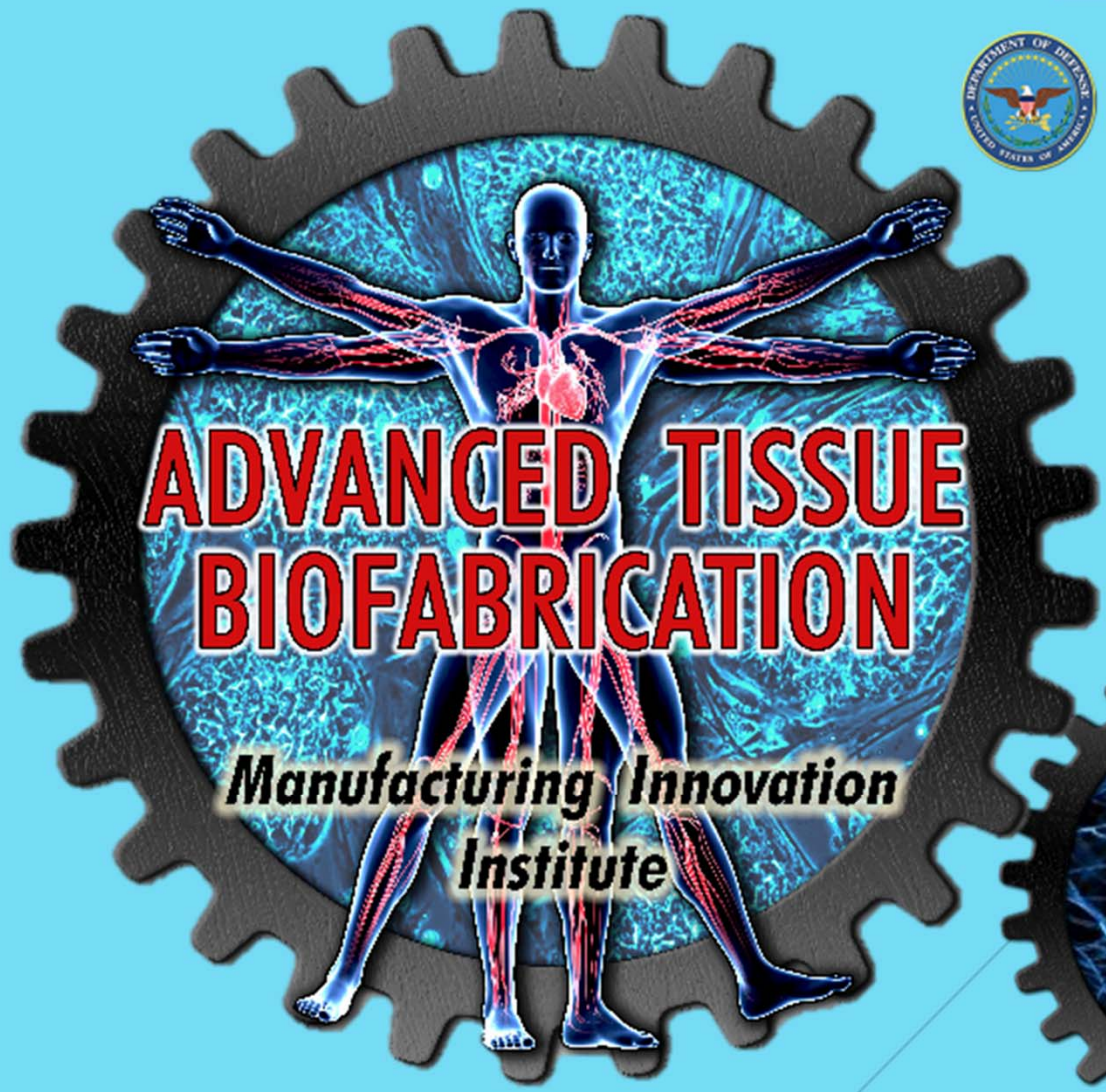
ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

PROPOSERS' DAY



June 23rd, 2016

Unclassified

AGENDA

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- 0900 – 0905: UILABS Conference Center Welcome (Dr. Caralynn Nowinski Collens, M.D., CEO UI Labs)
- 0905 – 0920: OSD Welcome
- 0920 – 0950: Institutes for Manufacturing Innovation - Objectives
- 0950 – 1005: Break
- 1005 – 1050: FOA Contracting Overview
- 1050 – 1150: FOA Advanced Tissue Biofabrication Manufacturing Innovation Institute Overview
- 1150 - 1200: Initial Q&A
- 1200 – 1300: No Host Lunch (Teaming discussions among potential Proposers encouraged)
- 1305 – 1335: Multi-Agency Tissue Engineering Science (MATES) Working Group
- 1335 – 1350: Additional Q&A
- 1350 – 1400: Concluding Remarks

UILABS CONFERENCE CENTER WELCOME

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

***Dr.* Caralynn Nowinski Collens, M.D.**
CEO UI Labs

OSD WELCOME

ADVANCED TISSUE BIOFABRICATION
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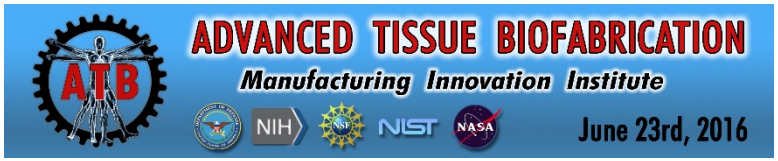
Ms. Adele Ratcliff

DoD ManTech
ODASD(MIBP)

LINKEDIN COLLABORATIVE SITE



- https://www.linkedin.com/groups/8545546
- Provided for collaboration
- Will post contacts from “Want to Lead” and “Want to Team” boards

OSD WELCOME

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

Ms. Tracy Frost

DoD ManTech
ODASD(MIBP)

MANUFACTURING GAPS WITHIN THE DOD

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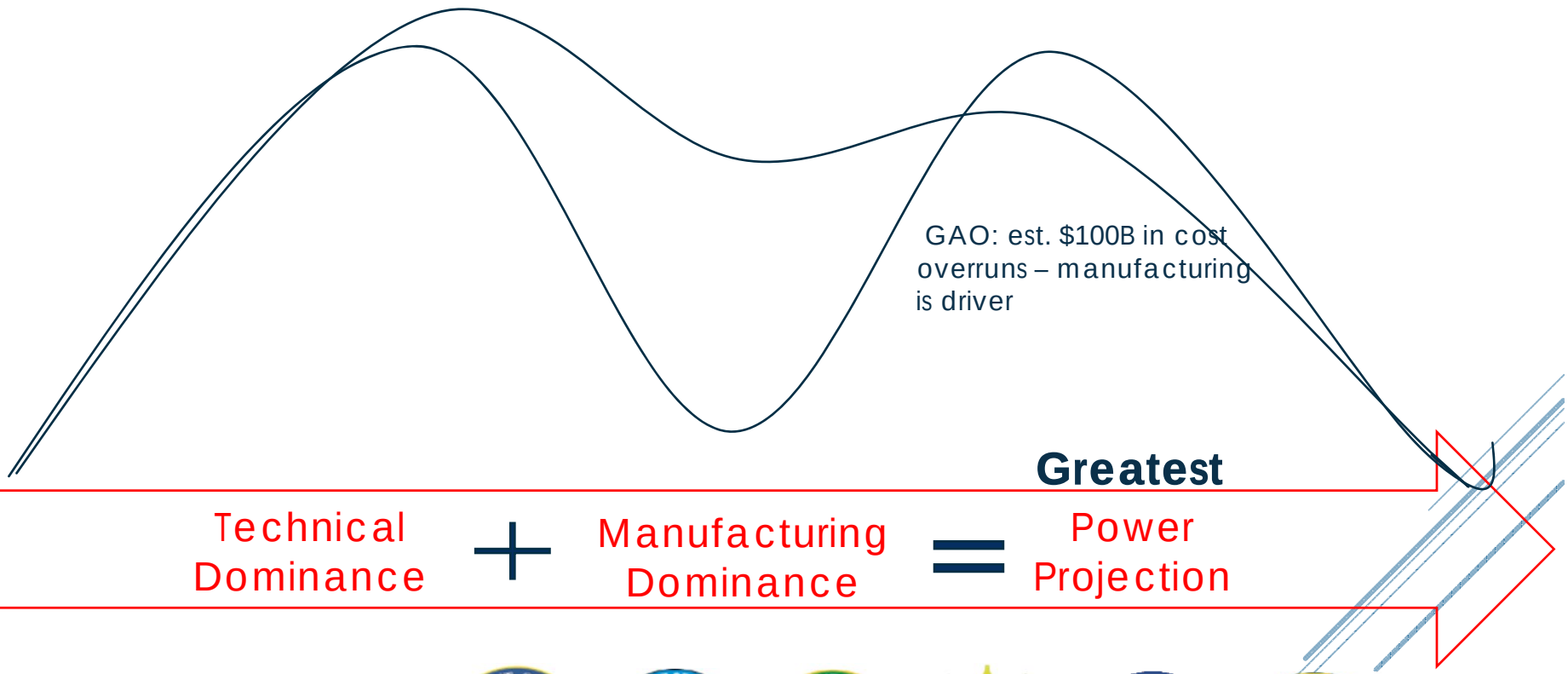
June 23rd, 2016



MANUFACTURING GAPS WITHIN THE DOD cont.

