regulatory challenges that may need to be addressed in terms of the use of unmanned aerial systems (drones), health and safety aspects of unmanned terrestrial farming equipment and other factors to be determined.

G. Platform Summary

Table 7: Precision and Digital Agriculture Platform Summary

Status	☐ Emerging R&D (core competency in research only, need to build industry) ■ Emerging R&D Plus (R&D core competency and small base of industry) ☐ Established Growth (R&D and significant base of industry with expansion potential)
Business start-up potential	There could be significant start-up potential. There have been some small start-ups in Iowa in precision agriculture already, and the proximity to major agricultural equipment companies is promising for collaborations.
Business expansion potential	Attraction of venture capital into the agricultural technologies sector is providing early-stage companies with capital access required for growth. Opportunities for acquisitions are also evident, with large companies having the resources to significantly scale-up production from emerging ventures.
Business attraction potential	Organized correctly, and with the right approach to marketing, Iowa's relevant academic R&D strengths and associated workforce education attributes, combined with Iowa's substantial base of advanced manufacturing capability, may be seen as attractive to inward investors.
Academic R&D growth potential	There is a potentially challenging environment for raising funds from traditional federal sources, with federal agencies facing funding cutbacks. However, ISU is ranked first in the nation for agricultural engineering, and has significant strengths in other disciplines, that likely support the development of highly competitive proposals. Industry funding is likely to be attracted to leaders in precision agriculture R&D.
Iowa competitive situation	This is an emerging sector, and no single state has established a robust leadership position. Iowa can be a highly competitive player in this sector if it organizes its assets appropriately and addresses identified weaknesses and gaps.
Key barriers to overcome	• Highly transdisciplinary nature of precision agriculture solutions development may require investment in faculty and infrastructure in identified under-resourced fields. • Applied nature of work in this space may not hold appeal to academics across each of the disciplines required. • Building interest and momentum with faculty to advance innovations along a commercialization pathway. • Distance between the AgriTech Accelerator in Des Moines and the major academic research hub in Ames.

H. Recommendations

As highlighted herein, precision agriculture or "digital agriculture" holds promise for development of a highly diverse range of products, technologies and solutions. Iowa should bring together key stakeholders in this sector to work in collaboration to identify best areas of opportunity rooted in existing and emerging Iowa research community and industry strengths.

Tying precision agriculture R&D to the agricultural profile of Iowa makes sense for enabling the development of innovations that may be tested in the Iowa production environment –whether on the

crop or livestock side of the equation. By directing technology development towards the needs of Iowa production agriculture, R&D activity is more likely to attract investment form commodity groups, cooperatives and other key financial stakeholders within Iowa.

Iowa State University should create an Institute for Digital Agriculture, or similar organization, comprising industry and academic stakeholders. This Institute should represent an umbrella organization for coordinating activities around thematic opportunities, assembling the teams from various disciplines required, providing seed funds for research teams, and developing undergraduate and graduate level curricula for precision agriculture engineering and digital agriculture cyber-physical systems and analytics.

Primary crosscutting recommendations for bioscience cluster development in Iowa are profiled in Chapter IV. Under the recommended new Iowa Bioscience Development Center, it is recommended that each platform has an individual sub-committee focused on platform advancement.

Platform 4: Vaccines and Immunotherapeutics

A. Description

A vaccine is an antigenic biological preparation typically prepared from the causative agent of a disease (the pathogen), or a synthetic substitute, and used to provide immunity against one or several diseases. A vaccine typically works by priming a host's immune system to recognize a disease-causing microorganism. This is done by exposing the subject being vaccinated to a dead or weakened version of the pathogen, its toxins or one of its surface proteins. Vaccines are usually used as a prophylactic agent to prevent or minimize a future infection that may be encountered by the vaccinated human (or animal in the case of veterinary vaccines). There is also work taking place in using vaccines as therapeutics, with most of this work focused particularly in human cancers (e.g. stimulating the immune system to attack cancer cells).

While incredibly effective public health agents, vaccines have tended to be seen by industry as a low profit business with slow growth. The rationale for the industry perspective is grounded in the fact that a person or animal may only need to receive one dose (or very infrequent doses) of a vaccine over a lifetime – and, therefore, will not represent a repeat customer in the same way that a person needing a therapeutic drug for a chronic condition will be. While this later observation still holds true, various factors have led to life sciences companies reconsidering their position on the vaccine business and seeing it as an attractive pathway to revenues. Among these factors are:

- Pressures to significantly reduce the use of antibiotics in livestock (which are associated with the spread of antibiotics resistant organisms) and instead use vaccination approaches to livestock health.
- Global population growth and rising global incomes enabling the purchase and more widespread use of vaccines.
- Increasing awareness of the threats of emerging infectious diseases opening new markets for novel vaccines.
- Rising global incomes increasing demand for animal-based protein, leading to increasing production of livestock needing to be vaccinated (and the short lifespan of livestock leading to more rapid turnover of these vaccine "customers").
- Spending by governments on vaccine R&D and vaccine stocks for biosecurity purposes (pandemic and bioterror preparedness).
- An increasingly global community, with widespread global travel requiring vaccinations of travelers, and increasing the threat of rapid transmission of infectious pathogens.
- Campaigns by governments and global non-profit organizations focused on increasing immunization rates.
- Research uncovering the link between infectious diseases and the later development of cancers and other chronic diseases. For example, the HPV vaccine being deployed as a preventative measure against the development of cervical cancer.
- Potential for therapeutic vaccine development for cancers, allergies and other conditions.
- Improvements in vaccine distribution, storage and delivery technologies (including medical devices).
- Increased spending on animal healthcare, especially in emerging economies, both in companion animals and livestock.

As a result of positive trends, BCC Research notes that vaccines are "now one of the brighter spots for pharmaceutical companies in terms of revenue streams."[16] Generally, BCC considers growth in the industry being especially driven by global population increases and also the acceptance of adult vaccines (as opposed to only childhood vaccinations). For animal vaccines, a key driver is the pressure to reduce use of antibiotics.

> *In developing countries, rapid industrialization of the livestock segment; an impending shift to international best practices; increased realization among progressive farmers about disease management and prevention; and more animal diseases being taken up by federal as well as state governments for mass vaccination programs are amplifying the market for food producing animal vaccines.*
>
> BCC Research

TEConomy sees vaccines as a potential platform for Iowa for several reasons. In particular there is a small, but recently expanding, cluster of vaccine companies in the area around Ames – especially companies focused on the animal vaccine market located in the ISU Research Park or affiliated with it:

- **AeroGenics, LLC** provides gene research for the development of veterinary drugs. The company was founded in 2013 and is based in Story City, Iowa.
- **BioProtection Systems Corporation**, a biotechnology company, develops antiviral vaccines to fight against bio terror agents and infectious diseases. The company was founded in 2005 and is based in Ames, Iowa. BioProtection Systems Corporation operates as a subsidiary of NewLink Genetics, Inc
- **Boehringer Ingelheim Vetmedica, Inc.**, (BIVI) is the fifth largest animal health company in the U.S. and produces innovative vaccine and pharmaceutical products for the prevention and treatment of diseases in the swine, cattle, equine and companion animal markets.
- **Merck Animal Health**, recently acquired Harrisvaccines. It offers a broad portfolio of products to "prevent, treat and control diseases across major farm and companion animal species."
- **NeoVax, Inc.** is an early stage company currently developing a range of novel protein subunit vaccines for use in humans and livestock/poultry against the Clostridial group of bacteria.
- **Pathovacs, Inc.** is developing novel, universal protein subunit vaccines for infectious agents. The company is using a proteome mining platform for protein-antigen discovery called Proteomics-based Expression Library Screening (PELS).

Also of potential relevance to this cluster in Ames are the following local company operations:

- **Clarus Validation Group**, which provides compliance and technical consulting services to companies in the regulated Life Sciences industries (pharmaceutical, biological, medical device, diagnostic and nutraceutical).
- **Hipra Scientific USA, LLC** is a veterinary pharmaceutical company focused on research, production and marketing of products for Animal Health. They are particularly focused in Biologicals.
- I**deopak** provides customized packaging solutions for food and pharmaceutical companies, including contamination detection technologies.
- **Versova Laboratory** provides animal health monitoring and veterinary diagnostic services to the poultry industry.
- **Veterinary Resources** provides contract services to companies doing research and development of biologicals and pharmaceuticals for poultry, swine, and cattle. The company performs studies using disease challenge models to meet USDA, FDA, or ECU regulatory requirements. Veterinary Resources owns and operates 15,000 square feet of infectious disease isolation facilities in

[16] BCC Research. 2017. "Global Markets for Vaccine Technologies."

addition to operating four additional leased livestock facilities near Ames. The company produces high health status swine for its research use and is expanding production to provide sales to other research companies and institutions.

The global animal vaccine market is also gaining in importance. Expanding demand for livestock products and an increase in the trend of pet ownership are the foremost reasons for increasing vaccination in animals. Significant developments in biotechnology, informatics and information system has prompted better planning and execution of animal disease prevention in many countries.

A vaccine company in Iowa City

Close to the University of Iowa, and located on the University of Iowa Research Park is Memcine Pharmaceuticals, Inc. which has vaccine platforms for both infectious diseases and oncology personalized medicine indications.

The global vaccine market has both human and animal market segments. BCC Research's latest report[17] places global revenues for both segments at nearly $33.3 billion in 2016 with strong growth predicted:

- The global market for vaccine technologies reached $33.3 billion in 2016 and should reach $45.2 billion by 2021, growing at a compound annual growth rate (CAGR) of 6.3% from 2016 to 2021.
- Human vaccines as a segment of this market reached $27.2 billion in 2016 and should reach nearly $37.5 billion by 2021, growing at a CAGR of 6.6% from 2016 to 2021.
- **Animal vaccines as a segment of this market reached nearly $6.1 billion in 2016 and should reach $7.7 billion by 2021, growing at a CAGR of 4.9% from 2016 to 2021**.

The animal vaccine market can be further segmented into:

- Vaccines used in food-producing animals, with sales of $3.3 billion in 2014 and $3.5 billion in 2015. This segment is expected to grow at CAGR of 4.9%.
- Vaccines used in companion animals is expected to reach $2.9 billion in 2021, at a five-year CAGR of 5.1%.
- The market for vaccines for other applications (such as for wild rabbits, pigeons and wildlife) stood at $177.2 million in 2014 and is expected to reach $216.3 million by the end of 2016.

It should be noted that members of the focus group for animal vaccines held at Iowa State University noted that they consider the above market projections to significantly underestimate the market size. It was noted that "industry believes the market will be much larger".

As the above data show, **vaccines used in food-producing animals are the market leader in animal vaccines, having a 60% market share** in 2015 versus vaccines in companion animals at a 36.9% market share. Vaccines used for other animals comprise only a small market (3.1%).

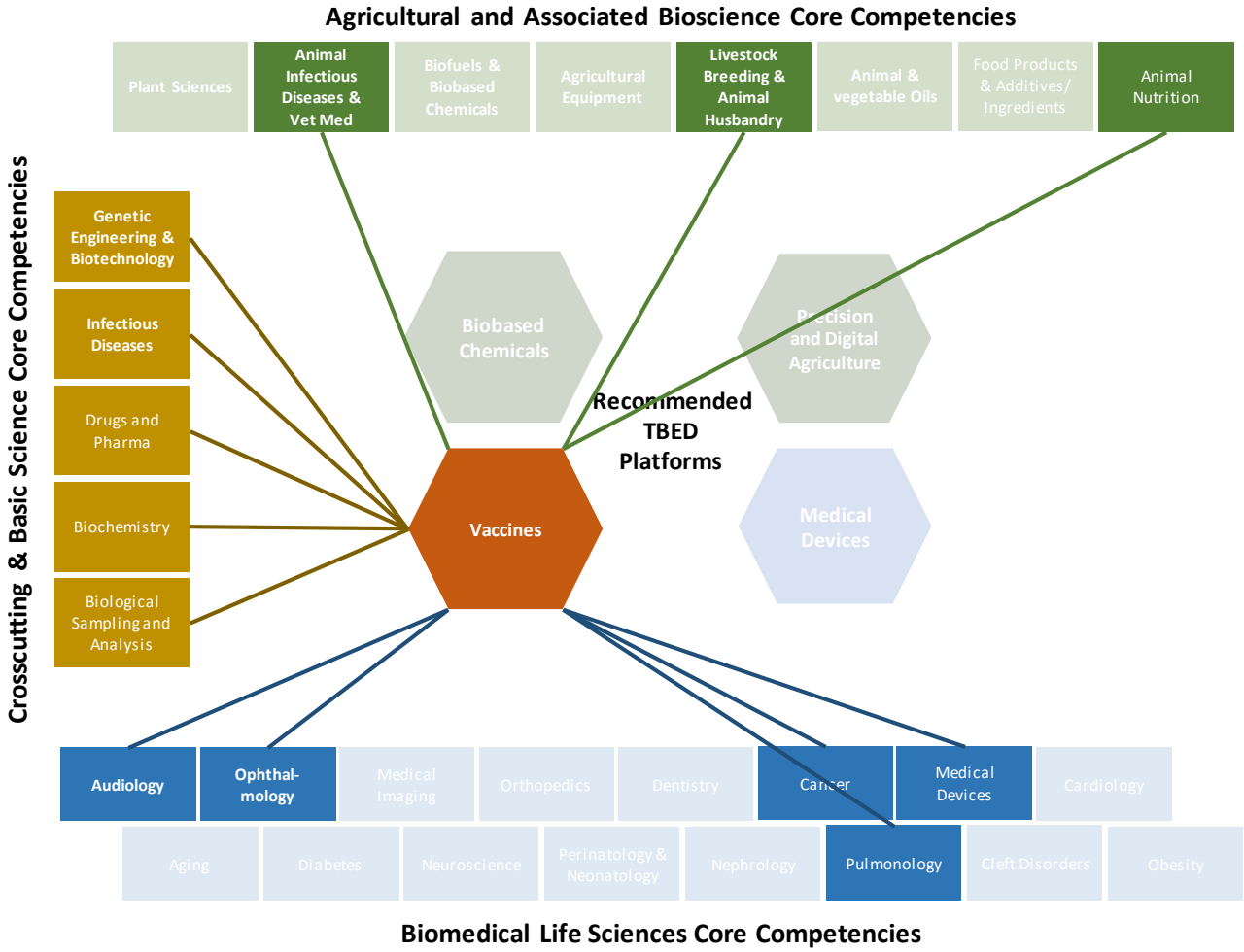
Compared to human vaccines, the development and approval of animal vaccines advances much more rapidly, at three to five years for USDA approval of veterinary vaccine (compared to five to ten years for FDA approval of human vaccines). The primary reason for the time difference is that fewer clinical trials are required for animal vaccines. Concerns over antibiotic use in food animals, and their connection to increasing challenges of antibiotic resistance, are expected to be a significant driver of animal vaccine growth although other factors also come into play. New and emerging diseases and the globalization of the food supply means diseases spread quickly. Global population growth and income growth are driving the global demand for food animals. The bottom line is that animal vaccines, especially for food animals, demonstrates strong prospects for significant ongoing growth.

