

**FA8650-19-S-5028**

**MANUFACTURING INNOVATION INSTITUTE**

**Request for Information:**

**Specific Synthetic Biology Manufacturing Focus Areas  
Suitable for a Manufacturing Innovation Institute**

**1. Contracting Office Address** Department of the Air Force, Air Force Research Laboratory (AFRL) – Wright Research Site, AFRL/RXKMC, Area B, Bldg. 45, 2130 8th Street, Wright-Patterson AFB, OH, 45433-7541.

**2. General Information** This is a Request for Information (RFI) only, as defined in FAR 15.201(e), to obtain information about pricing, delivery, capabilities, and other market information for planning purposes. This RFI is being published on behalf of the Office of the Undersecretary of Defense (OUSD) for Research and Engineering (R&E). This RFI is not a request for competitive proposals; therefore, responses to this notice are not considered offers and cannot be accepted by the Government to form a binding contract. Responses should include information identifying whether the responder's firm is a small or large business. A small business is defined as having 500 or fewer employees. The NAICS codes for this potential effort are 541713, 541714, or 541715. Companies that respond will not be paid for the information submitted. No telephone calls will be accepted requesting a bid package or solicitation. There is no bid package or solicitation. All information received shall be safeguarded from unauthorized disclosure. Please do not submit any proprietary or classified information.

**3. General Intent** The OUSD(R&E) has established Biotechnology as a Defense-wide Modernization Priority. A potential benefit offered to DoD by biotechnology is the ability to secure the supply chain for a wide range of non-medical products via biomanufacturing from domestically sourced feedstocks and reagents, including synthesized DNA. Other possible benefits include reduction in lifecycle costs by utilizing sustainable and self-renewing processes, enhanced or novel product performance, biosecurity, and potential for distributed manufacturing including in austere environments. Defense applications that may be addressed using synthetic biology-enabled manufacturing include but are not limited to small molecules or precursors of small molecules for monomers/pre-polymer/resins/coatings, materials to be used in extreme environments, energetics, electro-magnetic nanomaterials, catalysts (e.g., for fuel cells), structural materials (bio-inorganic hybrid materials), sensors, and living organism products (e.g., for growable biomaterials, bioremediation, bioleaching, probiotics, and sensors). The combination of defense priorities addressable by synthetic biology manufacturing and the commercial potential of these innovations to industry will require the expansion of a relatively small number of experts into an ecosystem and workforce capable of innovating and supplying U.S. defense and commercial requirements.

The Department of Defense (DoD) is therefore seeking input from industry, academia, non-profits, and other stakeholders as it considers the establishment of a Manufacturing Innovation

Institute (MII) dedicated to synthetic biology (SynBio) for non-biomedical applications. The SynBio MII will seek to enable a wide range of commercial and defense-relevant products and applications that can be customized to continuously evolving DoD and commercial needs. The information provided under this RFI will be used to determine the viability of using a public-private partnership business model and to select and scope the technology focus areas. The Department is requesting responses that will assist in refining the technology focus areas currently under consideration (section 5 below), based upon evidence of support for national security requirements, economic benefit, technical opportunity, relevance to industry, sustainability, and workforce development opportunities.

Today, the MII network contains 14 Institutes that each have a specific technology or market focus, led by a not-for profit organization that includes domestic-based members from industry and academia. The goal of the SynBio MII would be to create an impactful public-private partnership enabling the advanced development and scale-up of emergent biomanufacturing technologies and processes with the goal of successful transition of existing science and technology into defense and commercial manufacturing applications.