ADVANCED TISSUE BIOFABRICATION
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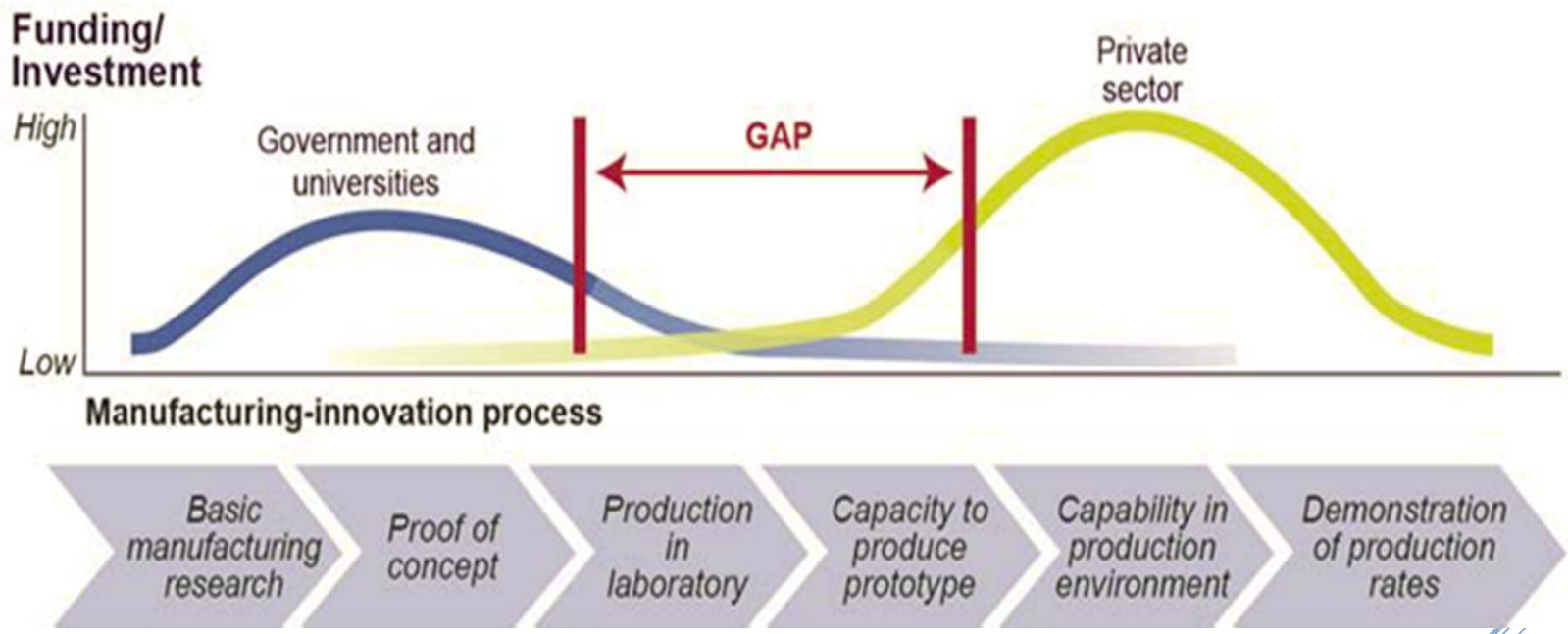
The "valley of death"
The "missing Bell Labs"
The "industrial commons"



US MANUFACTURING GAP REPORTED

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
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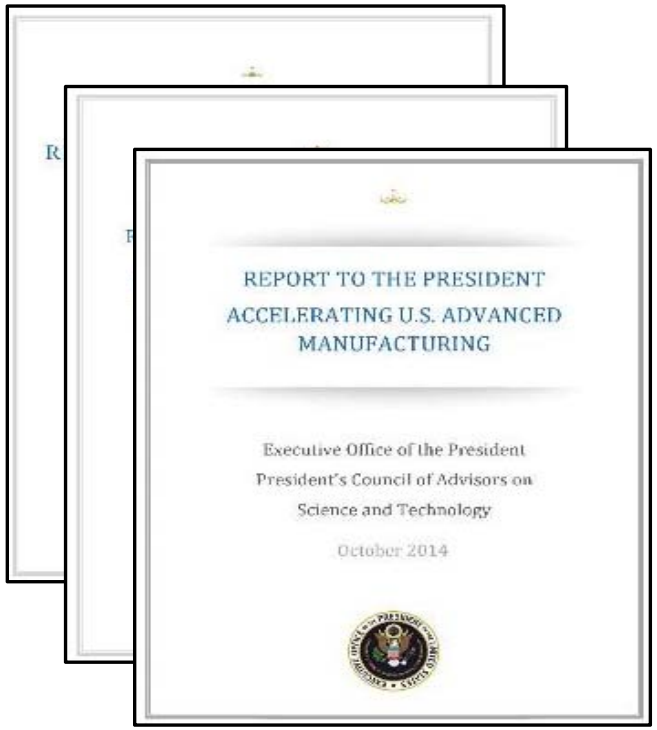

President's Council of Advisors on Science and Technology (PCAST)

2011, 2012 and 2014 reports recommended, respectively:

- ***Advanced Manufacturing Initiative as national innovation policy***
- ***Manufacturing Innovation Institutes to address key market failure***
- ***Strong, collaborative network of Manufacturing Innovation Institutes***

US MANUFACTURING GAP ADDRESSED

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

2012 Presidential Actions:

- Asks Congress to authorize initial network of up to 15 MIIs
- Directs pilot institute

Requirements:

A framework for government, industry and academia to intensely collaborate on industry-relevant manufacturing problems

Fundamentals:

(1) Leverage USG's power to convene and industry's leadership long-term

(2) Generate intense public-private collaboration through partnerships

(3) Encourage regional clustering while generating national impact

CONGRESSIONAL AUTHORIZATION

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
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Revitalize American Manufacturing & Innovation (RAMI) Act of 2014

118 bipartisan RAMI Bill Sponsors

Rep. Tom Reed
R NY-23

Rep. Joe Kennedy
D MA-4

Sen. Sherrod Brown
D Ohio

Sen. Roy Blunt
R Missouri

September 15, 2014 –
Passed House
100 Cosponsors (51D, 49R)

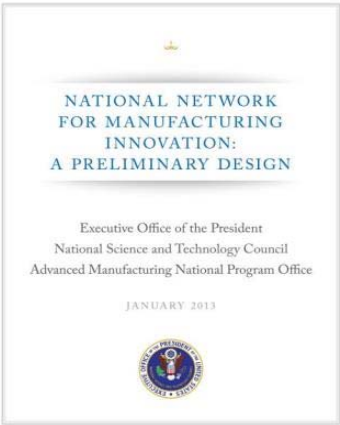
December 11, 2014 –
Passed Senate with 2015 Appropriations
18 Cosponsors (10D, 7R, 1I)

December 16, 2014 –
Signed By President Obama

Bipartisan Momentum Supporting the NNMI Initiative

THE MANUFACTURING INNOVATION INSTITUTES (MMIs) DESIGN

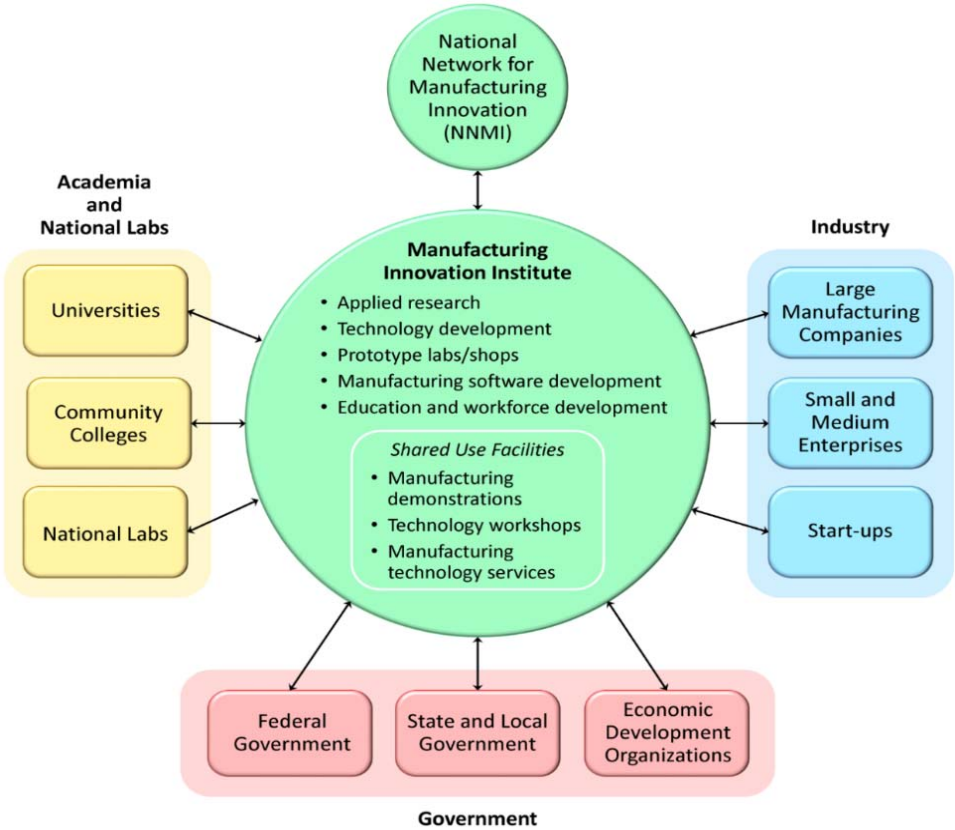
ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016


NATIONAL NETWORK FOR MANUFACTURING INNOVATION: A PRELIMINARY DESIGN

Executive Office of the President
National Science and Technology Council
Advanced Manufacturing National Program Office

JANUARY 2013

White House Report
NNMI Framework Design



Creating the partnership space for sustained and powerful, pre-competitive collaboration between Industry, Academia and Government

ESTABLISHED MIIs

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June 23rd, 2016

1. ***America Makes:*** **The National Additive MII**
   DOD-Led; Established August 2012

2. ***Power America:*** **Next Generation Power Electronics MII**
   DOE-Led; Announced January 2014