[17] BCC Research. 2017. "Global Markets for Vaccine Technologies."

B. Connectivity to Iowa Core Competencies

Figure 12 illustrates the connectivity between multiple core competencies and the Vaccines platform:

Figure 12: Vaccines Platform – Connectivity to Identified Core Competencies



C. Strengths

As noted above Iowa has established a notable cluster of animal vaccine companies in Ames and its immediate environs. This cluster includes several early-stage companies but also large market leaders with two out of the nine largest global companies in animal health products (see Table 8) having locations at the Iowa State University Research Park – Merck and Boehringer Ingelheim.

Outside of Ames, there are other significant operations of leading animal health companies in Iowa. Elanco U.S. Inc. (a subsidiary of Eli Lilly and Company headquartered in Indiana), acquired the Fort Dodge operations and manufacturing of Boehringer Ingelheim Vetmedica, Inc.'s (BIVI) U.S. feline, canine and rabies vaccines portfolio. The Fort Dodge facility is a fully integrated manufacturing and R&D site for animal vaccines. Zoetis (headquartered in New Jersey), the largest global company in animal health products, also has a major manufacturing facility for vaccines in Iowa. The Zoetis manufacturing site in Charles City, Iowa, produces vaccines for poultry, swine, equine and canine applications. The Zoetis Charles City facility includes 600,000+ square feet of buildings located on 256 acres and employs over 400 personnel.

Table 8: Global Market Leaders in Animal Health Products – Iowa Presence Highlighted (2014-16) ($ millions)

Company	2014	2015	2016*
Zoetis Inc. (Charles City, IA)	4,785.0	4,765.0	4,740.0
Merck Animal Health (Ames, IA)	**3,454.0**	**3,324.0**	**3,400.0**
Merial SAS (part of Sanofi)**	2,325.1	2,816.8	3,326.4
Bayer Animal Health**	1,476.2	1,668.8	1,868.2
Elanco Animal Health (Fort Dodge, IA)	2,346.0	3,181.0	3,228.8
Boehringer Ingelheim Vetmedica (Ames, IA)**	**1265.6**	**1,526.6**	**1,541.1**
Novartis Animal Health***	1,174.0	-	-
Virbac**	865.9	954.2	952.6
Ceva Santé Animale	857.1	959.2	1,019.2
Others	8,709.7	9,145.2	9,593.3
Total	27,258.6	28,340.8	29,669.6

*Estimated based on half-year financial results.
**Numbers reported in other currencies are converted to USD as per the exchange rate.
***Novartis sold its animal health business to Eli Lilly & Co. in January 2015. Elanco is Eli Lilly's animal health company.
Source: BCC Research

Particularly for R&D activity, Ames is viewed as a prime location. Dr. Albrecht Kissel, president and CEO of Boehringer Ingelheim Vetmedica, emphasized this at the opening of the company's 52,000 square foot, $22 million, R&D Center at the ISU Research Park, saying:

> *We are pleased to continue our relationship with Iowa State University as well as local and state leadership, and to be part of this community, which is considered to be the epicenter for animal health research in the country.*[18]

These operations have their roots in entrepreneurial ventures in Ames. NOBL Laboratories, a vaccine company, was started by Dr. Jan Schuiteman, Dr. Mike Daniel, and Dr. Hank Harris in 2005. The company was acquired by Boehringer Ingelheim Vetmedica in 1997. Dr. Harris also founded Harrisvaccines, based on a novel porcine vaccine, in 2005. Harrisvaccines received early-stage commercialization funding from IEDA, and the company was acquired by Merck Animal Health in 2015 which now conducts both R&D and manufacturing at its Ames facility.

BCC Research reports on the Merck acquisition of Harrisvaccines

In November 2015, Merck Animal Health signed an agreement to acquire Harrisvaccines, a privately-held company that develops, manufactures and sells vaccines for food production and companion animals. Harrisvaccines has a unique RNA particle technology for vaccine development. The company holds a highly versatile production platform that is able to target a wide range of viruses and bacteria. RNA particle technology involves the collection of pathogens from a farm and specific genes are sequenced and inserted into RNA particles to make safe and potent vaccines for herd-specific protection.

It is also of note that Iowa is a significant producer of pork and dairy and one of the leading egg-producing states—eggs are used in the production of vaccines. Indigenous animal therapeutics and vaccine companies, such as Iowa's Ames Vaccine Company (later part of Fort Dodge Animal Health and

[18] http://www.bi-vetmedica.com/company/company/newsroom/press_releases/boehringer_ingelheimvetmedicaincopensnewrdfacilityinamesiowa.html

now part of Elanco) and Charles City-based Salsbury Laboratories (acquired by Solvay, then Fort Dodge Animal Health, then Pfizer, and most recently, in 2013, by Zoetis) both date back to the 1910s.

In addition to the corporate presence in vaccines and animal health products in Ames and its immediate environs, **there are also notable government and academic capabilities that are complementary.** Chief among these is a **USDA** facilities constellation for APHIS-ARS that includes: the **National Animal Disease Center (NADC); National Veterinary Services Laboratories (NVSL), and the Center for Veterinary Biologics (CVB).** Primarily focused on the health of livestock species used in production agriculture, the USDA Ames facilities are modern (constructed between 2004 and 2009) and comprise:

- Consolidated laboratory and administrative facilities containing over 612,000 square feet of space. Includes labs are: the APHIS Pathobiology Lab; APHIS Diagnostic Bacteriology Lab; BSL-2 and BSL-3 laboratories, and caged animal facility.
- High Containment Large Animal Housing and Training Facility, comprising over 141,000 square feet of space serving ARS and APHIS research areas, including the diagnostics and biologics programs and associated training.
- Low Containment Large Animal Housing facility, providing housing for animals infected with BSL-2 or lower-level organisms.

A key competitiveness factor that reinforces the animal vaccine industry base in Iowa is the location of the USDA's veterinary vaccines regulatory body in Ames. This is the Center for Veterinary Biologics within USDA's Animal and Plant Health Inspection Services. The USDA National Animal Disease Center and National Surveillance Organization are also located in Ames. According to one animal health company with a vaccine manufacturing facility in Iowa, the company submits approvals to the USDA Center for Veterinary Biologics multiple times a week. The ability to develop good personal relationships and trust with USDA regulatory staff through face-to-face interactions is important. All the major animal health companies are members of the Animal Health Institute, which collectively meet with the USDA in Ames to work on regulatory issues.

As would be expected given the co-location in Ames, the USDA operations in Ames have collaborations with ISU, with the following projects:

- Evaluating the Epidemiology, Ecology, and Biology of Swine Viral Pathogens
- Investigate the Pathogenesis and Biology of Emerging and Re-Emerging Swine Viral Diseases
- Nanoparticle Microarray for High-throughput Chemical Phenotyping of Microbiomes
- Diversity of Antibiotic Resistance Genes and Transfer Elements Quantitative Monitoring for Environmental Samples.

The USDA operations are performing both basic and applied research in animal health, and relevant to vaccines, examining subjects such as:

- Disease mechanisms and pathogenesis
- Characterization of antigens, host immunity and virulence markers
- Disease intervention and control strategies
- Novel approaches to vaccination
- Exposure and methods of infection.

ISU has a number of strengths that contribute to the vaccines cluster – ranging from fundamental microbiological research through to applied veterinary sciences. Training of graduate students is particularly notable in terms of the Interdepartmental Microbiology (IM) Graduate Program which offers both M.S. and Ph. D. degrees in all aspects of prokaryotic and eukaryotic microbiology. Multiple ISU departments, and affiliated national laboratories in Ames, participate, bringing together faculty with expertise in biochemistry, ecology, genetics and molecular biology, biogeochemistry, biorenewables, food safety and security, veterinary microbiology, medical microbiology, plant pathology, virology, entomology, immunology, parasitology, mycology, and microbial genomics, among others. There is also an Immunobiology Interdepartmental Program.

The ISU College of Veterinary Medicine's Department of Veterinary Microbiology and Preventive Medicine is also a key asset. The Department notes that its:

> *Faculty promote the understanding of causes of infectious disease in animals and the mechanisms by which diseases develop at the organismal, cellular and molecular levels. Veterinary microbiology also includes research on the interaction of pathogenic and symbiotic microbes with their hosts and the host response to infection.*[19]

The College and Department specifically call-out the close relationship with the USDA NADC, noting that:

> *Unique to Iowa State is our proximity to the USDA animal health centers located in Ames. This provides outstanding opportunities for our faculty and graduate students to collaborate with USDA researchers to develop new vaccines and improved diagnostics*.[20]

Iowa State University has been a significant contributor to the establishment and growth of this sector in Iowa, with both its College of Veterinary Medicine and also its biological engineering program. Many of Iowa's animal vaccine companies with R&D portfolios and on-going R&D activities were either founded by, or have senior management who received a doctorate of veterinary medicine from, ISU—e.g., Dr. Jan Schuiteman (co-founded NOBL Laboratories), Dr. Hank Harris (co-founded NOBL Laboratories and founded Harrisvaccines, now Merck Animal Health), and Dr. Michael Roof (NOBL Laboratories, now Zoetis; developed salmonella vaccine at ISU that was licensed to NOBL). U.S. News & World Report ranked ISU's graduate veterinary medicine program 13th nationally in 2015.

From a research, tech transfer, and workforce perspective, ISU is an important pillar of the animal vaccine cluster in Iowa. ISU is one of Boehringer Ingelheim Vetmedica's three global strategic university partners, and the company targeted Ames for the location of its animal vaccine R&D, with approximately 65 employees located at its new $22 million R&D facility at the ISU Research Park. This is in spite of the fact that BIVI was headquartered in St. Joseph, Missouri—now Atlanta, GA, with its acquisition of Sanofi. BIVI has found ISU to be a very good and collaborative partner and source of talent.

ISU is also the leader in the emerging field of nanovaccine R&D. Centered within the Nanovaccine Initiative, ISU is leading a multi-disciplinary and multi-institutional team of 51 university, medical school, research hospital, national laboratory and industry researchers to design nanovaccines targeting diseases such as tuberculosis, malaria, biodefense pathogens and cancer. The leader of the Initiative, ISU Professor Balaji Narasimhan, notes that "this is truly one of the dream teams working on vaccine research anywhere in the world,"[21] Nanovaccines represent a novel approach to vaccine

[19] https://www.vetmed.iastate.edu/vmpm/about/about-department
[20] Ibid
[21] https://www.nanovaccine.iastate.edu/about/

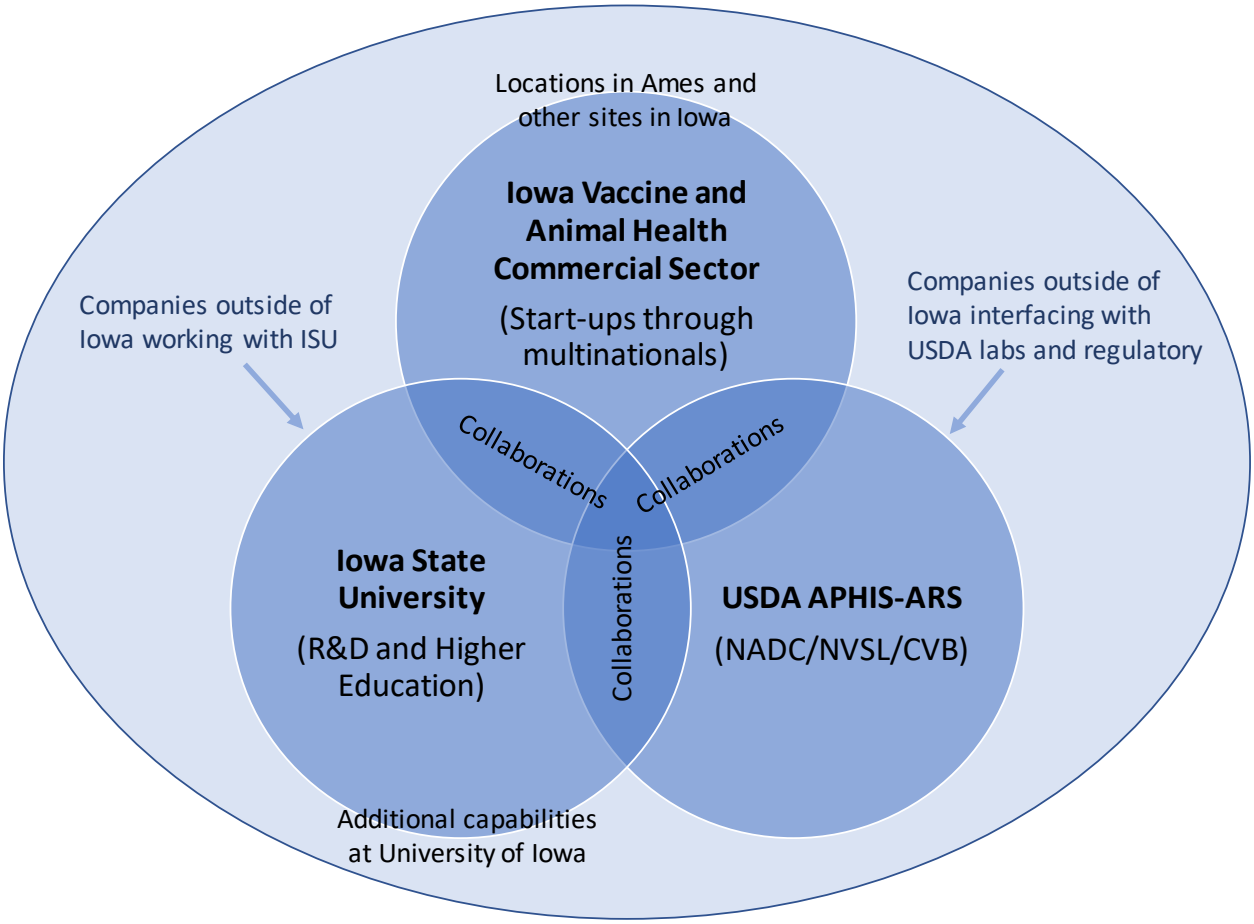
function which, unlike current vaccines, use nanoparticles which send "pathogen-like" signals to stimulate the immune system.

Other strengths noted at the focus group held at ISU include:

- Capability at ISU to study diseases across multiple animal models, and to test at scale across a large number of animals of the species of interest.
- Presence of BSL-3 facilities in Ames and personnel well-skilled in biosafety procedures and associated research activities.
- The Center for Public Health and Food Safety at ISU.

As illustrated on Figure 13, the triangulation of three core assets (vaccine and animal health companies, USDA animal disease labs, and Iowa State University with basic sciences, veterinary medicine and novel R&D approaches) provides the Ames region, and the State of Iowa, with a signature base of science and technology capacity around which to further build a cluster of R&D and production economic activity. Ames also represents a location that attracts companies, vaccine researchers and other relevant parties from outside of the state to interface with ISU, and all companies in the sector nationwide are engaged with the USDA operations. As noted in the sidebar on Page 57, all of the major animal health companies are members of the Animal Health Institute, which collectively meet with the USDA in Ames to work on regulatory issues. Because of the assets in Iowa it was noted in the focus group at ISU that "everyone in animal health globally knows Ames Iowa" and the veterinary biologics program in particular is attracting participants to come to Iowa for multiple events and training programs.

Figure 13: The Ecosystem for Animal Health and Vaccines in Ames and Iowa



It should also be noted that in addition to ISU research and education benefits, companies also recruit from the University of Iowa's biology program, and the Director of the UI Pharmaceuticals facility stated in an interview with TEConomy that some of its customers include Iowa animal health companies. For vaccine manufacturing facilities, animal health companies also recruit from a larger pool of Iowa colleges outside of UI and ISU, as well as community colleges.

Iowa's Research Activities Tax credit is also a notable strength, used by animal health companies that are working to commercialize new vaccines. As one company representative noted, the Research Activities Tax Credit and IEDA's jobs training programs are important tie-breakers when companies are comparing competing state offers. IEDA's Proof of Commercial Relevance and Demonstration Funds have also been critical sources of early-stage capital for startup vaccine companies, such as Harrisvaccines (now Merck Animal Health).

D. Weaknesses

While Boehringer Ingelheim Vetmedica, Merck Animal Health, Zoetis, and Elanco each have locations in in Iowa, principally through the acquisition of Iowa animal vaccine companies, the headquarters of these companies and their core R&D facilities are located outside of Iowa. The main exception is Boehringer Ingelheim Vetmedica's R&D facility at the ISU Research Park. The location of the headquarters and main R&D facilities of major animal health companies are:

- Zoetis: U.S. headquarters in in Parsippany, New Jersey and global R&D in Kalamazoo, MI; U.S. R&D teams in Iowa, Maryland, Nebraska and North Carolina
- Boehringer Ingelheim Vetmedica: U.S. corporate headquarters in Duluth, Georgia (near Atlanta) and U.S. R&D in Ames, Iowa
- Elanco: global headquarters in Greenfield, Indiana (near Indianapolis) and Vaccine Innovation Center also in Greenfield, Indiana;
- Merck Animal Health: headquarters in Madison, NJ and R&D in Nebraska, Kansas and Iowa.

An additional weakness is that despite the continued growth of the animal health and vaccine market, none of the animal health companies, trade associations, chamber of commerce, or other industry representatives interviewed by TEConomy for this project were able to suggest a particular path forward to greatly expand animal vaccine activity in the state. In addition to an opinion that there are no clear emerging opportunities, these companies may perhaps be waiting for the dust to settle following all the recent acquisition and divestiture activity across the state.

Perhaps the most notable weakness observed is a lack of communication and coordination across the sector in Ames or, more broadly, within Iowa. Figure 11 illustrates the significant and unique triangulation of assets that the Ames region has, yet without coordination and communication between these assets, the real potential for cluster-based economic development around animal vaccines and associated health products will not be realized.

It was noted that there are some gaps in research capabilities at ISU, with more expertise needed in innate immunity and associated genetic factors, systems biology, and a larger cluster of expertise required generally in immunology (especially in viral immunology).

E. Opportunities

A clear opportunity for the sector overall is presented by the pressure being placed on food animal operations to reduce the prophylactic use of antibiotics in animal production systems. Well-founded concerns regarding overuse of antibiotics contributing to more rapid emergence of antibiotic-resistant

pathogens is behind a robust imperative to find alternatives – with vaccines being the leading candidate technology to supplant antibiotics where feasible.

In recent years, the emergence of multiple viral and bacterial animal infections has posed a direct threat to production agriculture. In some cases, these have included zoonotic diseases with the potential to transfer from animals to humans, or vice versa. The ongoing an emerging nature of livestock infectious diseases creates an expanding need and opportunity for vaccines and other animal health products (including diagnostics and therapeutics). As BCC Research notes:

- *Viral, bacterial and parasitic infections such as avian flu, rabies, zoonotic infections (anthrax), bovine respiratory syncytial viral disease (BRSV), porcine circovirus type 2 (PCV2), West Nile virus (WNV), vibriosis, myxomatosis and many other animal diseases have created opportunities for animal vaccine manufacturers to develop innovative animal products.*[22]

In addition to vaccines developed from existing program foci in Iowa, some new, or developing areas in vaccines might also hold promise for potential Iowa research and development, including for example:

- Marker vaccines that allow differentiation of infected from vaccinated animals (known by the acronym DIVA). The market here is expected to be for use in regions considered to be free from a disease, but risks of one emerging, and in locations which may only have limited outbreaks.
- Potentially connecting the Medical Device Platform, because the development of advanced vaccine delivery systems is also an expanding area in the vaccines market. Traditionally, vaccines are administered intramuscularly with a needle and syringe but alternative options are in development (such as dermal patches, edible tablets, or addition of vaccines into livestock feed).
- Vaccines for aquatic species. The increasing market for aquatic food-animals, produced in confined systems via aquaculture, presents a large and expanding market for vaccines but a technological challenge, since it is not practical to use injections.

And, as noted previously, Iowa State University has a leading-edge position in the emerging technology of nanovaccines. A key potential advantage of nanovaccine technology lies in an ability to produce vaccines that would avoid the cost and logistical complexity of requiring cold storage and transportation. Thermally stable vaccines would have substantial market value.

The development of the cluster in animal vaccines offers a potential near-term path to technology-based economic growth in Iowa. This is largely because:

- There are considerably less clinical trials required for animal health products and the trials are conducted on the animals for which the product is being produced (as opposed to a model system).
- Adoption of vaccines into livestock and other animal markets does not face the "anti-vax" resistance that is present in human vaccines.
- The rapid turnover, especially of livestock, in terms of life-span assures a rapid replenishing of the customer base.
- Vaccines are the best solution to reducing antibiotic use in food animal production systems.

Currently, vaccines constitute approximately 21% of the overall global animal health market.

Given similar markets, there may be potential, in the medium to long-term, to build on the animal vaccines base in Iowa into other animal health products such as novel antibiotics, parasiticides and medicinal feed additives.

[22] BCC Research. 2017. "Global Markets for Vaccine Technologies."

Iowa's trifecta of existing industry base, USDA regulatory and research activity, and university research, higher education and tech transfer activity help position Iowa very well for growth in the animal vaccine area.

As the cluster builds in Iowa longer-term opportunities may be presented for expansion beyond vaccines into other related areas in animal health including: anti-infectives; diagnostics; biopharmaceuticals, and animal disease monitoring and surveillance systems.

At the focus group held at ISU it was put forward that there is a need and opportunity for ISU to establish a transdisciplinary animal health research and education building perhaps at the ISU Research Park. It was proposed that such a building could contain the Iowa State University Nanovaccine Initiative, together with other R&D, education and event programs that would help support collaborations across key stakeholders. It was also noted that the ISU Research Park would also benefit from having a multi-tenant building focused around nurturing new ventures in vaccines and animal health products.

F. Threats

One of the key challenges for further development of the vaccine cluster in Iowa, particularly any development on the human vaccine front, is the length of time required to go through the discovery, development, trials and regulatory approval process to bring a vaccine to market. Just as with medical devices and pharmaceuticals, the process of building a platform in vaccines takes patience and a willingness to commit to platform development over the long-haul. Animal vaccines may be developed and commercialized on a shorter-timeline than human vaccines, but they still require a relatively lengthy development and regulatory review process compared to many other areas of technology development. As BCC Research notes in relation to human vaccines:

> *Development of a vaccine is not only time consuming and expensive, but this complex process requires scientific expertise. Once a new vaccine is developed, it undergoes animal testing that does not necessarily reflect human immunity. It can take decades from the start of vaccine development to final FDA approval; at huge cost. Products developed by pharmaceutical companies and research institutes undergo comprehensive analysis prior to receiving regulatory approval. Vaccine development differs from the development of conventional drugs as these are intended for use in healthy people to prevent diseases. A higher number of subjects is required for vaccine clinical trials than for traditional drug trials. Before regulatory approval is granted, a vaccine undergoes a long and rigorous process of research, followed by many years of testing. On average, the period for vaccine development can last 12 to 15 years and involves various phases of clinical trials, namely preclinical, phase I, II, III and phase IV or pharmacovigilance.*[23]

As noted above, the pathway for animal vaccines is less time consuming versus human vaccines.

Growth in the animal vaccine and biologics market is driven by the consumption of livestock animals, which in turn is driven by population growth and rising incomes. Growth in U.S. exports of beef and pork, through free trade deals and other mechanism, also increases domestic production of livestock animals and the vaccines and therapeutics that keep them healthy. One recent blow to the U.S. beef and pork industry was the current administration's decision to pull out of the Trans-Pacific Partnership regional free trade agreement. Under this agreement, Japanese tariffs on U.S. exports of beef and pork would have fallen from the existing 38.5% to 9% over the next 15 years.

[23] Ibid

The current consolidation of the animal health sector, through merger and acquisition, joint venture, and divestiture, also have the potential for negative impacts. When acquisitions occur, it is always possible that the acquired company location may be closed and the production or other activities incorporated into existing facilities of the acquiring company.

Other risk factors include on-going state budget shortfalls and continued cuts to Iowa's major research universities. Year-on-year cuts to universities can signal a pull-back in commitment to academic excellence—especially research and tech transfer activities—and can cause mid-level and senior faculty to move to parts of the country that are providing more academic research support.

Similarly, state legislative cuts to Iowa's Research Activities Tax Credit and early-stage capital for startup vaccine companies would also weaken Iowa's competitive position in the animal health sector vis-à-vis competitors.

Another threat is that "animal health" and/or vaccines as economic development clusters are also a focus for other regions of the country. Two key regions seeking to focus and cement their assets in animal health and vaccines include:

- **Kansas City region**. The Kansas City Animal Health Corridor, anchored by Manhattan, Kansas, and Columbia, Missouri, is home to more than 300 animal health companies, representing the largest concentration in the world. The Corridor organization claims that companies with a strategic location in the KC Animal Health Corridor now represent 56 percent of total worldwide animal health, diagnostics and pet food sales.
- **The Research Triangle** region of North Carolina, where the Biological Agents and Infectious Diseases Cluster has seen vaccine makers Novartis and Medicago and public health research and consulting company SciMetrika lead investments which contributed $1.1 billion and nearly 600 jobs over just two years. The North Carolina Biotechnology Center is well funded by the State, and has been a leading convener of focused bioscience-based economic development programs, supports and investments.

At the ISU focus group, it was also noted that Texas A&M represents an additional competitor, with the university having established good infrastructure and collaborative work with the University of Texas Medical Branch in Galveston. Lincoln Nebraska was also noted as being "Ames light" in terms of potential in the sector.

G. Platform Summary

Table 9: Vaccines Platform Summary

Status	☐ Emerging R&D (core competency in research only, need to build industry) ☐ Emerging R&D Plus (R&D core competency and small base of industry) ■ Established Growth (R&D and significant base of industry with expansion potential)
Business start-up potential	Evidence shows that Iowa-based R&D can lead to the development of successful start-up companies in animal vaccines. With a cluster of companies in and around Ames, other vaccine companies within the state, together with USDA and ISU related-core competencies, there should be a conducive environment for innovation and commercialization. However, this optimism is tempered by interviews with sector representatives who have been unable to identify specific pathways forward.

Business expansion potential	Potentially strong, given positive factors influencing market growth for animal vaccines and the cluster of related companies formed in and around Ames, and more broadly across Iowa.
Business attraction potential	Potentially strong environment for business attraction given significant cluster of Iowa assets, especially in Ames.
Academic R&D growth potential	Challenging environment for raising funds from traditional federal sources, with federal agencies facing funding cutbacks. Potential though for "atypical" federal Homeland Security and defense-related funding applications.
Iowa competitive situation	Iowa is well positioned in terms of having industry, academic and federal government R&D assets co-located in the sector – together with regulatory organizations and vaccine product manufacturing. A key will be moving to the next level by achieving another significant external investment or fast-growing start-up company to sustain growth momentum in the face of competition such as the Kansas City Animal Health Corridor.
Key barriers to overcome	• Building continued interest and momentum with faculty and federal lab personnel to advance innovations along a commercialization pathway. • Early stage capital availability for proof of concept and early-stage business formation and growth. • Development of joint industry-university-USDA research and cluster development collaborations, particularly in Ames.

H. Recommendations

While the assets in Iowa for vaccine development and associated economic development are strong, especially in animal vaccines, the academic, industry and government lab R&D assets and expertise have not naturally coalesced into an organization focused on cluster development. This is needed. Having R&D, manufacturing, regulatory and government affairs, veterinary medicine research and education, and a large livestock industry in Iowa (with much of this co-located in Ames) presents a unique opportunity to come together to develop a vision for the cluster's development. Development of this organization should be the first step in advancing a vision for the cluster, and for providing advisory services into the R&D enterprise to assist in research question development and pre-commercial technology evaluation. Creating a unified voice for the platform comprising industry, academic, government lab and other key stakeholders is a necessary first step in advancing this platform. This organization should be affiliated with the overarching Iowa Bioscience Development Center (see Chapter IV)

It was noted in ISU focus groups that the platform should perhaps be expanded in its nomenclature to include, more broadly, "immunotherapeutics" as a theme (rather than just vaccines). This is a "hot" area of R&D and presents opportunities in immunoadjuvants, immunomodulation, personalized immunotherapeutics and other technologies. Thus, a recommendation was made to name the platform Vaccines and Immunotherapeutics.