3. ***DMDII:*** **Digital Manufacturing & Design Innovation Institute**
   DOD-Led; Established February 2014

4. ***LIFT: Lightweight Innovations for Tomorrow*** **(Lightweight & Modern Metals)**
   DOD-Led; Established February 2014

5. ***IACMI:*** **Institute for Advanced Composites Manufacturing Innovation**
   DOE-Led; Announced January 2015

6. ***AIM Photonics:*** **American Institute for Manufacturing Integrated Photonics**
   DOD-Led; Established July 2015

7. ***NextFlex:*** **Flexible Hybrid Electronics Manufacturing Innovation Institute**
   DOD-Led; Established August 2015

8. ***AFFOA:*** **Advanced Functional Fabrics of America**
   DOD-Led; Established April 2016

REGIONALLY LOCATED; NATIONALLY IMPACTFUL

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

Building a National Network of Institutes

Network Status and Growth Plans

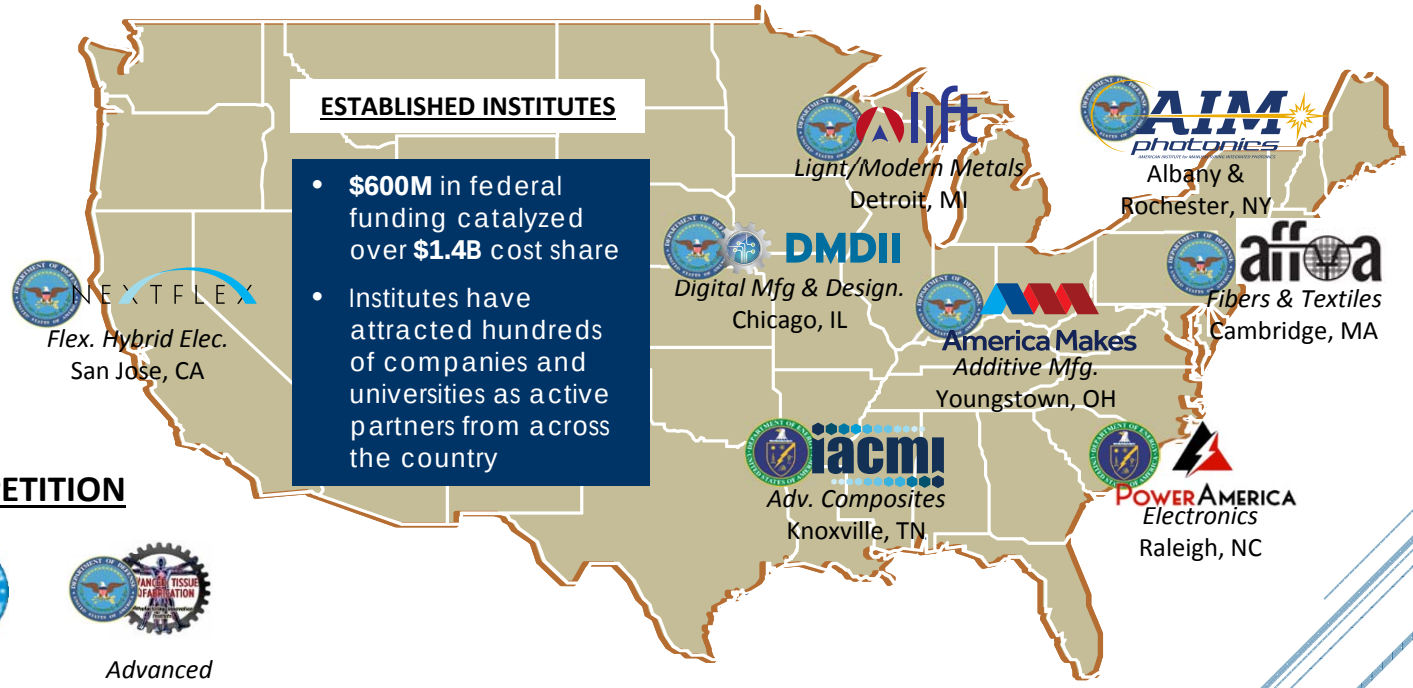
INSTITUTES IN DEVELOPMENT

1. *Process Intensification*
2. *Topic TBA*

Robotics in Manufacturing Environments

ESTABLISHED INSTITUTES

- **$600M** in federal funding catalyzed over **$1.4B** cost share
- Institutes have attracted hundreds of companies and universities as active partners from across the country



INSTITUTES IN COMPETITION

Smart Mfg. for Energy Efficiency
Proj. Award TBD

Open Topic Competition for up to 2 MIIs
Proj. Award TBD

Advanced Tissue Biofabrication
Proj. Award TBD

As of 1 June 2016

DOD's CURRENT ROLE

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- **DoD established six (6) of the first eight (8) existing institutes**
  - **Over $600 million in DoD funding matched by well over $1 billion in committed industry cost share**

- **DoD-led MIIs established/overseen by OSD's ManTech Office**
  - **DoD, Federal-level Interagency, and Industry/Academia coordination**
  - **Built deep trove of lessons, analytical data, policy insights supporting the full NNMI Program enterprise**

DOD MII ACQUISITION STRATEGY

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- **Technology Focus Area**
  - Significant coordination across DoD & federal S&T enterprises
  - Deep engagement with Industry/academia via RFIs, workshops
- **Solicitation Phase (6-8 months)**
  - DoD uses 2-step funding opportunity announcement (FOA) process:
    - Step 1: Concept Papers
    - Step 2: Full Proposals (by-invitation only)
  - DoD and DOE require award to 501(c)(3) non-profit
  - Award instrument: Cooperative Agreement or *Technology Investment Agreement (TIA)*
  - Pre-award negotiations last one to several months
- **MII award typically announced by cabinet level or higher principal (previous officials: SECDEF, VPOTUS, POTUS)**

15 MINUTE BREAK

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

W911NF-16-R-0021 **OVERVIEW**

Christopher Justice, U.S. Army Contracting Command - Aberdeen Proving Ground, RTP Division

AGENDA

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- General Information
- Award Instrument
- Eligibility
- Foreign Participation
- Cost Share
- Evaluation Process
- Evaluation Factors
- Notification – Concept Papers
- Notification – Negotiation and Award
- Schedule

GENERAL INFORMATION

- Army Contracting Command – Aberdeen Proving Ground (Research Triangle Park) (ACC-APG(RTP))
  - Specialize in grants, cooperative agreements and other assistance instruments in addition to contracts
  - Primarily support Army Research Laboratory, Army Research Office and various other DoD initiatives

GENERAL INFORMATION

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- **Read the FOA Instructions**

- Proposal Due Date and Times
  - Concept Papers Due 29 July 2016 no later than 3:00 PM local Durham, NC time.
  - Proposal due date and time will be specified at the time of Proposal Invitation

- Proposal Requirements, Sections
  - Reference Section IV of FOA for specific Concept Paper and Proposal Requirements and Sections

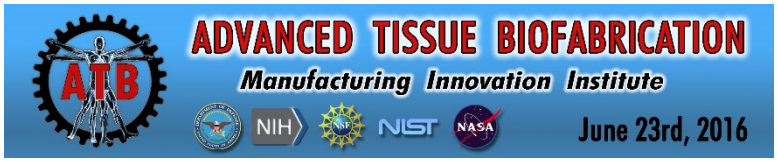
GENERAL INFORMATION

- **Read the FOA Instructions**

- Page Limitation
  - Concept Paper – 40 pages total
  - Proposal – 90 pages total

- Other Requirements
  - Concept Papers must be submitted to usarmy.rtp.rdecom-aro.list.atb-foa@mail.mil
  - Full Proposals must be submitted via grants.gov

AWARD INSTRUMENT



- Technology Investment Agreement (TIA) under the authority of10 USC §2371, as implemented by the Department of Defense Grant and Agreement Regulations (DoDGARS)
  - https://www.gpo.gov/fdsys/pkg/CFR-2011-title32-vol1/xml/CFR-2011-title32-vol1-subtitleA-chapI-subchapC.xml (Part 37)
- Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards2 CFR 200
  - http://www.ecfr.gov/cgi-bin/text-idx?tpl=/ecfrbrowse/Title02/2cfr200_main_02.tpl

AWARD INSTRUMENT

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
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- What is a Technology Investment Agreement (TIA)?
  - A special class of assistance instrument used to increase involvement of commercial firms in defense research programs and for other purposes related to integrating the commercial and defense sectors of the nation's technology and industrial base.
- Why a TIA?
  - Financial management systems
  - Patent rights/Intellectual Property

ELIGIBILITY

- **(See Section III of the FOA)**

- Limited to *U.S. non-profit organizations* who will serve as the lead and will be the recipient of the TIA

- The U.S. non-profit is expected to team with any combination of businesses, manufacturing firms, institutions of higher education, associated institutes, or non-profit industry consortia.

FOREIGN PARTICIPATION, ETC.

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- The recipient of the award must be registered as a U.S. organization
- U.S. incorporated companies that are wholly owned subsidiaries of foreign companies may be eligible to be members of the ATB-MII, and sub-awardees
- FFRDC's are not eligible to receive an award under this FOA or team with an applicant

COST SHARE

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- Minimum 1:1 Cost Share Required
  - AT LEAST $80M cost share
  - Cost-sharing is not required to precisely align with this funding profile on a yearly basis
- May Include
  - State and Local Funding (not origination from Federal dollars)
  - Private Sector Investment
  - In-Kind Cost Sharing
    - Equipment, facilities, man-power (see OMB Circulars, DoDGARs)

EVALUATION PROCESS

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- 2 Step Process (Concept Paper and Proposal)
- Multi-Agency Scientific/Technical Review
  - Not a FAR Part 15 Source Selection Process
  - Evaluation Team is "Government Only"
- Evaluation Process
  - Preliminary review for proposal completeness, eligibility requirements, conformance with FOA requirements
  - Individual Proposals will be evaluated against the evaluation criteria – not against each other
- Award Selection:
  - Based on overall merit of proposal in response to the FOA, Agency need, and Available funding

EVALUATION CRITERIA

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- The following four factors will be evaluated in descending order of importance: (1) Business Plan; (2) Technical Plan; (3) Educational Workforce Plan; and (4) Cost.
  - Factor 1 is broken down into 7 subfactors of equal importance.
  - Factor 2 is broken down into 3 subfactors of equal importance.