IV. Recommended Strategies and Actions to Advance Bioscience-Based Economic Development in Iowa

A. Advancing Iowa Bioscience Development to the Next level

It should be noted that the strategies listed in the Phase I report herein are preliminary and have been modified and detailed more specifically in TEConomy's Phase II report titled:

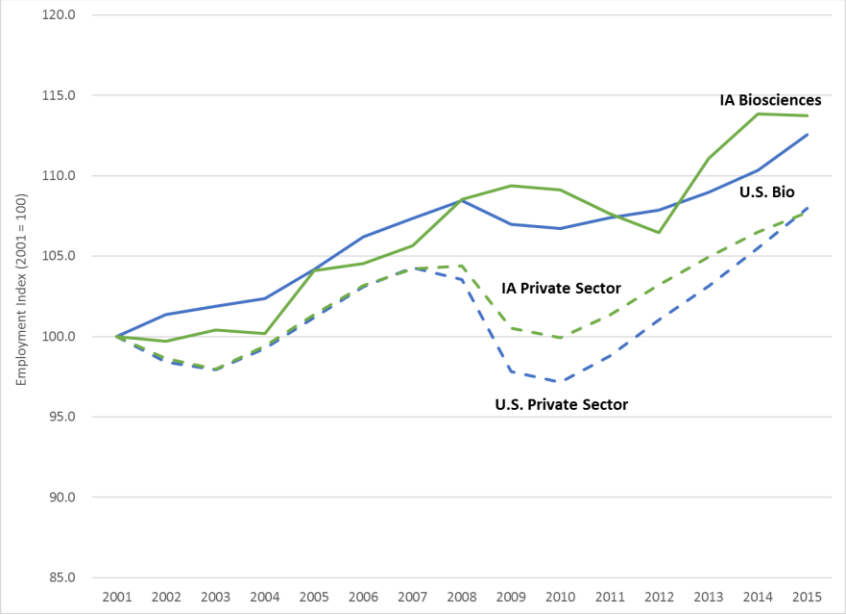
"Phase II Report: Strategies and Actions for Iowa Bioscience Development. Crosscutting and Platform Specific Strategies and Actions."

There should be little doubt, that over the past decade, bioscience and associated sectors of the Iowa economy have made critically important contributions to Iowa's economic growth and societal wellbeing. The most recent report for BIO by TEConomy discusses Iowa's bioscience strengths and performance, noting that:

Iowa's bioscience industry is sizable, specialized and diverse in its employment concentration, and has grown significantly since 2012. The state's bioscience firms employed nearly 25,000 in 2014, up 7 percent over a 2-year period. Iowa is a national leader in the agricultural biosciences where the state accounts for 10 percent of U.S. employment, has a very high and specialized concentration relative to the national average (location quotient is 9.07), and has grown rapidly since 2012 (up 5 percent). Iowa also has a specialized employment concentration in bioscience-related distribution, which has grown by 3 percent since 2012. While employment is relatively modest, Iowa is emerging with strong recent job gains in two areas—medical devices and drugs and pharmaceuticals.

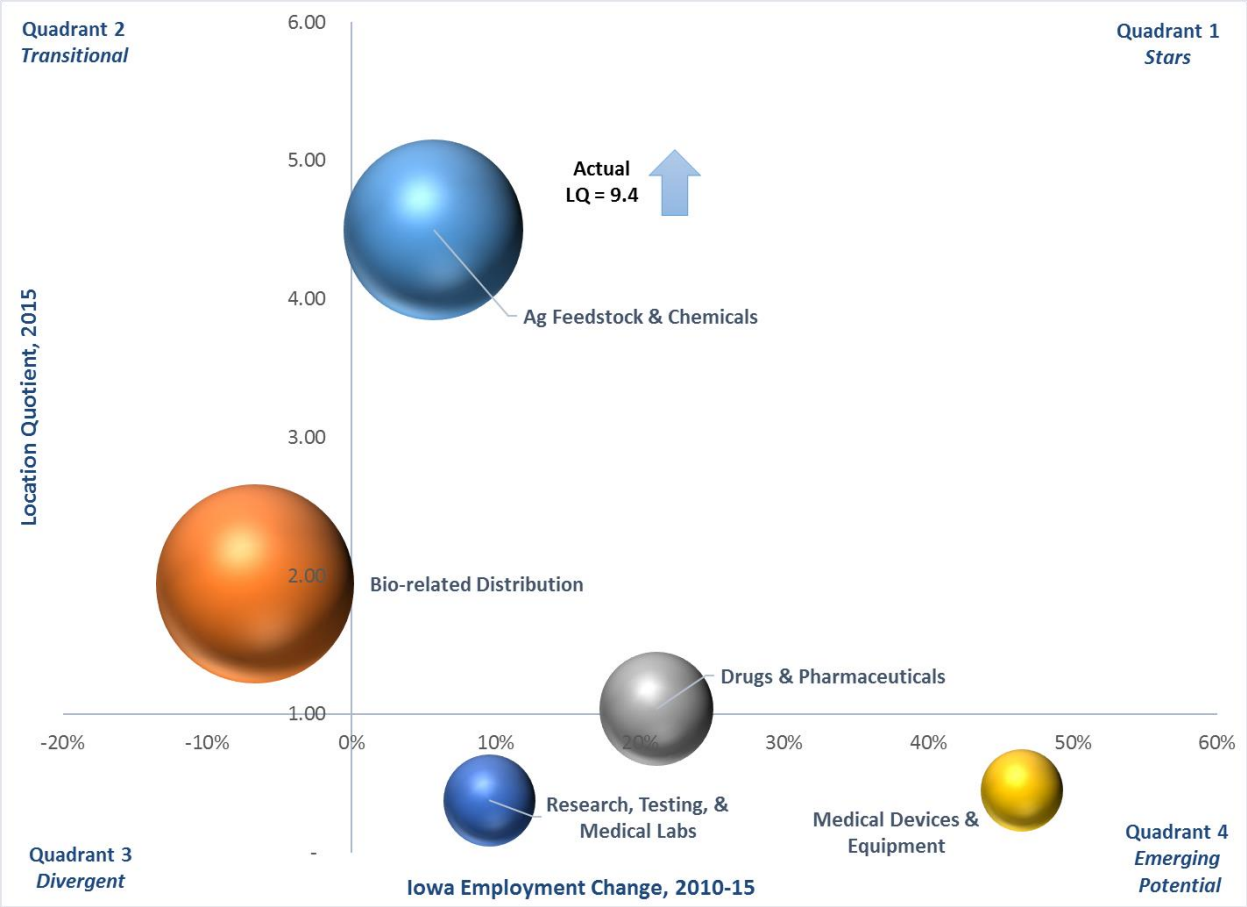
Biosciences have consistently outperformed the overall private sector in Iowa in terms of employment growth rate, and helped bolster Iowa's economy through the great recession. As Figure 14 illustrates, since 2008, Iowa's indexed bioscience growth rate has been higher than that for the nation every year (except in 2012).

Figure 14: Iowa Bioscience and Private Sector Employment Growth Versus the Nation



Iowa's bioscience profile is different to that of the U.S. overall, reflecting a much more intensive focus on agricultural biotechnology and life sciences, and less of an emphasis on job growth in biomedical life sciences. However, recent trends show that, while agricultural biosciences remain a core of overall bioscience activity in Iowa, biomedical sectors are up-and-coming. As illustrated on Figure 15, both the **Medical Devices and Equipment** sector and the **Drugs and Pharmaceuticals** sector have been experiencing quite robust growth in the state, and represent 'Emerging Potential" sectors for the state.

Figure 15: Iowa Bioscience and Private Sector Employment Growth Versus the Nation (Bubble size proportionate to total sector employment in Iowa in 2015)



Source: TEConomy analysis of Bureau of Labor Statistics, QCEW data, enhanced file from IMPLAN.

To-date, Iowa has achieved this relatively robust performance in advancing bioscience-based development despite lacking a truly coordinated approach to sector development. The state has received strategic action plans (from TEConomy's forerunner organization at Battelle), but has lacked the organizational structures to fully implement the strategies and actions recommended, except on an ad hoc basis. Unlike other high-performance states in bioscience development (such as Massachusetts, North Carolina and Indiana), Iowa lacks a well-supported public/private organization dedicated to implementation of a strategic bioscience development implementation plan. In the face of expanding domestic and international competition for technology-based economic development and the high

skill/high wage jobs supported in STEM-related sectors, it is necessary for Iowa to move to a more sophisticated next-level of bioscience development coordination and strategy implementation.

The strategies and actions recommended herein, are built around recognition that both the public and private sectors in Iowa need to advance a new public/private organization dedicated to focused bioscience-based economic development for Iowa. The biosciences present great ongoing opportunities for economic growth in Iowa, but realizing these opportunities in a shifting competitive playing field mandates a new way of operating . Consider for example that:

- Growth in the renewable fuels sector has tapered-off as national commitment to alternative fuels wanes and fossil fuel prices declined.
- Federal investment in scientific and technological research is under threat, and universities are having an increasingly challenging time competing for major grants and funding the early career development of junior faculty.
- Individual U.S. states, including Iowa, are having to make tough budget decisions regarding support for infrastructure, education, health care, social services and business development incentives
- Major international competitors, such as China, India and European nations are increasing their investment in science, and catching-up to, or overtaking, the United States in the innovation stakes.
- Highly skilled talent in scientific and engineering disciplines, trained in U.S. world-class universities, are increasingly being attracted to jobs overseas.

These, and other challenges, mean that ongoing TBED growth is far from assured for U.S. states. The stakes have been raised, and less-organized, ad hoc approaches to R&D, innovation, entrepreneurship, skilled talent development, and related factors will likely place a state at a disadvantage. Based on these trends, and a review of the current status of technology-based economic development and supporting organizations in Iowa, TEConomy recommends that Iowa adopt a more aggressive, formalized approach to organizing for life sciences development. The strategies and actions recommended herein are rooted in this conclusion.

B. Organizing Iowa Bioscience-Based Economic Development

At the present time, Iowa has multiple organizations who conduct work that either directly or indirectly impacts bioscience-based state development (Table 10). This includes: organizations operating statewide in support of general and technology-based economic development; organizations specifically focused on bioscience sectors, and activities within the Regent's universities.

Table 10: Major Organizations in Iowa Effecting Bioscience Development General Economic Development and Technology-Based Economic Development

Organization	Focus	Organization Type
Iowa Economic Development Authority	Statewide economic development, including TBED as a component	State government authority. Reports to the Governor.
Iowa Innovation Corporation	Innovation-based economic development	Public/private, with primary financial support via contract with IEDA
Iowa Innovation Council	Advice to Governor and senior administration in Iowa regarding economic development and innovation	Advisory council
VentureNet Iowa LLC	Entrepreneurial business development	Private corporation

Organization	Focus	Organization Type
Cultivation Corridor	Agricultural bioscience and ag tech investment attraction and promotion	Non-profit
Iowa Biotechnology Association	Association for companies, institutions and other parties engaged in Iowa biosciences sectors.	Non-profit
Iowa Renewable Fuels Association	Association representing the needs and interests of Iowa's renewable liquid fuels industry	Non-profit

University R&D Advancement and Economic Development

University	Program Name	Focus
Iowa State University	Office of Economic Development and Industry Relations	Streamline industry access to ISU resources and capabilities.
	ISU Research Park	Sites, leased space and business incubation space.
	Center for Industrial Research & Service (CIRAS)	Providing access to ISU expertise and resources to help advance and improve Iowa business performance.
	ISU Pappajohn Center for Entrepreneurship	Entrepreneurship guidance, assistance and resources to support new venture development.
	ISU Startup Factory	52-week intensive education and coaching program for university entrepreneurs.
	Office of Intellectual Property and tech Transfer	Works together with ISURF to identify, protect and develop ISU innovations in the form of intellectual property.
University of Iowa	Office of Research and Economic Development	VP Research office plus economic development function coordination for UI.
	University of Iowa Research Park	Sites, leased space and business incubation space.
	UI Research Foundation	Works to identify, protect and develop UI innovations in the form of intellectual property.
	UIVentures	Entrepreneurship guidance, assistance and resources to support new venture development.
	UI ProtoLabs	Provision and coordination of UI resources for prototyping.

	University of Iowa John Pappajohn Entrepreneurial Center	Entrepreneurship guidance, assistance and resources to support new venture development.
University of Northern Iowa	Business and Community Services	Coordination of UNI economic and community development activities
	The Center for Business Growth and Innovation (CBGI)	Assists small businesses or entrepreneurs with business planning
	UNI John Pappajohn Entrepreneurial Center	Entrepreneurship guidance, assistance and resources to support new venture development for students.
	AdvanceIowa	Business consulting support for mid-size Iowa companies.

In addition to the above, there are multiple regional and local economic development organizations providing services across the state, including groups such as:

- The Greater Des Moines Partnership
- Des Moines Office of Economic Development
- Corporation for Economic Development in Des Moines
- West Des Moines Department of Community and Economic Development
- Cedar Rapids Metro Economic Alliance
- Iowa City Area Development Group
- Ames Economic Development Commission
- Greater Dubuque Development Corporation
- and many others…

It is not unusual for states, and individual regions within states, to have multiple layers of organizations engaging in economic development activities – in fact it is typical. Multiple organizations can provide different services or complementary services, and individual communities, cities and regions provide local-level expertise and focus. **What is problematic, however, is that technology-based economic development (TBED) focusing on defined clusters of economic activity and focused innovation platforms requires a coordinated approach to be taken by key stakeholders and this has been lacking in Iowa.** Even though biosciences is a key growth sector in Iowa, there is no single organization focused on strategic advancement of bioscience development in the state. Parts of this function are distributed across multiple organizations and are uncoordinated against a shared strategy or action plan.