EVALUATION CRITERIA

ADVANCED TISSUE BIOFABRICATION
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June 23rd, 2016

- Factor 1: Business Plan
  - Assess the business plan which will describe how the ATB-MII will design, integrate and sustain the ecosystem within the membership and its external stake holders
- Factor 2: Technical Plan
  - Assess technical strategy, innovation beyond current practice, and personnel qualifications
- Factor 3: Educational and Workforce Plan
  - Asses the quality and degree of integration of educational and workforce/professional development and training to support advancing technology
- Factor 4: Cost

COST PROPOSAL

ADVANCED TISSUE BIOFABRICATION
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June 23rd, 2016

- Concept Paper
  - The cost portion of the Concept Paper shall include a ROM cost estimate. No detailed price or cost support information should be forwarded; only a time-phased bottom line figure should be provided.

- Proposal
  - Breakout of all costs by FY
  - Labor hours (mix and type), material costs, sub-recipient cost (breakout)
  - Supporting documentation (basis for cost estimate)
  - Vendor quotes for equipment/materials etc.
  - Basis for travel estimates etc.

COST PROPOSAL

ADVANCED TISSUE BIOFABRICATION
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June 23rd, 2016

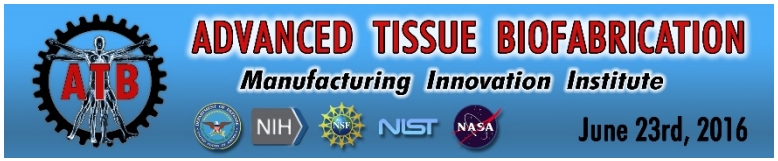
- Cost will be evaluated on reasonableness and realism of the proposed costs, to include cost share, consideration of proposed budgets and funding profiles. Cost Realism Analysis will ensure proposed cost:
  - Is realistic for work to be performed
  - Reflects a clear understanding of the requirements
  - Is consistent with the unique methods of performance and material described in Applicants' technical proposals

NOTIFICATION – CONCEPT PAPERS

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- Concept paper evaluations complete the week of 15 AUGUST 2016
- Request for full proposal notification sent Mid-Late AUGUST 2016
  - Only applicants invited to submit a proposal may do so
  - Unsuccessful concept paper proposers are encouraged to team with other entities
- Site visits may be scheduled
  - Dates TBD based on date of Proposal Invitations

NOTIFICATION – NEGOTIATION AND AWARD



- Selection for Negotiation Notification is not to be construed as an "assured award"
  - Successful Negotiations are required for award.
  - Inability to come to agreement on terms and conditions of the TIA within a reasonable time may result in moving to the next highest rated proposal.

Scheduled Award Date 16 DECEMBER 2016

SCHEDULE

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

MILESTONE	DATE
• Funding Opportunity Announcement	13 JUNE 2016
• Proposer's Day 1	17 JUNE 2016
• Proposer's Day 2	23 JUNE 2016
• Concept Paper Due	29 JULY 2016
• Concept Paper Evaluations Complete	WEEK OF 15 AUGUST
• Proposal Invitation	MID-LATE AUGUST 2016
• Proposals Due	On or about 18 OCTOBER 2016
• Proposal Evaluation Complete	
• Negotiations Complete	
• TIA Award	16 DECEMBER 2016

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

ADVANCED TISSUE BIOFABRICATION MII OVERVIEW (ATB-MII)

Kristy Pottol, Program Manager, *U.S. Army Medical Material Development Activity*

Brad Ringeisen, Chief Science Officer, *Navy Research Laboratory*

AGENDA

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- Introduction
- Government Team
- Vision
- Ecosystem Overview
- Evaluation Criteria
- Summary

INTRODUCTION

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- The broad field of regenerative medicine has the potential to be a game changer
- The federal government has invested significant amount of research funding for many years and we are at a point of inflection
- "What will it take to advance the industry forward?"
- This question has been explored in a number of road mapping efforts, workshops, special reports, and inter-agency meetings
- The distillation of these efforts has led to the first bio-focused manufacturing innovation institute

BRIDGING THE CAPABILITY GAP

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

ENABLING FEDERAL PROGRAMS

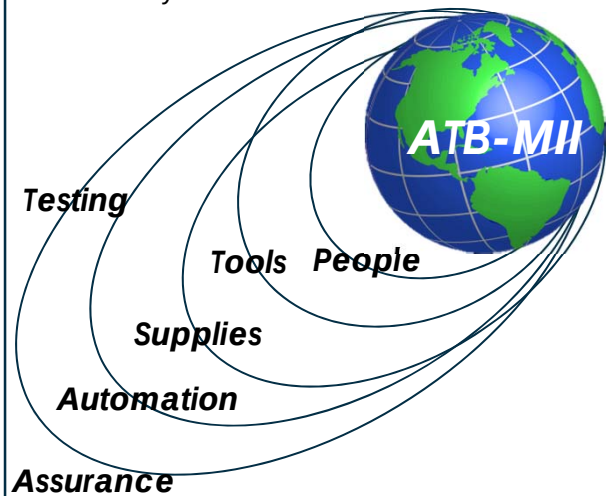
- ✓ Advanced Manufacturing, A Snapshot of Priority Technology Areas Across the Federal Government
- ✓ Regenerative Medicine: Federal Investment, Information Sharing, and Challenges in an Evolving Field

PROCESSES

- ✓ Measurement Science Standards
- ✓ Inspections
- ✓ Workforce Development
- ✓ Scale Up/Out
- ✓ Delivery Methods

TECHNOLOGIES

- ✓ Growth Media
- ✓ Cell Sourcing
- ✓ Preservation and transportation
- ✓ Biofabrication Platforms
- ✓ Testing platforms; sensors & assays
- ✓ Automation and Integration
- ✓ Software Design and Interoperability
- ✓ Central Taxonomy Databases



PRODUCTS & MEDICAL USES

- ✓ Pharmaceutical
- ✓ Biologic
- ✓ Precision & Personalized
- ✓ Regenerative Medicine
- ✓ Immunotherapy
- ✓ Devices
- ✓ Diagnostics
- ✓ Screening

ENABLING TECHNOLOGY MATURITY — ***Technology Available***

FDA REGULATORY PROCESS

PRODUCT & MEDICAL OUTCOMES MATURITY — ***Medical Solution Available***

GOVERNMENT TEAM

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- OSD Leadership: Office of the Secretary of Defense (OSD), Manufacturing and Industrial Base Policy (MIBP
- Contracting: U. S. Army Contracting Command, Aberdeen Proving Ground, Research Triangle Park having lead responsibilities to execute the solicitation and award management functions
- Program Manager (PM) & Deputy PM, represented by U.S. Army Medical Material Development Activity
- Chief Technology Officer (CTO), represented by U.S. Navy
- Gov't team: Army, Navy, Air Force, OSD, NSF, NIH, NIST, NASA

ENABLING FEDERAL PROGRAMS

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Discovery | **Development** | **Production**

- Bio-printing -> additive manufacturing
- Organ bioengineering roadmaps
- Methods to manipulate & track cell and tissue function
- Global Assessment of Biological Engineering & Manufacturing

- Bio-printing -> additive manufacturing
- Tissue on a chip
- Biopharmaceutical Development Program

- Tissue on a chip

- AMTECH Cell manufacturing consortium
- Measurement assurance for product characterization

- Manufacturing quality control development and research
- Regulatory oversight

- Medical Technology Enterprise Consortium (MTEC)
- MTEC-led Regenerative Medicine Manufacturing Technology, FY 16

- Additive Manufacturing Innovation Institute

VISION

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- Create an institute whose primary objective is to foster innovation in the U.S. for Advanced Tissue Biofabrication
  - How? It's all up to **YOU**
- Intent of DoD's investment is to have an ecosystem that if formed by organizing the currently fragmented U.S. capabilities in Advanced Tissue Biofabrication technology resulting in U.S. being better positioned relative to global competition
  - Structure:
    - Allows government, industry and academia to come together
    - Addressing both DOD and commercial applications, with a focus on maturing/scaling technologies from Manufacturing Readiness Level (MRL) 4 to 7

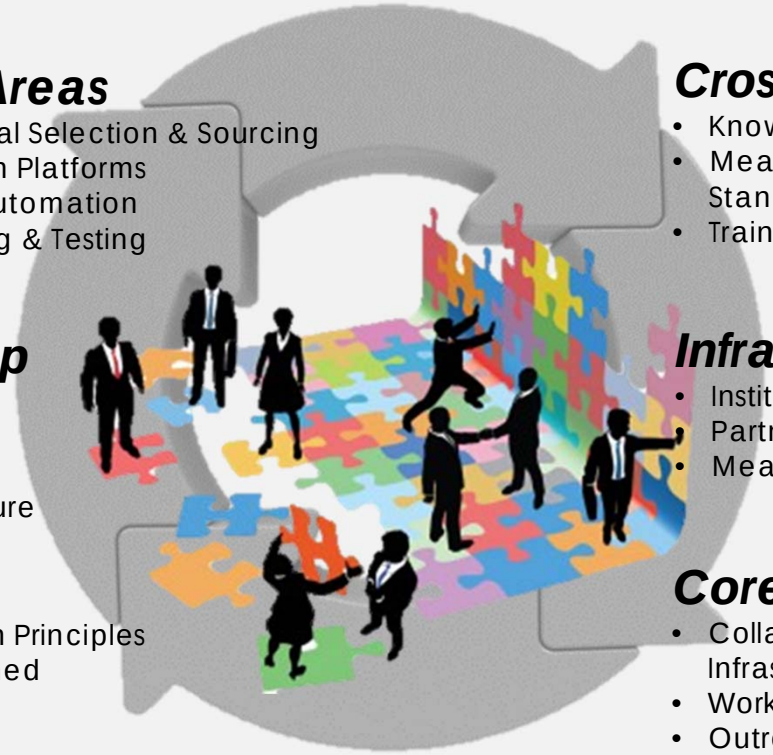
OPERATIONAL OVERVIEW

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

Thrust Areas
- Cell & Material Selection & Sourcing
- Biofabrication Platforms
- Bioprocess Automation
- Tissue Finishing & Testing