This current situation in Iowa runs counter to best practices in TBED and bioscience development, where major states and regions that have distinct clusters in bioscience, and are seeking to advance them further, have a major dedicated organization (typically public/private organizations) focused on bioscience strategy development, long-term coordination of strategy and action plan implementation, and provision of a unified voice for the sector spanning industry, government, universities and other core stakeholders. Examples of such organizations include:

Table 11: Three States with Focused Bioscience Development Organizations

Organization	Structure and Primary Functions
The Massachusetts Life Sciences Center (MLSC)	MLSC is an investment agency that supports life sciences innovation, education, research & development, and commercialization across the state of Massachusetts. The MLSC is charged with implementing a $1-billion, state-

	funded investment initiative. MLSC claims to offer "the nation's most comprehensive set of incentives and collaborative programs targeted to the life sciences ecosystem." It operates with a staff of 19 and the 2017 State Appropriation is budgeted at $10 million.
North Carolina Biotechnology Center	NCBiotech is a non-profit with headquarters in Research Triangle Park and offices in Asheville, Charlotte, Winston-Salem, Greenville and Wilmington. The North Carolina General Assembly funds the organization. The organization has a multi-faceted mission to connect: company and university researchers; funders to small companies, and job seekers and job providers. NCBiotech provides early stage funding and identifies emerging biotech sectors to make sure North Carolina stakes a leadership position.
BioCrossroads (Indiana)	BioCrossroads is an independent non-profit, funded by philanthropic, corporate, university and other stakeholders in Indiana. It serves the central role in the state in advancing Indiana's signature strengths in the life sciences (in areas such as medical devices, agricultural biotech, etc.) by connecting with corporate, academic and philanthropic partners; facilitating investments in promising start ups and building new enterprises; and educating through conferences, reports and market development knowledge. BioCrossroads has stood-up multiple subsidiary organizations specializing in individual bioscience platforms for the state including, for example: OrthoWorx focused on advancing Indiana's orthopedic device sector, and AgriNovus Indiana focused on advancing the agricultural bioscience sector in Indiana as a nationally recognized leader in the development of new, innovative products and services.

TEConomy has direct experience in performing multiple projects with both NCBiotech and BioCrossroads, and is currently starting a project with the MSLC. Writing in a recent report for the Washington Life Science and Global Health Advisory Council, TEConomy noted the following regarding life science development and the Massachusetts and North Carolina organizations:

"The bar for advancing life sciences and global health innovation and industry development is much higher than for other innovation-led industries. The complexity of translating scientific advances to improve human, animal, and plant health, along with the rigorous regulatory requirements to ensure the efficacy and safety of new life sciences products, results in a lengthy, costly, and uncertain innovation process. These characteristics and challenges to innovation are much different from other technology-based sectors, such as software and applications development, and require committed, long-term partnerships between industry, government, and academia.

To overcome the challenges inherent in these high-risk sectors, other states and regions invest significantly in public-private partnerships. For example, consider the investments of two leading states when it comes to life sciences economic development:

> ***Massachusetts:** In 2008, a $1 billion, 10-year investment in the Massachusetts Life Sciences Initiative was made to advance a comprehensive effort overseen by a new state-sponsored nonprofit known as the Massachusetts Life Sciences Center. Its results are outstanding: 1.4 million square feet of new life sciences facilities, including incubators and accelerators as well as shared-use biomanufacturing facilities; $115 million in tax credits to over 75 companies that have committed to create more than 3,750 jobs; and 1,900 postsecondary interns placed since 2009 at more than 450 life sciences companies from across more than 160 colleges and universities. Across all of the Massachusetts Life Sciences Initiative efforts, it has been reported that $3.4 in additional nonstate funding has been leveraged for every $1 invested.*
>
> ***North Carolina:** In 1984, North Carolina developed a unique model for biotechnology-related economic development, centered on the formation of the North Carolina Biotechnology Center (NCBiotech)—a state-*

funded, private nonprofit organization. Just from its long-term commitment to biotechnology business development targeting emerging new ventures with a range of financing, NCBiotech-funded companies in 2014 employed 2,188 workers (the most recent analysis available), with the total economic impact supporting 8,945 jobs in North Carolina. Annual revenues resulting from the total economic activity of these companies generate more than three times the tax revenue, an estimated $44.9 million in state revenues in 2014, than the state's appropriation for NCBiotech of $13.6 million in 2014."[24]

In comparing Iowa performance against these three competing states with highly focused statewide bioscience development organizations (MA, IN and NC) it can be seen that (when normalized for population size) Iowa is generally underperforming. Iowa is specialized in biosciences, with a location quotient of 1.36, but each of the three benchmark states have higher LQ's, ranging from a high of 1.95 in Massachusetts to a low of 1.46 in North Carolina. Academic R&D in biosciences per capita is stronger In both Massachusetts and North Carolina, than in Iowa, although Indiana's is lower still (and a key component of BioCrossroads strategic work is now focused on increasing the attraction of academic R&D funding to the state). Where Iowa clearly falls short is in attracting crucial venture capital to scale bioscience enterprises. Iowa, at only $2.72 in bioscience VC invested per capita, runs at less than half the VC investment level of Indiana. Compared to Massachusetts and North Carolina in VC funding per capita, Iowa isn't remotely close (with only 0.2% the level of funding per capita that Massachusetts bioscience companies achieve, and only 2.2% compared to North Carolina). In terms of patenting activity in biosciences, Iowa exceeds North Carolina (normalized at a rate per 100,000 population), is less than Indiana and much lower than Massachusetts.

Table 12: Iowa Compared Against Three States with Focused Bioscience Development Organizations

State	Population (2015)	Gross State Product (2014) $ millions	Bioscience Employment (2014)	Bioscience Location Quotient	Academic Bioscience R&D (per capita, 2014)	Bioscience Venture Capital 2012-15 (per capita)	Bioscience and Related Patents 2012-15 (per 100K population)
Massachusetts	6,794,422	$459,937	81,495	1.95	$224	$1,394.63	158.6
Indiana	6,619,680	$317,840	58,461	1.64	$88	$5.97	60.6
North Carolina	10,042,802	$483,126	70,466	1.46	$206	$125.67	30.9
Iowa	**3,123,899**	**$170,613**	**24,762**	**1.36**	**$159**	**$2.72**	**46.8**

TEConomy considers that Table 12 shows that Iowa is "in the hunt" when it comes to biosciences when compared to these three benchmarked states. It is competing in academic bioscience R&D, not far off two out of three benchmarks in location quotient, and has a similar situation in patenting (although Massachusetts is considerably advanced there). Where Iowa clearly falls short, however, is in raising venture capital investments to advance companies forward on a significant growth trajectory. In part, this may reflect Iowa's larger relative concentration in agricultural biosciences (versus human biomedical sciences) and the fact that new ventures in agricultural biosciences have not been a traditional focus of VC (but that situation is changing, particularly in ag tech where VC is becoming more engaged nationally). Iowa's location quotient in the BIO/TEConomy classification focused on agricultural

[24] Mitch Horowitz and Ryan Helwig. 2017. *"Life Science and Global Health Development in Washington State: Future at Risk."* Prepared for the Washington Life Science and Global Health Advisory Council by TEConomy Partners, LLC. February 2017.

biosciences shows Iowa with a 9.07 LQ, compared to Indiana (2.86), North Carolina (1.38) and Massachusetts (0.10).

Examining location quotients across five subsectors of biosciences tracked by BIO/TEConomy (Table 13), the quite different bioscience structure of Iowa is evident – again indicating a quite robust emphasis on the agricultural biosciences, and a higher LQ in the less innovative "bioscience-related distribution" sector.

Table 13: Iowa Bioscience LQ's Compared to Three States with Focused Bioscience Development Organizations

Bioscience Sector	Iowa	Massachusetts	North Carolina	Indiana
Agricultural Feedstock and Chemicals	**9.07**	0.10	1.38	2.86
Bioscience-Related Distribution	**2.05**	0.74	1.05	1.16
Drugs and Pharmaceuticals	0.94	1.35	2.54	**2.76**
Medical Devices and Equipment	0.45	**2.37**	0.84	2.23
Research, Testing and Medical Laboratories	0.37	**3.43**	1.66	0.78
Overall Life Sciences LQ	**1.36**	**1.95**	**1.46**	**1.64**

Among eight midwestern states (comprising Iowa and the seven states surrounding Iowa) Iowa performs quite well – having the 3rd highest location quotient for biosciences (behind Minnesota and Nebraska) and being 1st in terms of academic bioscience R&D expenditures per capita (Table 14). Iowa also performs relatively strongly in patenting per 100,000 population in biosciences (3rd, behind Minnesota and Wisconsin). Again, where Iowa shows weak performance regionally is in bioscience venture capital, where it ranks last (8th) among these states (by a wide margin).

Table 14: Iowa Compared to Seven Surrounding Midwest States

State	Population (2015)	Gross State Product (2014) $ millions	Bioscience Employment (2014)	Bioscience Location Quotient	Academic Bioscience R&D (per capita, 2014)	Bioscience Venture Capital 2012-15 (per capita)	Bioscience and Related Patents 2012-15 (per 100K population)
Minnesota	5,489,514	$316,204	49,658	1.48	$114	$176.90	128.7
Nebraska	1,896,190	$112,159	15,906	1.42	$158	$23.63	26.0
Iowa	**3,123,899**	**$170,613**	**24,762**	**1.36 (3rd)**	**$159 (1st)**	**$2.72 (8th)**	**46.8 (3rd)**
South Dakota	858,469	$45,867	5,787	1.2	$70	$24.35	29.6
Illinois	12,859,995	$745,875	80,965	1.14	$108	$88.57	34.3
Wisconsin	5,771,337	$292,891	31,687	0.94	$154	$31.40	52.2
Kansas	2,911,641	$147,075	14,202	0.89	$108	$40.39	26.1
Missouri	6,083,672	$284,462	26,857	0.84	$139	$57.05	35.7

Iowa has not performed badly in terms of bioscience development, but much of its success has been through biofuels development. Moving to the next level of TBED performance, diversifying bioscience development generally and specific to the four recommended Iowa bioscience platforms, mandates advancing Iowa along the best practice route of standing-up a dedicated bioscience development organization – focused on strategy implementation to leverage Iowa's strengths and address its shortcomings. This conclusion leads to Strategy One:

C. Preliminary Recommendations for Cross-Cutting Strategies

Strategy One: Establish a Public/Private Iowa Bioscience Development Center

Description: Iowa will benefit through establishing an Iowa Bioscience Development Center as a public/private economic development initiative focused on coordinating existing assets and strategy implementation and actions to advance Iowa bioscience platforms and overall sector growth. It is recommended that this bring together existing assets in the Iowa Innovation Corporation and other related entities, rather than being a separate freestanding operation.

With biosciences representing an existing economic strength for the state, together with presenting broad-ranging opportunities for further technology-based economic development growth, this highly specialized sector now deserves and requires standing-up an organizational structure that will assure strategy and action plan implementation occurs in a centrally organized manner. Based on TEConomy's deep experience working with bioscience development programs across the United States, it is recommended that the activity areas of the North Carolina Biotechnology Center be considered as model for organizational activities within Iowa together with BioSTL (in St. Louis).

North Carolina Biotechnology Center

The NC Biotechnology Center is a private, non-profit corporation created by the State in 1984 and supported by the NC General Assembly. The Biotechnology Center's mission is to provide long-term economic and societal benefits to North Carolina by supporting biotechnology research, business development and education statewide. The Biotechnology Center has three core programs:

- Science and Technology Development – targeted at assuring NC sustains and builds leadership positions in academic and industrial R&D in targeted established and emerging biotechnology-fields.
- Business and Technology Development – focused on helping technologies advance towards commercialization from universities, and assisting new and emerging companies advance their promising technologies and business development.
- Education and Training -assuring that NC develops the workforce, research, entrepreneurial and business management talent required to meet the human capital needs of a growing biotech sector.

For 2016 and 2017, the State is providing $13.6 million in annual funding for both fiscal years. The Center's funding is divided into the following classifications:

- $1.86 million for the center's operations.
- $8.83 million for centers of innovation, business and technology development, education and training, and related activities.
- $2.92 million for job creation, including agriculture biotech initiatives, economic and industrial development and related activities.

The Biotechnology Center operates with a staff of 64. It has a 36-member Board of Directors comprising leaders from the NC biotechnology industry, research institutes, universities and colleges, and state government agencies. The Center, recognizing

As envisioned for Iowa, the NC Biotechnology Center operates a series of initiatives focused on advancing not only existing strength platforms, but also emerging strategic technology platforms. The Centers of Innovation grants program directs resources to support emerging platforms in: advanced medical technology; marine biotechnology; nanobiotechnology, and precision health.

In the NC Biotechnology Center model, primary funding comes from the State through a direct appropriation from the NC State Legislature. The dedicated annual funding for the Center, representing supporting continuous operations since 1984, shows a long-term commitment to growing the biotechnology sector in North Carolina – and this commitment has yielded significant dividends:

North Carolina Biotechnology Center

Helping to Achieve Substantial Results Through Biotechnology Growth in NC

- At more than 70,000 industry jobs, North Carolina is among the nation's largest life science industry clusters and the state is highly specialized in its concentration of jobs.
- The life science industry has added nearly 20,000 net new jobs since 2001, increasing its base by 40 percent.
- During this same period, the state's private sector payrolls increased by less than 6 percent. Since 2001, the life sciences have accounted for one in ten net new jobs in North Carolina.
- More recently, the industry has seen strong job growth since 2012, rising 6.6 percent or three times the national growth rate of 2.2 percent.
- North Carolina's life science industry base is diverse. It has much higher levels of employment concentration than the nation, and is in fact specialized in i) drugs and pharmaceuticals, ii) research, testing, and medical labs, and iii) the agricultural biosciences. In addition, its presence in bioscience-related distribution employment also exceeds the national average.
- The jobs generated in the life science industry pay wages nearly double that of the overall private sector in North Carolina. In 2014, the average wage for a life science worker topped $87,000 compared with just over $45,000 for workers across the private sector.
- In North Carolina, average life science industry wages have grown by 13 percent since 2001 in real, inflation adjusted terms. This is twice the real wage growth for the average state private sector worker over this same decade and a half (6 percent).

Source: TEConomy Partners. *"2016 Evidence and Opportunity: Impact of Life Sciences in North Carolina"*. Prepared for the North Carolina Biotechnology Center.

BioSTL is a much more recently established organization, with less track record versus the NC Biotechnology Center. The Vision of BioSTL is:

> *St. Louis will be recognized globally as a leading center for bioscience research and commercialization with a vibrant entrepreneurial start-up community that is a magnet for attracting talented people and enterprises. Success will generate quality jobs for St. Louis in a high-growth industry and will enhance regional prosperity by attracting substantial investment and revenues from outside the region.*

The BioSTL organization represents a recent (2011) reorganization of the previous Coalition for Plant and Life Sciences (established in 2001). The organization was designed to leverage regional strengths in medical and agricultural biosciences coordinating assets including internationally recognized scientific research universities and institutions, including Washington University in St. Louis and Saint Louis University, and multinational corporations such as Monsanto and Sigma-Aldrich. The Coalition for Plant and Life Sciences has played a leadership role in helping to facilitate the development of a bioscience entrepreneurial infrastructure and ecosystem in the region (including new company creation, increasing local venture capital access, establishing science districts with lab facilities, and promoting public policies to support science, entrepreneurship and the growth of the bioscience industry). Evaluation of

the ecosystem in the St. Louis region recently identified that there are still challenges and gaps that need to be addressed. In particular more emphasis was considered to be needed in:

- Increasing the pace of new company formation around competitive strengths
- Strategically growing access to capital
- Improving the ability to attract experienced entrepreneurs and corporate relocations.

It was determined that these enhanced efforts mandated creation of a more formal organization to "coordinate and integrate the elements, set priorities and ensure the St. Louis bioscience community is speaking with a single, coherent voice to the public, policymakers and funders."[25] The restructured organization, BioSTL is designed to focus on the above and build on the momentum created through the past decade of the Coalition for Plant and Life Sciences (see below):

St. Louis Region

2001-2011 Accomplishments of the Coalition for Plant and Life Sciences[26]

The Coalition was founded at the behest of St. Louis' major regional business organizations and has been led since its inception by Dr. William H. Danforth, chancellor emeritus of Washington University in St. Louis and founding chairman of the Donald Danforth Plant Science Center. See the list of regional leaders who make up the Coalition, renamed the BioSTL Coalition in 2011.

Over the past decade much has been accomplished in these and other areas:

- The BioGenerator – The Coalition established the BioGenerator in 2003 to work closely with universities, scientists, entrepreneurs and investors to start new companies. To date, the BioGenerator has created more than 40 new seed and pre-seed stage start-ups, investing more than $5 million in these companies and leveraging $140 million in additional private co-investment.
- Facilities for start-up companies – In 2002, the Coalition established the Center of Research Technology and Entrepreneurial Exchange (Cortex), which has developed two successful buildings and assembled more than 40 acres of urban land for further development. In parallel, Bio-Research & Development Growth (BRDG) Park on the Donald Danforth Plant Science Center campus has developed a successful multi-tenant building for emerging plant science companies.
- Local venture capital – Since 2001, St. Louis has grown to nearly $1 billion in biosciences venture capital under local management. Much of this growth was triggered by three separate commitments of $40 million each from Washington University in St. Louis, the Danforth Foundation and the McDonnell family.
- Businesses and organizations recruited to the region, including start-ups attracted by leveraging our institutional strengths and our start-up support infrastructure, including the BioGenerator.
- Improved university technology transfer.
- Federal support and state tax credits for Cortex, the BioGenerator, and the Center for Emerging Technologies.
- Bioscience state legislation, including establishment of the Life Sciences Research Trust Fund, which has funded nearly $30 million in research capacity projects overall, about $7.7 million of that flowing to St. Louis projects.

[25] http://www.biostl.org/about/history/
[26] Ibid

- Developed and built a statewide coalition to pass MOSIRA (the Missouri Science and Innovation Reinvestment Act), a potentially transformational state program to support industry-building efforts.
- MOBIO – Worked with statewide partners to develop MOBIO – The Missouri Biotechnology Association, which has become a strong statewide advocate for pro-science policies and has helped to develop legislative champions for the biosciences.

BioSTL is now focusing on strategy execution and actions including:

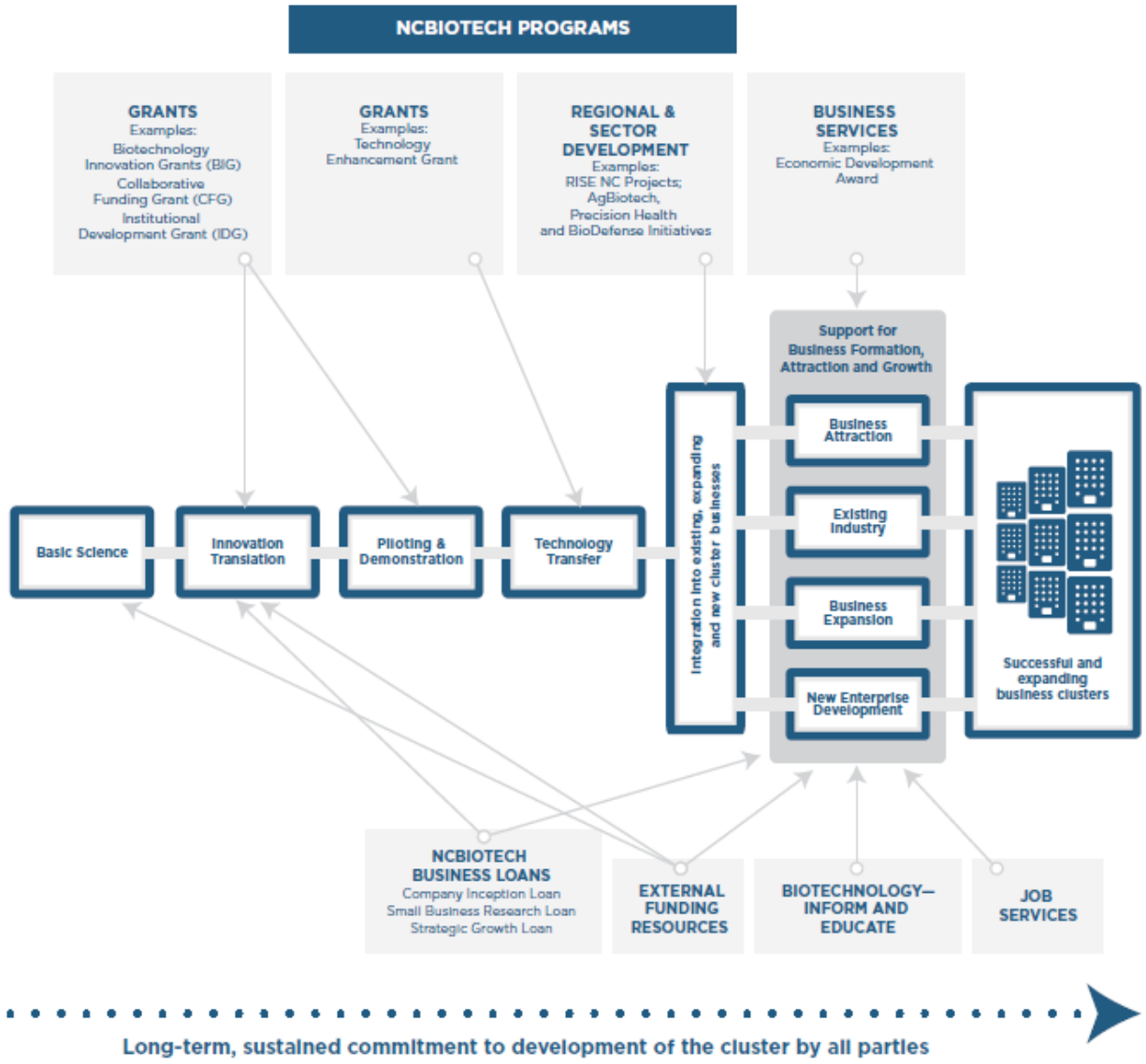
- Building regional capacity in capital and entrepreneurship in the biosciences, including training and recruiting entrepreneurs and increasing venture capital investment in the region.
- Marketing and branding St. Louis biosciences to local and national audiences.
- Data collection to help market St. Louis' assets and to connect scientific and business talent with jobs in emerging companies.
- Government relations and setting state and national legislative priorities.
- Guiding regional efforts to apply for large-scale public and private grants.
- BioSTL ensures the St. Louis biosciences community is speaking with a single, coherent voice to the public, policymakers and funders.

TEConomy notes that this mission is very similar to that of BioCrossroads, and organization formed by the Central Indiana Corporate Partnership, which has been very successful in raising the profile of Indiana in life sciences and coordinating activities and assets to grow Indiana's life science sector (which includes medical, agricultural and industrial life science activities).

TEConomy recommends that Iowa considers the NC, St. Louis and Central Indiana organizations as models for taking a similarly focused approach to bioscience sector development. This requires organizing a well-staffed and resourced structure able to coordinate, guide and advance the implementation of focused, long-term strategic actions that assure the bioscience technology-based ecosystem in Iowa is complete and that the most promising sectors, technologies and new business ventures are provided with optimized conditions in Iowa to advance their growth and success. As shown on Figure 16, the North Carolina Biotechnology Center's programs are designed with focused programs and supporting initiatives that assure each component of a complete bioscience development ecosystem are in-place and supported.

The NC Biotech Center provides leadership and strategic plan development for the overall sector in the State and then acts as a convener, facilitator, investor, and partner to universities and industries, to assure strategies and actions are implemented. By focusing its strategic actions on assuring a complete bioscience-development ecosystem is sustained, NC Biotech helps build basic and applied bioscience research capacity, support the advancement of innovations through piloting and scale-up, help start-ups and existing industry access commercialization and growth funding, and develop the workforce needed to staff sector growth.

Figure 16: NC Biotechnology Center Program Connectivity to Key Ecosystem Elements



Primary Activities:

TEConomy recommends that an Iowa Bioscience Development Center (IBDC) be established as an expansion of the existing Iowa Innovation Corporation (IIC). This would represent a state-supported initiative with dedicated staff and focused mission to support bioscience development across the state.

The IIC-IBDC will support bioscience research & development, innovation, commercialization and education through developing a series of focused initiatives to leverage bioscience development opportunities presented in the state, and to address weaknesses or gaps in the Iowa bioscience development ecosystem. It will serve as the accepted strategic development agency for biosciences in Iowa, providing central convening and coordinating functions for key Iowa stakeholders representing bioscience industries, research institutions, higher education and workforce training providers, and government/economic-development agencies which affect the bioscience development ecosystem. The IIC-IBDC should be structured such that all state funding and development resources for biosciences

R&D enhancement and business commercialization be administered through the IBDC, giving it the resources and power-of-the-purse to provide effective strategic leadership and strategic plan implementation.

Funding: One option to consider would be to fund the IIC-IBDC proportionate to the current size difference between the North Carolina and Iowa economies and bioscience sectors. Examining both gross state product (as an overall measure of the size of their respective economies) and bioscience employment (as a direct measure of bioscience sector size in each state) shows that Iowa is at around 35 percent the size of North Carolina on both measures (Table 15).

Table 15: Iowa Compared to NC in Gross State Product and Bioscience Employment

	Iowa	North Carolina	Iowa as a Percent of North Carolina
Gross State Product	$170,613 million	$483,126 million	35.3%
Bioscience Sector Employment	24,762	70,466	35.1%

Standing-up an organization at 35 percent the scale of the NC Biotech Center would result in the following basic figures:

- Staffing – circa 20 personnel
- Total budget (including operations and funds for investment in programs and companies) $4.76 million.

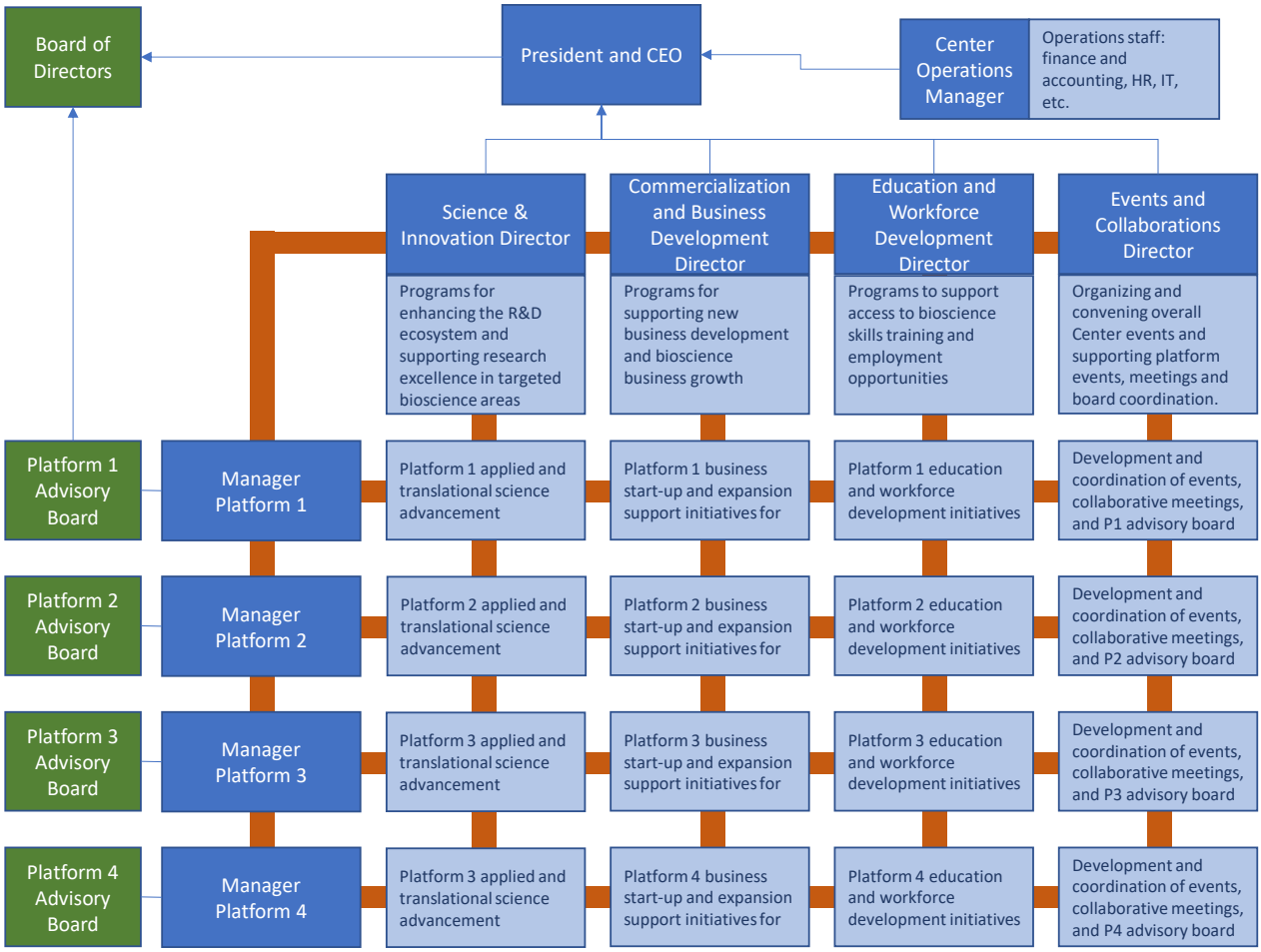
It should be noted that such a level of resources is already being devoted to activities through IEDA and IIC, and a restructuring of activities (rather than an entirely new appropriation) may accomplish much of what is envisioned.