Leadership
- Vision
- Strategy
- People
- Defined Culture

Culture
- MII Operation Principles
- Lessons Learned
- Expectations



Cross Cutters
- Knowledge Gateway
- Measurement Science & Standards
- Training

Infrastructure
- Institute Design
- Partnerships
- Measures of Success

Core Process
- Collaborative Infrastructure
- Workforce Development
- Outreach for Relevancy

7. Results
- Current Performance
- SWOT
- ROI
- Cost Share
- Investments
- IP
- Service Sales
- Data Use
- Regulatory Pathways

MRL 1 - 3
Foundational Research

Pressure to System

ECOSYSTEM PRODUCT SERVICE & STRATEGY

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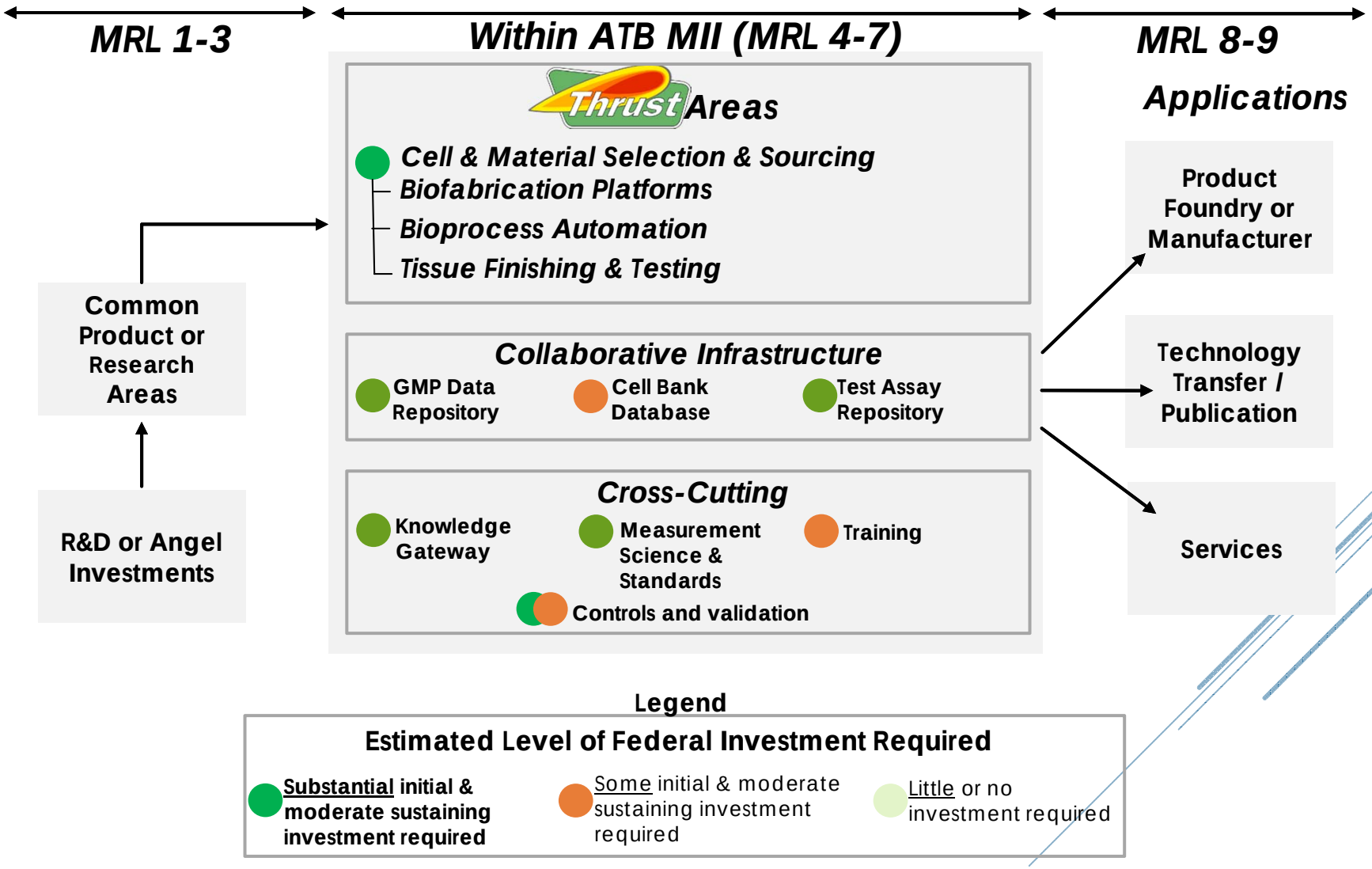

EXAMPLE PRODUCT LINES

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

MRL 1-3

DHA 4DBio3
"Bioprinting Consortium"
$9.5M POP 2016-2020

NIH NCATS
"Tissues Chips"
$70M POP 2012-2016

NSF EAGER
Investor-led Research
POP 2016-2018

DARPA
Microphysiological Systems
$70M POP 2012-2016

DTRA
eX vivo Capability for Eval and Licensure
$50M POP 2013-2017

Within ATB MII (MRL 4-7)

BIOMANUFACTURED PRODUCTS

Enable and support innovation in a range of technologies: pharmaceuticals, biologics, precision medicine, detection, diagnostics

MATURATION OF BIOFABRICATION TECHNOLOGIES

Bioprinting tools
Cell printing
Robotics/automation
Software
3D printing
Bioreactors

RECENT SCIENTIFIC ADVANCES

Stem cell biology
3D Printing
Biomaterials
Microfluidics
Systems biology
Cell sourcing
Stem cell differentiation
Biopolymers
Micro- and nanofabrication
Decellularized tissues

MRL 8-9
Industry Pull

Pharmaceutical
Drug efficacy and toxicity screening
Vaccine development
Immunotherapy
Teaming with organ-on-a-chip start-ups

Personalized & Precision Medicine
Precision medicine via patient-derived screening tests
Scale-up requires high throughput and automation

Cell Manufacturing & Sourcing
Established consortia
New stem cell products
Scale-up to meet demand for cell-based products

EVALUATION CRITERIA FACTOR-1 BUSINESS PLAN

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

- For the evaluation of **Factor 1**, the Government will assess the **Business Plan** which will describe how the ATB-MII will design, integrate, and sustain the ecosystem within the membership and its external stakeholders
- Discuss the coordination and operation of the ATB-MII through integration of the business plan sub-factors and enabling the advancement of the manufacturing readiness levels across the tissue biofabrication-related technology thrust areas
- Focused discussion on how these technology transitions will generate revenue for the ATB-MII
- Business and technical merits of the strategy for innovation and technology deployment/ dissemination should also be discussed
- **Factor 1 includes seven (7) sub-factors which will be evaluated and are equal in importance**

EVALUATION CRITERIA FACTOR-1 BUSINESS PLAN

ADVANCED TISSUE BIOFABRICATION
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- **<u>Organization, Governance, and Operations</u>**: Completeness and quality of the vision, culture, governance, and plan for the proposed organization and operation of the ATB-MII. This criterion includes the level and role of for-profit and non-profit organizations, institutions of higher education and multiple tiers of industry, end users, networked institutes, and the Government
  - Ability to bind all other participants to the terms and conditions of the award and to administer the award on behalf of the other participants
  - An agreement that the award terms and conditions take priority over those in the governance plan
  - Acknowledgement of the sub-recipients of their respective cost sharing and that no sub-recipient is responsible for the cost-sharing commitment of any other sub-recipient
  - The methods by which decisions will be made (e.g., with respect to operations, membership, capital investments, project selection, funding allocation, and progress toward self-sufficiency)
  - Draft ATB-MII organizational design, membership structure, governance agreements, and quality systems

EVALUATION CRITERIA FACTOR-1 BUSINESS PLAN

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- **<u>Management Capabilities</u>**: Caliber (experience / knowledge), commitment, quality, leadership, technical capabilities and successful track record of the Lead Organization, the Lead Organization Director and key personnel to design, establish, grow, and sustain the ATB-MII. This includes the capacity and capability to execute the ATB-MII operational plan
  - Degree of leadership, technical capabilities and successful track record of the Lead Organization, Organization Director and key personnel and level of commitment to the ATB-MII
  - The relevant experience in successfully developing collaborative shared user facilities, capital equipment, and integrated workflows
  - Years of experience, areas of experience, relevancy of leadership and managerial experience and the ability to bring diverse stakeholders together for a common goal
  - Specific skills of key personnel necessary to execute the business of the ATB-MII and support the plan to take scientific efforts and translate them so that industry can understand and adopt

EVALUATION CRITERIA FACTOR-1 BUSINESS PLAN

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- **<u>Physical Infrastructure</u>:** Soundness, availability, and access of the overall infrastructure proposed within existing facilities, including quality, capabilities, and availability of existing and proposed equipment, to include future infrastructure potential
  - Describe relevant physical infrastructure to include the sufficiency of geographic concentration to support the overall ATB-MII processes, including the manufacturing hub and other needed nodes
  - Capability to attain critical mass of capability and foster an active advanced tissue biofabrication manufacturing innovation ecosystem
  - There is a preference for existing facilities that are currently owned or leased. **No new construction is allowed with federal funds**.

EVALUATION CRITERIA FACTOR-1 BUSINESS PLAN

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- **<u>Cost Share</u>**: The makeup, extent, and quality of commitments, of the cost share plan proposed over the life of the award. This includes the amount, source of the cost share, the timing of availability, the quality/applicability of any cost share, conditions of the cost share, and the impact of the cost share to the program over the period of performance
  - Overall cost share, source, category, and conditions associated with the cost share must be provided
  - A minimum 1:1 cost share against federal dollars is required, and greater cost share is encouraged
  - The cost share should be fully auditable and traceable
  - Cost share that is **evenly dispersed throughout the period of performance** is preferred over front-loaded or rear-loaded cost share
  - As a part of the Business Plan it is noted that cash contributions support the self-sustaining aspect of the ATB-MII more than in-kind contributions, although both categories are desirable and will be used to evaluate quality and make-up

EVALUATION CRITERIA FACTOR-1 BUSINESS PLAN

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- **Intellectual Property (IP) Management:** Soundness of plan for managing and protecting intellectual property and the extent to which the IP management plan incentivizes private sector involvement as sub-recipients and sustainment
  - The treatment of confidential information between recipient and sub-recipients
  - The treatment of background IP
  - The treatment of inventions made under a project
  - The treatment of data produced, including technical data, software and documentation, under the project The treatment of any intellectual property issues that may arise due to a change in the make-up of sub-recipients
  - The handling of conflicts of interest of consortia or recipient and sub-recipients
  - The handling of disputes related to intellectual property between the recipient and sub-recipients
  - Government Use Rights
  - The manner in which Cyber Physical Systems Security measures will be addressed and managed to protect intellectual property

EVALUATION CRITERIA FACTOR-1 BUSINESS PLAN

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- **<u>Self-Sufficiency</u>:** Viability of the plan for the ATB-MII to achieve financial self-sufficiency beyond the end of ATB-MII agreement performance period while maintaining an enduring industrial ecosystem and workforce development programs to meet technology needs
  - Plan for the ATB-MII to achieve financial self-sufficiency within the 7-year period of performance
  - Plan for developing additional revenue outside of the funding provided by the Government in support of financial independence and the plan for leveraging federal funds to optimize advancement of programmatic goals appropriate for the maturity of the technology under development
  - Describe the potential sources of outside funds (*e.g.*, membership fee structure, etc.)
  - Describe the management approach of focusing the research of the ATB-MII to develop the breadth and depth of research to specific areas that lend themselves to supporting a self-sustaining applied research ATB-MII
  - Include specific target metrics to track progress

EVALUATION CRITERIA FACTOR-1 BUSINESS PLAN

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- **<u>Defense and Economic Impact</u>**: Viability of the plan for the ATB-MII to achieve financial self-sufficiency beyond the end of ATB-MII agreement performance period while maintaining an enduring industrial ecosystem and workforce development programs to meet technology needs
  - Relevance and potential U.S. economic impact (job creation, spin-off companies, etc.) of the proposed ATB-MII on the technology transition for commercial and defense applications
  - Relevance and contributions of the proposed effort to advance the manufacturing readiness level and accessibility to industry and/or the government and Government missions and the extent to which the overall ATB-MII proposal enables ecosystem development
  - Describe the proposed transition pathway to commercialization and give examples of previous successful transitions that have been executed.
  - Include more detailed expected contributions in the near (2-3 years), mid (4-7 years) and long term (8+ years)
  - Include any technology transfer and commercialization requirements or arrangements between the recipient and sub-recipients

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- As part of the evaluation of **Factor 2,** the **Technical Plan**, the Government will evaluate **three (3) subfactors of equal importance** they are: **Technical Strategy, Innovation Beyond Current Practice and Technical Personnel Qualifications**

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- **<u>Technical Strategy</u>**: Overall scientific and technical merits, quality, and level of innovation within the thrust areas and cross-cutting areas of the proposed approach with clear technology advancement goals or milestones. The breadth of the technical strategy to utilize each element of the ATB-MII ecosystem to its maximum potential in order to realize manufacturing advances
  - Approach to establish a national ATB-MII as a resource to focus on the complex issues in advanced tissue biofabrication, develop solutions to create cost-effective manufacturing capabilities that offset the risk to the U.S industrial base in adopting these new technologies, using a collaborative approach between industry, academia, government, and the workforce
  - address the technical aspects of an end-to-end 'ecosystem' in the U.S. for advanced tissue biofabrication.
  - Provide a detailed structure addressing both DoD and commercial applications, with a focus on maturing technologies from Manufacturing Readiness Level 4 to 7.

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- **<u>Innovation Beyond Current Practice</u>**: Relevance, approach and potential impact to defense and other government/ commercial applications as detailed in four example applied research projects that address each of the core technical areas of the ATB-MII. These four example applied research projects will be divided into quick start, stop-gap, cross cutter, and self-select project categories in order to evaluate the Applicant's ability to exercise an ambitious and integrated ATB-MII technical plan

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- **Example Manufacturing R & D Projects for Advanced Tissue Biofabrication Technical Areas are: CRITICAL TECHNOLOGY, CROSS-CUTTER, QUICK-START and PROPOSER OPTION**

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- **Example Manufacturing R & D Projects for Advanced Tissue Biofabrication: CRITICAL TECHNOLOGY**
- Provide a solution to a critical technology hurdle. As an example, the proposer would outline the design, development, testing, optimization and standardization of non-destructive, in-line sensing or detection technologies to monitor environmental and/or cellular conditions during a tissue biofabrication process. In order to mature a tissue biofabrication technology into manufacturing practice, process monitoring at all stages is required that would aid in process optimization, real-time feedback, verification of process accuracy and precision as well as validation of the final tissue product. Important environmental and cellular conditions to monitor may include oxygen concentrations and gradients, cell viability, cell number, pH, molecular and/or ion diffusion and detection of secreted biofactors

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- **Example Manufacturing R & D Projects for Advanced Tissue Biofabrication: CROSS-CUTTER**
- Provide a solution for an end-to-end, cross-cutting tissue biofabrication process. As an example, the proposer would outline the entire manufacturing process for creation of a high throughput tissue-based assay. The proposer would describe solutions to each of the four technology thrust areas (detailed in Appendix A), providing a description of: (a) cell sourcing and differentiation, (b) biofabrication platform choice, description and validation, (c) process design, integration and automation and (d) finishing and testing technologies that will be used to mature the tissue-based assay and validate its viability and efficacy. For this example it will be important for proposers to address how cross-cutting technologies such as measurement science, workforce training and accessibility of technology will be used to enhance the manufacturing process and product

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- **Example Manufacturing R & D Projects for Advanced Tissue Biofabrication: QUICK-START**
- As an example, the proposer would describe the set-up and execution of a virtual knowledge gateway. This enhanced data repository would make critical information on tissue biofabrication processes (cell sourcing and differentiation protocols; bioprinting protocols including bio-ink formulations, software, and process controls and settings) available and accessible to team members. This gateway would improve information dissemination, team-to-team coordination, process and foundational component standardization, protocol optimization and collaboration throughout the ATB-MII

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- **Example Manufacturing R & D Projects for Advanced Tissue Biofabrication: PROPOSER OPTION**
- The fourth example project must be determined by the proposer and should highlight the strengths and uniqueness of the proposed ATB-MII technologies and team members. The project should be representative of one or more thrust areas.

EVALUATION CRITERIA FACTOR-2 TECHNICAL PLAN

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- **<u>Technical Personnel Qualifications</u>**: The qualifications, capabilities and experience of the technical personnel
  - Illustrate the qualifications, capabilities and experience of the technical personnel and their ability to effectively manage and perform the research and development activities of the ATB-MII
  - Provide a summary of the plan for a proposed technical management structure of the ATB-MII
  - Short biographies for the key technical personnel
  - Qualifications of technical personnel include, but are not limited to, certifications, advanced degrees, professional licenses, etc. Capabilities include, but are not limited to, knowledge of the ATB-MII thrust areas
  - Relevancy and extent of work performed in the domain of the ATB-MII thrust areas

EVALUATION CRITERIA FACTOR-3 EDUCATIONAL AND WORKFORCE

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- **<u>Education and Workforce Development Plan</u>:** The quality and degree of integration of educational and workforce/ professional development and training to support advancing technology will be evaluated
  - Description of the educational and workforce development components of the ATB-MII
  - Plan should consider all levels of education and position within the supply chain, including workforce retraining, 2 and 4 year undergraduate programs, graduate and post-graduate engagement, faculty engagement, internships, sabbaticals, and professional development necessary to ensure the next-generation tissue biofabrication workforce has the knowledge and skill required to enable U.S. advanced tissue biofabrication enterprises
  - The plan should establish an effective development with TRL/MRL 1-3 performers at colleges and universities and include how the ATB-MII will partner with intermediary organizations to enhance the involvement of students, teachers, and faculty
  - Degree of integration will be measured based on the level of consideration given to the inclusion of all levels of education and the opportunities provided by the ATB-MII for industrial personnel, faculty, students, researchers, and the commercial workforce to collaborate in the development of the materials, coursework and the research and practical experiences needed to ensure the availability of a workforce that is prepared for an effective transition to employment in the U.S. advanced tissue biofabrication manufacturing industry