Organization:

The IIC-IBDC may be designed with a matrix organizational structure to accomplish the key functional activities envisioned for the organization – as shown in Figure 17. This organizational structure is designed to be:

- Fully responsive to the need to develop and administer programs across the full bioscience development ecosystem, including functions in support of R&D and innovation, new business development and growth, and workforce development.
- Fully responsive to the needs of a development model focused on advancing bioscience development platforms that have unique characteristics, needs, gaps and opportunities. Plus, scalable for the addition of further platforms that may be identified and advanced in the future.
- Structured as a central hub that will be an effective convener, facilitator, investor, and partner to the research community, industry, external investors, and R&D stakeholders.
- Connected to existing external resources in the bioscience ecosystem in terms of existing business incubators and accelerators, research parks, entrepreneurship centers, regional development organizations, and business associations.
- Accountable to a Board of Directors, and advised by a series of dedicated advisory boards for each platform comprising scientists, educators, entrepreneurs, business leaders, representatives of the investment community, and government/economic development agency advisors.
- Promotional, working to advance the internal and external image of Iowa as a leading location for bioscience innovation and associated business development and growth.

Figure 17: Proposed Matrix Organization Structure for IIC-Iowa Bioscience Development Center



Timescale: Immediate. Both Governor Reynolds and IEDA Director Durham understand modern economic development and the role that state government plays as a convener, facilitator and investor in advanced technology-based economic development. This was ably demonstrated in the support for the recent Iowa Energy Strategy. Similarly, they understand that the biosciences represent a signature high technology sector for Iowa, providing jobs and opportunities for further development across the state – building upon existing and emerging R&D and industry strengths. While state government certainly has constrained budgets, the size of the opportunity for Iowa in biosciences is such that the timing is right to invest in expanding the scope of the Iowa Innovation Corporation to encompass the scope and strategic functionality as described for the IBDC.

Strategy Two: Increase Capital Available for Investment in Iowa Bioscience Companies

Description: As seen in TEConomy's analysis, Iowa is quite competitive in terms of performance of academic bioscience R&D and in terms of innovation (as measured using patents as proxies). Where it is far less than competitive is in venture capital to finance growth of companies based on Iowa innovations. Increasing Iowa's bioscience employment, especially in high paying technology ventures is hampered by a comparative lack of risk capital investment – particularly investment required to scale an enterprises post proof-of-concept. Iowa's performance in attracting venture capital places it at the bottom of performance among surrounding Midwestern states, and in the fourth quintile overall among all U.S. states.

Continuous innovation—the successful introduction of new products and services to the marketplace—is critical to sales and market share for both new and existing companies. Young, rapidly growing companies based on new product or service innovations drive net employment creation in the U.S.[27] and they, themselves, are driven by capital investment. Venture capital, however, continues to move toward larger and later stage deals.[28] According to CB Insights, $150K to $1M rounds from institutional VCs are increasingly on the decline.[29] This seed stage of funding is critical to helping startup companies hit milestones required before private sector investors will invest.

Solving the VC access challenge for Iowa is no easy task. The state's prior experience with an unsuccessful Fund of Funds program (which closed under threat of default in 2012) justifiably makes the administration and legislature gun-shy of revisiting such an approach. Yet, fund of funds models are working in other states. BioCrossroads in Indiana, for example, has established two bioscience-oriented fund of funds to 1) catalyze venture capital funding of emerging bioscience companies in Indiana, and 2) to advance relationships for merging Indiana bioscience companies with other regional and national venture capital funds. In 2003, BioCrossroad's "Indiana Future Fund" was established, investing $73 million across six venture capital firms. In December 2009, BioCrossroads established the INext Fund as a successor fund, capitalized with $58 million. Four VC firms received investment through the INext Fund. BioCrossroads has helped advance companies towards venture funding rounds through also operating a Seed Capital Fund, used by early-stage companies for technology-validation in advance of being ready for VC funding. BioCrossroads has formed multiple seed funds, totaling $14.25 million via funding received from a variety of State of Indiana, philanthropic and industrial investors. The impact of the seed and fund of funds venture financing in Indiana has been significant. A study commissioned by BioCrossroads in 2014 concluded that:

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[27] Haltiwanger, J., Jarmin, R., and J. Miranda (2013). "Who Creates Jobs: Small Versus Large Versus Young?" *The Review of Economics and Statistics*, May 2013, 95(2): 347-361. http://www.mitpressjournals.org/doi/pdf/10.1162/REST_a_00288 and J. Wiens and C. Jackson (2015). "The Importance of Young Firms for Economic Growth," *Entrepreneurship Policy Digest*, 13 September 2015. http://www.kauffman.org/what-we-do/resources/entrepreneurship-policy-digest/the-importance-of-young-firms-for-economic-growth

[28] According to Dow Jones VentureSource data, the median size of all venture capital financings in 2015 was $6.0 million, the highest level since 2008, and the median pre-money valuation for all venture capital financings in 2015 was $59.1 million, the highest level since 1996, when this data started to be collected. The median size of first-round financings was $3.2 million in 2015.

[29] CB Insights (2015). "The Growing Pre-Seed Opportunity in VC Financing." June 27, 2015. https://www.cbinsights.com/blog/pre-seed-venture-capital/

"Indiana has made substantial gains in life science venture capital over the past decade. Total venture capital investment in the life sciences in Indiana over the period 2003 to 2013 rose to $349 million across 100 deals and 39 companies."[30]

Utah has also achieved success using a fund of funds approach. Started in 2003, the Utah fund of funds approach comprised a $300 million state investment. The program has led to investment of $785 million in 73 Utah companies since its inception, of which 60 remain in operation supporting over 4,000 jobs.

Tennessee has deployed a different approach. The state created a state-sponsored, "venture capital type" program providing capital to local venture capital companies. Rather than trying to use a fund of funds mechanism or limited use of tax incentives, Tennessee instead created a pool of capital that was competitively awarded to venture capital firms formed in Tennessee and competitively selected by the state as Tennessee Investment Companies or TNInvestcos. Each of the TNInvestcos were allocated rights to $20 million in tax credits and sold the future years' tax credits for up-front capital from the state's insurance companies to invest in Tennessee businesses. The 2013 Annual Report for the program indicates that 132 Tennessee companies received direct investments of $108 million from TNInvestcos, and an additional $221 million in follow-on capital from other sources. These 132 TNInvestcos companies generated 1,605 jobs, of which 687 were new jobs generated after investment. Other states, including Pennsylvania and Maryland for example, have employed similar tax credit approaches to generate venture capital investment in their states.

Activities for Consideration:

Increasing major early stage and expansion capital, especially VC, needs to be a priority for Iowa over the next several years in order to realize growth and expansion of Iowa bioscience enterprise. In particular, given characteristics of early stage bioscience company development, the consideration should be given to:

1. **Expanding early-stage risk capital for pre-revenue companies**

Creating a private seed capital fund through the use of a tax credit may be one option. The goal here would be to incentivize the formation of an early-stage life sciences-focused fund by investors with a good track record and strong networks in sectors of relevance to the platforms. According to TEConomy research, 18 other states have created seed capital funds to provide targeted assistance to early-stage technology companies to help get to the point that the private sector takes over. These seed funds take an equity position in companies and are privately managed by either for-profit or non-profit entities. Review of these and their typical scale suggests a potential need to:

Note: The complexity of the capital access situation in Iowa is such that IEDA has contracted with TEConomy Partners to perform an additional focused analysis of the situation and make specific recommendations in a separate report to be completed before the end of 2017. Recommendations made in the current document, therefore, should be considered preliminary and may be subject to change.

- Create a 15-year, $50M-$60M fund focused on early stage ventures;
- Use 50-100% tax credits to compensate investors for very high risk and long-term time horizon projects;

[30] Battelle Technology Partnership Practice. 2014. "*Re-Examining the Need for Innovation Capital to Advance Life Science Development in Indiana*". October 2014.

- Sell up to $4M in tax credits per year;
- Require 1:1 co-investment by other private investors
- Performance metrics should include capital raised by portfolio companies and milestones hit in the short term; capital raised, product sales, and employment in the mid-term; and all of the above plus successful exits and return on investment in the long term.

Note: As discussed in the sidebar above, such conclusions are highly preliminary and subject to further review.

As shown on Table 16, development of venture organizations by states to advance company access to convertible debt or equity capital are not unusual. The 18 programs shown on Table 16 average $4.64 million in investments made per year.

Table 16: State-Supported Venture Development Organizations that Invest via Convertible Debt or Equity, 2016

	State	Venture Development Organization	Year Founded	Type of Corporation	Total Assets Under Management ($M)	Average Amount Invested/Year ($M)	Total Employees
1	CT	Connecticut Innovations	1989	Quasi-state	$134.749	$20.0	38
2	IN	Elevate Indiana	1999	501c3	$3.398	$6.0	13
3	KY	Kentucky Science & Technology Corporation	1987	501c3	$19.021	$2.0	27
4	MA*	MassVentures (Mass Technology Dev Corp)	1993 (1979)	Quasi-state	N/A	$1.5	6
5	ME	Maine Technology Institute	1999	501c3	$26.967	$0.2	11
6	MD*	Maryland TEDCO	1998	Quasi-state	N/A	N/A	20
7	MI	Ann Arbor SPARK (Michigan Economic Dev. Corp.)	2005	501c6	$19.756	$3.5	19
8	MS	Innovate Mississippi	1998	501c3	$0.120	$0.2	9
9	NE	Invest Nebraska	2002	501c3	$6.862	$1.0	3
10	NY	New York Ventures (Small Bus Tech Invest Fund)	2012 (1981)	Quasi-state	N/A	$3.0	6
11	ND	North Dakota Development Fund	1991	For-profit	N/A	N/A	N/A
12	OH	JumpStart (Ohio Third Frontier) CincyTech (Ohio Third Frontier)	2003 2006	501c3 for-profit	$41.327 N/A	$9.0 $3.0	50 13
13	OK	Innovation to Enterprise (i2E)	2004 (1998)	501c3	$11.696	$5.9	19
14	PA	Innovation Works (Ben Franklin Tech Partners) Southeastern BFTP (Ben Franklin Tech Partners)	1999 1983	501c3 501c3	$22.918 $65.736	$5.5 $10.0	25 27
15	SC	SC Launch	2006	501c3	$4.696	$2.5	10
16	TN	Launch TN	2012	501c3	$30.657	$7.0	10
17	VA	Center for Innovative Technology	1985	501c3	$5.722	$3.0	31
18	VT	Center for Emerging Technologies	2003	501c3	$4.038	$0.2	4

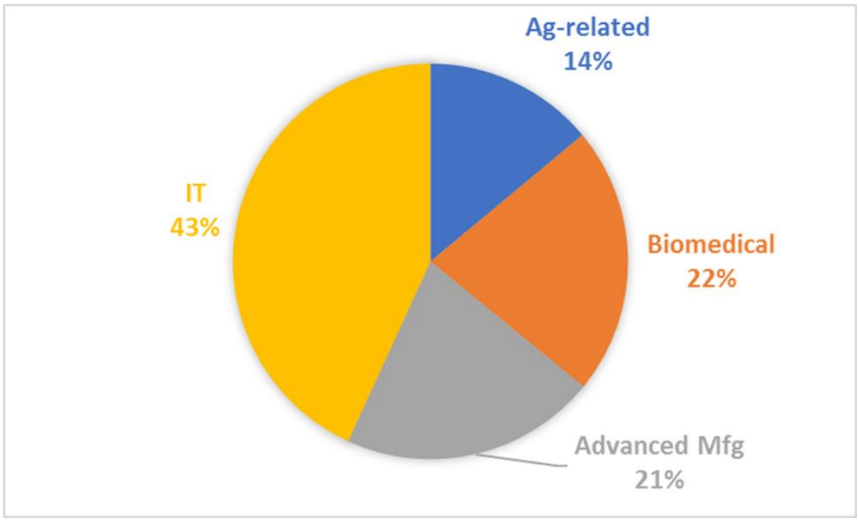
Note: *The employees of Maryland TEDCO and MassVentures are not state employees.
Source: TEConomy Partners, LLC analysis of websites, annual reports, and FY2015 990 tax filings in *Compensation Benchmarking and Performance Audit* prepared for Connecticut Innovations, December 2016.

Special Financing Needs for Platforms: Example of the Medical Device Platform.

It should be noted that capital availability is not uniform across the types of companies likely to be represented in each of the recommended Iowa bioscience Technology Platforms. The bioscience sector is an important industry sector for Iowa, yet the entrepreneurial ecosystem is generally less developed for medical technology than it is for agricultural technologies. In agricultural technology, one finds serial entrepreneurs with agricultural industry backgrounds, primarily because Iowa has a robust and diversified agricultural industry base and has experienced significant start-ups in the biofuels sector. These entrepreneurs understand business development and can identify important needs and customers. In the biomedical/med tech sector, there are a fewer Iowa companies, and the base of expertise and experience in medical device, diagnostics, therapeutics, or health technology company formation is less developed. This limits the pool of potential entrepreneurs, as well as the pool of potential investors (since investors invest in the entrepreneur and their track record alongside the business concept/technology).

What Iowa does have are the Regents universities which are the overwhelming source of intellectual property for many of Iowa's medical technology startups (according to VentureNet data for the past four years) compared to agricultural tech in which the private sector is the predominant source of IP for startups (Figure 18).