EVALUATION CRITERIA FACTOR-3 EDUCATIONAL AND WORKFORCE

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- **<u>Education and Workforce Development Plan</u>:** The quality and degree of integration of educational and workforce/ professional development and training to support advancing technology will be evaluated
  - Illustrate the design for education and workforce development as part of the ATB-MII operating structure
  - Provide a summary of the educational and workforce/professional development training components
  - Describe how the ATB-MII will partner with intermediary organizations, such as the National Institute of Standards and Technology Manufacturing Extension Partnerships, National Science Foundation Advanced Technological Education Centers, Engineering Research Centers, Industry/University Cooperative Research Centers, Trade Adjustment Assistance Community College and Career Training Centers, regional and state economic development organizations, and other intermediaries that provide manufacturing outreach and training
  - Plans for encouraging efficient access by graduate- and undergraduate-level researchers and community college technicians-in-training to specialized equipment and facilities in the ATB-MII and opportunities for students to interact with industry-based engineers should be included

EVALUATION CRITERIA FACTOR-4 COST

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- **Reasonableness and realism of the proposed costs**, to include cost share, consideration of proposed budgets and funding profiles. Cost Realism Analysis will ensure proposed cost:
  - Is realistic for work to be performed
  - Reflects a clear understanding of the requirements
  - Is consistent with the unique methods of performance and material described in Applicants' technical proposals

ATB-MII REVIEW

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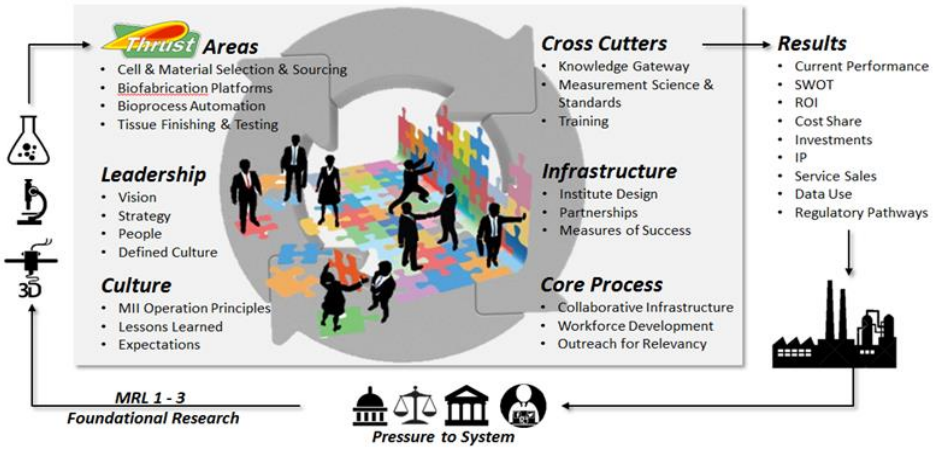
Thrust Area Overview

- Cell & Material Selection & Sourcing: standardization of starting materials, post-delivery assurance of tissue identity, viability, function and efficacy
- Biofabrication Platforms: transform standardized starting materials into novel and evolving tissue and tissue-related end-products
- Process Design and Automation: improve the scale, throughput, automation, and reproducibility of engineered tissues
- Tissue Finishing and Testing Technologies: non-destructive or minimally destructive test/sensors, real-time monitoring/sensing technologies

Biofabrication Innovation Ecosystem



- ATB-MII ecosystem assembles broad multi-disciplinary sub-recipients that are currently fragmented into a cohesive unit that provides prototyping and process advancements across multiple technology thrust areas

Funding and Acquisition Schedule

Fiscal Year	FY17	FY18	FY19	FY20	FY21	FY22	FY23	Total
Federal Govt Funding	$18	$18	$18	$18	$8	$0	$0	$80M
Non-Federal Government Cost Share (Minimum)								$80M
Total Program (Minimum)								$160M

- NOI released 23 May 2016; FOA released 13 June 2016
- Award Target: MID December 2016

Desired Results

- Bring together diverse and synergistic biologic science and engineering disciplines with traditional manufacturing processes
- Accelerate industrialization of emerging Biofabrication technologies
- Establish a manufacturing hub that supports standardization of starting materials as well as post-delivery assurance of tissue identity, viability, function and efficacy

SUMMARY

ADVANCED TISSUE BIOFABRICATION
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- **Excellent opportunity to create a center of excellence for ADVANCED TISSUE BIOFABRICATION**
- Successful partnership between Government, Academia, and Industry
- Benefits for DoD, the Federal Government and Commercial Industry will be substantial
- Opportunity to network with other Innovative Manufacturing Institutes
- Will Provide a technological leap to further U.S. economic competitiveness
- **All questions will be addressed later in the day**

INITIAL QUESTION AND ANSWER SESSION

LUNCH

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MULTI-AGENCY TISSUE ENGINEERING SCIENCE (MATES) INTERAGENCY WORKING GROUP

Richard McFarland, PhD, MD

MATES Chair, US Food and Drug Administration (FDA)

PRE-MATES HISTORY

1980's-1990's

- Ad hoc interactions among various agencies (NSF, NIH, ONR, DOE, NASA)
- Coining of term "tissue engineering"
- UCLA Symposium ("Keystone Conference") on "Tissue Engineering" in 1988

WHAT IS MATES?

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- **M**ulti-**A**gency **T**issue **E**ngineering **S**cience Interagency Working Group

- ***A longstanding means by which Federal agencies involved in tissue engineering stay informed of each other's activities and coordinate their efforts***

GOALS OF THE MATES INTERAGENCY WORKING GROUP

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- Facilitate communication across departments/agencies by regular information exchanges and a common web site.
- Enhance cooperation through co-sponsorship of scientific meetings and workshops.
- Monitor technology by undertaking cooperative assessments of the status of the field.
- Provide support for tissue engineering research through interagency funding opportunity announcements.
- Foster technology transfer and translation of research advances into practical applications.
- Promote the formulation and use of standards for both research tools and product development.

MATES HISTORY 1999-2009

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- **MATES** formally organized under the auspices of the Subcommittee on Biotechnology of the National Science and Technology Council. Office of Science and Technology Policy, Office of Management and Budget
- Strategic Plan for Tissue Engineering, "Advancing Tissue Science and Engineering: A Multi-Agency Strategic Plan" **2007**

ADVANCING TISSUE SCIENCE AND ENGINEERING

A MULTI-AGENCY STRATEGIC PLAN

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OVERARCHING GOALS FOR TISSUE SCIENCE AND ENGINEERING

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- Understanding and controlling the cellular response
- Formulating biomaterial scaffolds and the tissue matrix environment
- Developing enabling tools
- Promoting, scale-up, translation, and commercialization

2007 Strategic Plan

CATALYSTS AT EVERY STAGE OF DEVELOPMENT

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- Basic Science and Engineering
  - NSF
- Basic and Translational Research
  - NIH
- Mission-supportive Material and Functions
  - DoD
- Development of Enabling Technology
  - NIST
- Regulatory- Science, Policy, Review
  - FDA

STRATEGIC PRIORITIES FOR FEDERAL GOVERNMENT AGENCIES

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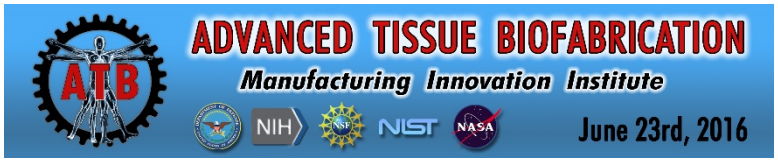
- Understanding the cellular machinery
- Identifying, Validating Biomarkers and Assays
- Advancing Imaging Technologies
- Defining cell/environment interactions
- Establishing computational modeling systems
- Assembling and maintaining complex tissue
- Improving tissue preservation and storage
- Facilitating effective applications development and commercialization

2007 Strategic Plan

MATES HISTORY 2009-2014



- Standing NSTC committees status changes as result Presidential transition
- MATES members chose to continue to use this mechanism for information sharing, collaboration and leverage of their agency's efforts.
- Continuing implementation of strategic plan by MATES agencies
- Highly active agencies during this era: NIH, FDA, NIST, DOD, NSF

MATES RECENT HISTORY 2014-2016

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- TERMIS Preconference Workshop (2014)
- GAO Report (2015)
- MATES Strategic Retreat (2015)
- NSTC Snapshot Advanced Manufacturing (2016)

PRE-CONFERENCE WORKSHOP TERMIS-AMERICAS 2014 "RESTORING LIVES THROUGH REGENERATIVE MEDICINE"

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- "Government Efforts on the Path to Patients for Regenerative Medicine Therapies: A MATES symposium"
  - Paired talks- Govt. and Private Sectors
    - NSF
    - NIH
    - DoD
    - NIST

United States Government Accountability Office

Report to Congressional Requesters

GAO

June 2015

REGENERATIVE MEDICINE

Federal Investment, Information Sharing, and Challenges in an Evolving Field

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DEFINITIONS USED IN THE GAO REPORT

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- **Tissue Engineering**: an interdisciplinary domain that combines engineering and materials science with Medicine. In general, constructs are made in vitro, and transplanted in vivo

- **Regenerative Medicine**: self-healing through endogenous recruitment or exogenous delivery of appropriate cells, biomolecules, and supporting structures