Figure 18: Sector Breakdown of Startups for Which VentureNet Organized Focus Groups, 2012-2016



Source: VentureNet

In TEConomy's interviews with Iowa VC investors and startup companies, the gaps identified include:

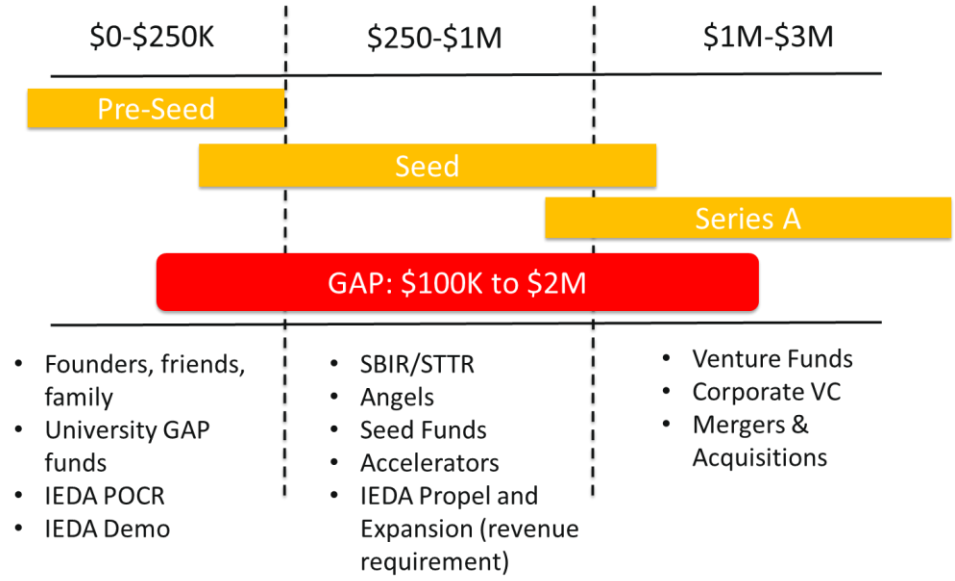
- Very few serial entrepreneurs in the biomedical space. However, several Iowa biomedical startups have been successful in recruiting CEOs with startup and industry backgrounds from outside the state.
- Very few Iowa VC funds that will lead rounds or be the "first money in" in biomedical startups: existing Iowa angels and VCs tend to prefer to co-invest alongside others.
- Iowa angels and VCs not well syndicated, so they do not pull in capital and industry sector expertise from Minneapolis and the Coasts. Commercialization of products for med tech companies requires significant capital.

Looking specifically at the demand for risk capital by Iowa's biomedical startups versus the availability of risk capital, TEConomy finds:

- Iowa innovation programs currently provide $25K to $500K rounds of funding via loans to startup companies, e.g., Proof of Commercial Relevance ($25K), Demonstration ($100K), Propel ($300K), and Expansion ($500K).
- However, from the $100K Demonstration Fund level on, these funds are no interest or low interest loans, and from the $300K Propel Fund level on, companies must show revenue.
- Many biomedical startups will not generate revenues for many years while going through FDA approval, so access to capital is a challenge for these companies after the $100K Demonstration Fund. In addition, IEDA loans can count against firms applying for SBIR Phase IIs.

Therefore, despite existing state innovation funding programs, there is still likely an excess demand for risk capital after the $100K round. Figure 19 shows the $100K to $2M early-stage rounds gap for Iowa's med tech, health tech and therapeutics startups.

Figure 19: Gap in Iowa's Early-Stage Risk Capital Market for Med Tech



Source: TEConomy Partners, LLC

As noted above, TEConomy has been retained by the IEDA to do a "deeper dive" study into VC availability and associated early stage capital – which will be provided in a separate report before the close of 2017.

Strategy Three: Ensure continued legislative support for existing innovation ecosystem development programs

Investors and entrepreneurs are risk takers, but they do seek to minimize risks to the extent possible. One of the key risks that a state should have control over is the stability of its government sponsored programs and incentives (and control of a predictable and stable regulatory and tax environment for commercial enterprise). The State of Iowa needs to assure that a long-term commitment is sustained in terms of maintaining the programs and incentives in its current economic development portfolio that have relevance to bioscience development as shown in Table 16.

Table 16: Existing Iowa Programs Relevant to Iowa Bioscience Sector Development and Growth

Support Area	Existing Programs
Private Sector Innovation, Technology Advancement, Entrepreneurship and Business Development	• **Refundable Research Activities Credit:** Iowa sets itself apart as being one of the few states to offer a refundable research activities credit. Iowa companies earn refundable tax credits for research and development investments that may be paid directly in cash to the company once its tax liabilities have been met. A company must meet the qualifications of the federal research credit in order to be eligible. • **The Proof of Commercial Relevance (POCR) program** is designed to define and articulate the opportunity for businesses that demonstrate a proof-of-concept for innovative technology. It is designed to assist in market validation of products/services and the business model prior to commercial launch. The program awards up to $25,000 in low interest loans with a 1:2 (private:public) match. Funds can be used for: validation of market potential, Beta testing; business model and marketing/distribution strategy/tactics; IP development and evaluation; competitive analysis and furthering translational development of a scientific discovery. To be eligible an Iowa company has to have been formed, and the program is focused on advanced manufacturing, bioscience or information technology industries • **Demonstration Fund:** This fund is designed to provide assistance to companies with market-ready innovative technologies or products that have a clear potential for commercial viability. It assists companies with marketing and business development activities and helps businesses with high-growth potential reach a position to attract follow-on private sector funding. Awards are up to $100,00 and are primarily loans or royalty arrangements with a 1:2 (private:public) match. • **Iowa Innovation Acceleration Fund**: Provides funds to Iowa-based companies (with <500 employees) with innovative technology solution(s). It is focused towards companies in advanced manufacturing, bioscience or information technology industries. Funds seek to accelerate market development and result in significant leveraged capital investment. The fund is split into: 1) PROPEL awards up to $300,000 to accelerate market development for companies that have critical management in place, have a validated business model and an established customer base that's generating substantive revenue, and 2) INNOVATION EXPANSION awards up to $500,000 to encourage expansion of product lines in companies that have a complete management infrastructure, a demonstrated historical profitability and an established customer base; funding provides assistance for product refinement and market expansion activities for unique, innovative and competitive products. • **SBIR/STTR Outreach Program**: Delivered by the Iowa Innovation Corporation, this program assists Iowa companies by reviewing SBIR/STTR grant proposal applications and providing commitments to matching grant funds for Phase I SBIR/STTR awards. • **The High-Quality Jobs (HQJ) program** provides qualifying businesses assistance to off-set some of the costs incurred to locate, expand or modernize an Iowa facility. This

	flexible program includes loans, forgivable loans, tax credits, exemptions and/or refunds. Actual award amounts based on the level of need; quality of the jobs; percentage of created or retained jobs defined as high-quality; and the project's economic impact
Investor Incentives	• **Angel Investor Tax Credits** are offered to increase the availability and accessibility of venture capital, particularly for ventures at the seed capital investment stage. The total amount of tax credits available per fiscal year (July 1 – June 30) is $2 million. Investors can receive a maximum of $100,000 in tax credits per calendar year for a household, and the investors in any one business can be issued a maximum amount of $500,000 in tax credits per calendar year. The tax credit is equal to 25% of an investor's equity investment and refundable to investors who file personal net income tax. • The **Innovation Fund Tax Credit** was created to stimulate VC investment in innovative Iowa businesses. Individual investors receive tax credits equal to 25 percent of an equity investment in a certified Innovation Fund. In turn, those certified Innovation Funds make investments in promising early-stage companies that have a principal place of business in Iowa. Innovative businesses include, but are not limited to, businesses engaged in advanced manufacturing, biosciences and information technology. The total amount available for investment in Innovation Funds is $8 million this fiscal year.
Workforce	• **New Jobs Tax Credit:** This one-time, corporate income tax credit is available to participants in the New Jobs Training (260E) Program that are planning to expand their workforce by at least 10%. Iowa offers this credit as an incentive for businesses that provide additional training to employees and expand their workforce. The maximum tax credit in 2017 is $1,758 per new employee. Unused tax credits may be carried forward for up to 10 years.
Place and Space	• While the IEDA has programs that help support city or place-based investment in businesses (The Economic Development Set-Aside and the Targeted Jobs Withholding Tax credit), it does not have specific funds to support development of incubators, accelerators, research parks or innovation districts specifically. This does not appear to represent a significant problem at the present time, since university-based and other incubators and accelerators have formed in the state, and both ISU and UI operate major research parks.

Given the demand and impact of Iowa's existing innovation funding programs, TEConomy believes it is important for the state to maintain its long-term commitment to these programs and the startup activity in the state that they support. Realistically it takes 10 to 15 years for startup companies in the biomedical sector to commercialize a product and grow to the point of sustainability or exit (e.g., a merger or acquisition, initial public offering, etc.), and some agricultural technologies (such as transgenic crops) can require an equally long timescale. Iowa's individual funds should be assessed to ensure that the terms and requirements (e.g., the fact that they are loans, rather than grants, and the fact that they require revenue) are appropriate for the stage and sector of companies that the state is trying to support. If they are not—as evidenced by lower demand by biomedical startups for some programs compared to others—changes should be considered to make them work better.

Strategy Four: Improve Connectivity and Collaboration Opportunities Between Key Stakeholders in Each of the Focused Bioscience Development Platforms

Interviews and discussions held throughout the program of core competency review and platform identification provided a consistent theme of a lack of awareness and connectivity between key companies, university research teams and other key stakeholders in Iowa. This is related to the need to

the need for standing up the recommended IIC-IBDC as an organization that will coordinate activities and communication across the full bioscience spectrum – but also, and in particular, provide for the development of platform specific committees that will bring together key platform stakeholders. Each of the platforms has significantly different sector foci, companies, university research teams and markets associated with it – and thus bringing these parties together to coordinate actions within their specific platforms is critically important. This is the approach, for example, taken by the Central Indiana Corporate Partnership (CICP) which operates specific programs for biopharmaceuticals development, medical devices, and agricultural biosciences.

Platform specific committees will need funding for staff support at IIC to assure that events and meetings are well coordinated, recorded and acted-upon. Once established it is imperative that Iowa be committed to coordinating and operating the IIC-IBDC and its individual platform operations and committees over a long-term time horizon. As shown in the successful bioscience initiatives in other regions of the country, there is significant pay-off for regional economic development to be accomplished through life sciences pathways, but robust development within life science sectors takes time (often decades) and a long-term, sustained commitment of resources to realize.

Appendix A: Plant Metabolic Engineering

There is also another, quite different pathway open to science in driving opportunities to realize product variety and functionality from plant chemistry – that of plant metabolic engineering. Plant metabolic engineering (PME) provides a significantly different way of viewing plants in the chemical production value chain. Instead of thinking about existing plants and their oils and starches as inputs to chemical refineries (e.g. converting basic oil and starch into intermediate chemicals and then refining them or processing them into specialty chemical products), PME provides a pathway to using plants themselves as the chemical factories.

Plants have evolved into sophisticated chemical micro-factories which use sunlight as a power source and atmospheric CO2 as the carbon feedstock. Plants have evolved metabolic pathways to the production of chemicals that attract pollinators, provide defense against feeding animals, pests, disease and competing plants, and send signals to symbiotic organisms, such as bacteria, promoting beneficial interactions. The chemicals produced by these metabolic pathways are typically referred to as secondary plant metabolites – while first metabolites are the chemicals more directly involved in plant growth and development (carbohydrates, proteins, and fats). By one estimate "within the plant kingdom alone, over 25,000 different organic chemical structures are produced."[31] The challenge is not just in characterizing this large diversity of chemical compounds that are produced regarding their functional characteristics, but also in the fact that the chemicals may be expressed in very small quantities and only at certain times in the plant life cycle, or only when the plant faces certain stressors.

Plant metabolic engineering, as the name suggests, presents opportunities for plant metabolisms to be specifically engineered or tuned to express useful volumes of desired chemicals. This may be achieved through the transfer of genes from another organism (such as another plant or microbes), known as transgenics, or using modern innovations in gene editing. The new technology of CRISPR/Cas9, for example, is providing an efficient and versatile tool for gene editing and makes possible plant transformations previously unthinkable. Almost any gene, in any plant, can potentially be edited to alter its functionality. This ability opens-up opportunities to custom engineer plants to be individual production factories for desirable chemical compounds. That makes it sound simple, but it is far from it. As noted by Lau et al: "adding new nodes to a plant metabolic

Recognizing the opportunities for R&D in metabolic engineering, ISU has also developed the **Center for Metabolic Biology (CMB)** to facilitate, encourage, and sponsor:

Innovative and fundamental molecular research that will lead to a comprehensive understanding of metabolic networks and systems. The goal of the Center is to generate the fundamental understanding of metabolism that will provide the basis for designing novel biological pathways for biochemical constituents that improve the nutritional quality of agricultural products and generate novel biorenewable sources of industrial feedstocks. Members of CMB are affiliated with various Iowa State University departments, including Agronomy, Biochemistry, Biophysics and Molecular Biology, Chemical and Biological Engineering, Chemistry and Genetics, Development and Cell Biology. Research is focused on integrating modern technologies in functional genomics, bioinformatics and computer sciences to comprehensively decipher metabolic networks. Researchers within the CMB are thus developing new resources in the area of metabolomics and computational modeling of metabolic networks.

Iowa State University. "About the Center for Metabolic Biology". Website content. http://www.metabolicbiology.iastate.edu/about

[31] John Ohlrogge. 1999. "Plant metabolic engineering: are we ready for phase two?" Current Opinion in Plant Biology 1999, 2:121–122

network is a difficult task that will benefit from advances in targeted genome modification, tissue-, cell-, and organelle-specific gene expression, and the controlled expression of multi-gene pathways."[32] The complexity of plant genomes, the impact of environment/epi-genetic factors on chemical expression, and the standard scientific issues of us "not knowing what we don't know" has made plant engineering on a commercial scale a challenging proposition. Despite the challenges, the fact is that biologically produced products can provide significantly greater diversity and oxidation states for the chemical industry than can the limited, highly reduced hydrocarbon structures found in crude oil.

In Iowa, the chemical/process-engineering approach comprises an established focus with expertise embodied in organizations such as the NSF-funded Center for Biorenewable Chemicals and particularly within the Center for Metabolic Biology (see sidebar). The plant metabolic pathway is a smaller focus area, and certainly a longer-term economic development opportunity for Iowa, but represents an opportunity for Iowa to build upon existing capacity to generate leadership in what will be an exciting and productive novel approach to the development and production of useful biobased molecules.

[32] Warren Lau, Michael A. Fischbach, Anne Osbourn, Elizabeth S. Sattely. 2014. "Key Applications of Plant Metabolic Engineering." Published: June 10, 2014. https://doi.org/10.1371/journal.pbio.1001879