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GAO REPORT CONCLUSIONS

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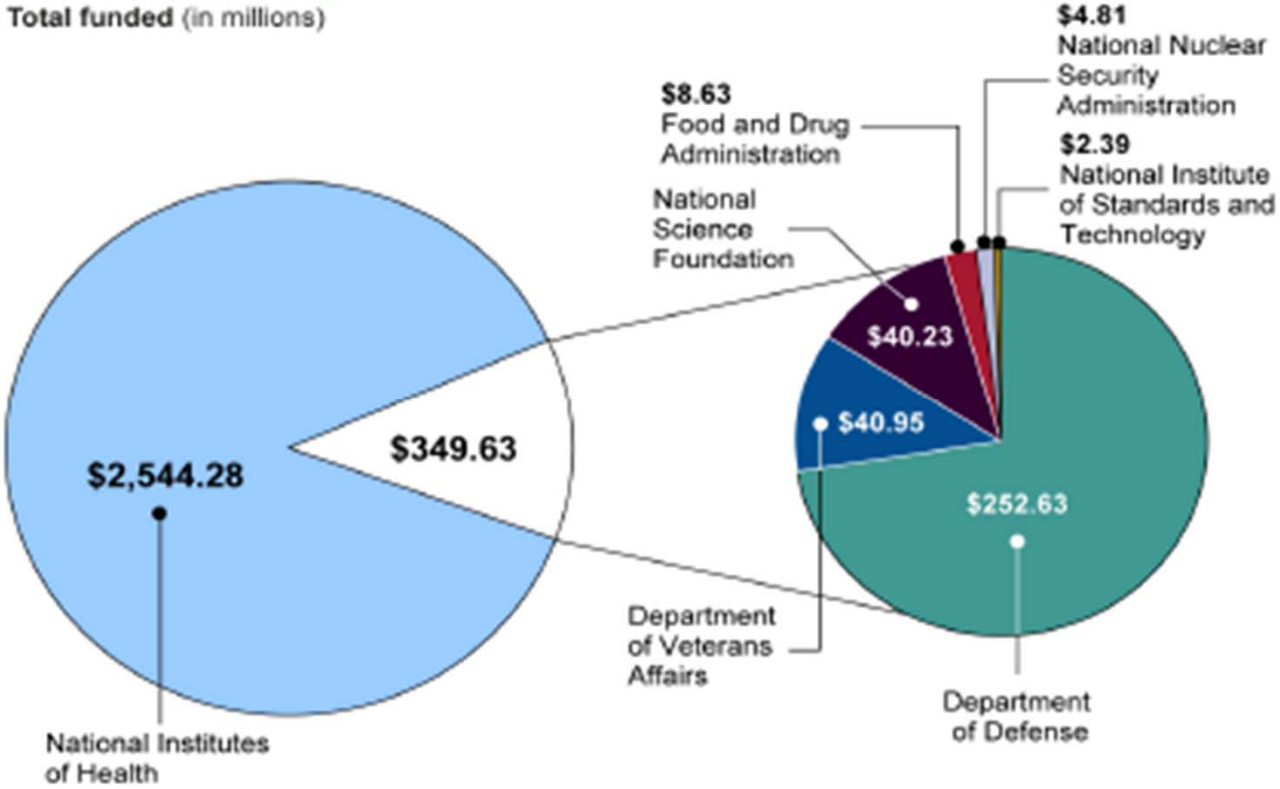
- Seven federal agencies invested $2.89 billion in regenerative medicine research (as defined by the GAO) in FY 12-14
- These agencies have established mechanisms for sharing information
- Challenges identified for field

Federal Funding for Regenerative Medicine Research, Fiscal Years 2012 through 2014

Total funded (in millions)



Source: GAO analysis of agency funding on regenerative medicine research. | GAO-15-553

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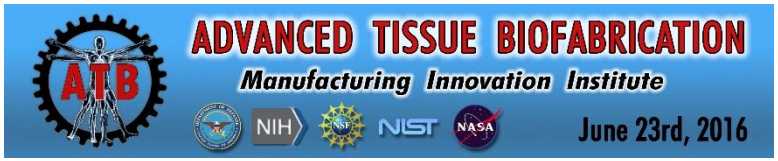
ESTABLISHED MECHANISMS FOR SHARING INFORMATION AMONG GOVERNMENT AGENCIES



- MATES meetings
- Co-funding research
- Co-sponsoring workshops

GAO

Table 1: Federal Agencies That Conducted or Funded Regenerative Medicine Research, Fiscal Years 2012 through 2014

Federal agency	Agency mission	Regenerative medicine research conducted includes
Department of Defense	Provide the military forces needed to deter war and to protect the security of the country	Research and applications for active-duty personnel including limb repair, traumatic brain injury, and battlefield injuries
Department of Veterans Affairs	Provide veterans and eligible beneficiaries with benefits and services	Research and applications for the veteran population, including limb repair, traumatic brain injury, and care for wounded warriors, as well as for stroke, glaucoma, and other conditions for an aging veteran population
Food and Drug Administration within the Department of Health and Human Services	Protect the public health by ensuring the safety, efficacy, and security of human drugs, biological products, medical devices, food supply, cosmetics, and products that emit radiation	Safety and effectiveness research related to regulation of regenerative medicine products and standards development
National Institute of Standards and Technology within the Department of Commerce	Promote innovation and industrial competitiveness by advancing measurement science, standards, and technology	Measurement science and development of consensus documentary standards and standard reference materials to facilitate commercialization of regenerative medicine products[a]
National Institutes of Health within the Department of Health and Human Services	Seek knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability	Biomedical applications and basic, clinical, and translational research, including stem cells and tissue engineering
National Nuclear Security Administration within the Department of Energy	Enhance national security through the military application of nuclear science; responsible for issues of nuclear defense, nonproliferation, and naval research	Research and development, including basic research and experiments designed to determine the utility of new scientific ideas, technical concepts, or devices
National Science Foundation	Promote and advance fundamental scientific progress	Basic research with a focus on expanding current scientific knowledge

Source: GAO analysis of agency interviews and information. | GAO-15-553

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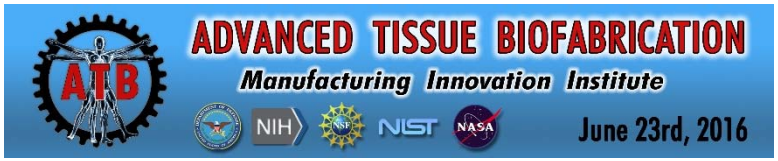
CHALLENGES FOR THE RM FIELD



- Establishing effective collaborations between federal and nonfederal stakeholders
- Recruiting scientists and engineers with RM expertise to the federal workforce
- Navigating the regulatory and product approval processes
- Making decisions about Medicare coverage, reimbursement rates for newly approved products

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TECHNICAL CHALLENGES FOR THE RM FIELD

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- Transitioning from an academic enterprise to an industry-based, commercial enterprise
- This transition requires a rigorous focus on starting materials, process, and final product characteristics to assure that products are safe, effective, and have a known potency and predictable shelf-life

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TECHNICAL CHALLENGES FOR THE RM FIELD

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- Continued maturation is dependent on designing and developing robust production-scale manufacturing techniques
- Refined set of measurements and standards that provide confidence in the product
- Workforce development
- Supply chain diversification

MATES STRATEGIC RETREAT

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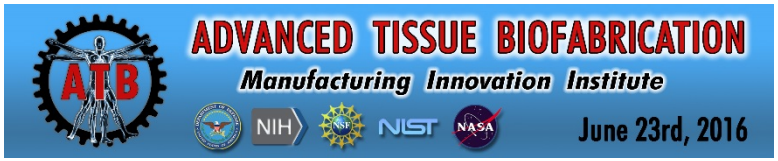
Food and Drug Administration

Silver Spring, Maryland

April 8, 2015

MATES STRATEGIC RETREAT



- The "Overarching Goals" outlined for the field in the 2007 plan remain
- Agencies have made progress toward reaching these goals by working on the "Strategic Priorities" in the 2007 Plan
- Sufficient progress toward the goals have been made to consider a pivot of emphasis toward the overarching goals of
  - Developing enabling tools
  - Promoting, scale-up, translation, and commercialization

TACTICAL PRIORITIES FOR MANUFACTURING

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- 1. Scale-up and quality control for batch processing of both suspension and adherent cells, including advanced separations technologies for product purification

- 2. Scale-out and quality control of 3D tissue units (e.g. Microphysiological Systems, or "tissue chip" prototypes) that can be made patient-specific

- 3. Controlled, user-friendly processes for differentiation of pluripotent (e.g. stem) cells and induction of tissue morphogenesis

TACTICAL PRIORITIES FOR MANUFACTURING

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- 4. Additive Manufacturing/Bioprinting of 3D constructs containing both cells and their support matrix in desired configurations

- 5. Bioreactor systems with continuous on-board, in-line, non-destructive process monitoring, and real-time manipulation of tissue morphogenesis within the bioreactors' environment

- 6. Standards and assays (potency, metabolic profile and phenotype/genotype fidelity) along the entire production line

- 7. Preservation technologies to sustain and assure functionality of fragile cells and tissues under biologically optimized conditions for storage, shipment and handling

ADVANCEDMANUFACTURING

A Snapshot of Priority Technology Areas Across the Federal Government

PRODUCT OF THE
Subcommittee for Advanced Manufacturing
OF THE NATIONAL SCIENCE AND TECHNOLOGY COUNCIL

February 2016

ADVANCED TISSUE BIOFABRICATION
Manufacturing Innovation Institute
June 23rd, 2016

CONTINUED STRONG MULTI-DISCIPLINARY AND COLLABORATIVE APPROACHES FOR FUTURE SUPPORT OF MANUFACTURING TECHNOLOGIES

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- To manufacture specific tissues, a project team must have advanced engineering skills combined with a deep understanding of the physiology of those tissues and the organ systems in which those tissues function.
- Statistics and computational modeling will be critical for designing and testing the platforms that will shape the product development plan and the regulatory strategy.
- Controlling and characterizing the biologic activity through discovery, triggers, and terminations of the appropriate effector and control mechanisms at the individual cell and population levels will require the expertise of genomic scientists.

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- A fundamental knowledge and understanding of developmental biology is required to deliver an adult phenotype and to regulate growth reproducibly over time.
- Efficiencies at each step are essential to keep costs and raw materials usage down, and to keep fragile products (i.e., cells, tissues) viable, while a constant focus on usability will ultimately help enable adoptability.

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ADDITIONAL QUESTION AND ANSWER SESSION

CONCLUDING REMARKS