The SynBio MII would be distinct from two other existing MIIs associated with biotechnology: the Department of Commerce (DOC) sponsored National Institute for Innovation in Manufacturing Biopharmaceuticals (NIIMBL) and the DoD's Advanced Regenerative Manufacturing Institute: BioFabUSA. NIIMBL's focus is on innovation leading to flexible and agile manufacturing processes for biologic therapies to treat debilitating illnesses. BioFabUSA is focused on establishing large-scale manufacturing of engineered tissues and regenerative medicines. Because both NIIMBL and BioFab USA are focused on products ultimately for human use, the subject matter experts, regulatory environment, methodologies, and toolsets used to produce molecules and materials envisioned in the SynBio MII are substantially different than those employed by them. None-the-less, we anticipate the SynBio MII to interact closely and collaborate with all MIIs, including NIIMBL and BioFabUSA, to seek areas of common interest and reduce or eliminate areas of potential overlap.

The overall goal of the SynBio MII is to reduce the cost and time to achieve robust biomanufacturing with a focus on fostering and sustaining a globally-competitive U.S. manufacturing base. It is anticipated that the SynBio MII will deliver:

- 1) Commercializable amounts of target molecules, materials, or cell-based products through scale-up manufacturing and down-stream processing, and
- 2) Platforms for testing and evaluation in order to rapidly and thoroughly assess and identify novel functionalities of target molecules, materials or cell-based products.

As part of the RFI process, the government will host two workshops to solicit feedback and foster in-depth discussions on this topic. For additional information and to register for one of the following workshops: <https://synbio.anser.org>

- **October 23, 2019** (eastern U.S location): Sheraton Boston Hotel, 39 Dalton Street, Boston, MA 02199
- **October 25, 2019** (western U.S. location): NextFlex, 2244 Blach Pl Suite 150, San Jose, CA 95131

**4. Background** Information related to the DoD MII network managed by the OUSD(R&E) Manufacturing Technology (ManTech) Program can be found via <https://www.dodmantech.com/>. A national MII network overview, including annual reports and a current strategic plan, is available at <https://www.manufacturing.com/>. Respondents to this RFI may wish to use these sources as reference material for additional information during formulation of inputs.

**5. DoD SynBio MII Potential Technology Focus Areas** The ManTech program invites responders to provide information in support of a potential future solicitation for a SynBio MII. While current MIIs are led by non-profit organizations, MIIs are ultimately industry-driven in order to be sustainable over time and promptly address both commercial and defense needs. Therefore, all responsible sources are encouraged to submit information that shall be considered by the Government.

We ask respondents to align their inputs with one or more of the three following technology focus areas of interest: A. *Scale-Up Manufacturing* (SUM), B. *Down-Stream Processing* (DSP), and C. *Testing and Evaluation* (T&E). Response should address the general questions listed in section 5.D. below as they relate to each technology focus area of interest addressed.

**A. Focus Area 1: Scale-Up Manufacturing (SUM)** For the SUM topic, the DoD is interested in approaches that facilitate domestic biosynthetic production of molecules (organic molecules, biopolymers, inorganics) and cells. Central to synthetic biotechnologies is the engineering of chassis organisms that are designed to reliably perform an intended function. However, while cellular behavior/yield/growth may be optimized in small-scale systems, engineered organisms often do not behave predictably when introduced into larger scale fermentation systems or other scale-up methods (e.g., via distributed systems or co-location with domestic feedstocks). To increase the use of engineered organisms in manufacturing, the community needs better tools for scale-up manufacturing, including models to relate lab-scale and full-scale fermentation, analytics, and reactors that monitor and adjust growth conditions, metabolites, yield, and other parameters in real time.

*Focus Area 1 (SUM) key areas are of interest include:*

- Predictive models and simulations for fermentation to optimize control parameters at multiple scales
- In situ, real-time, responsive fermentation processes
- Cost-effective and scalable bioreactors for a variety of engineered organisms
- Cost-effective and scalable bioreactors for a variety of feedstocks or adaptable to different feedstock formats, preferably domestically sourced

- Artificial Intelligence (AI)/Machine Learning (ML)-enabled data analytics for optimization, quality control, or to inform cross-platform applications
- DNA sequencing, synthesis, and secure data sharing platforms, allowing tracking of sample/organism provenance, storage and access to datasets

**B. Focus Area 2: Down-Stream Processing (DSP)** DSP refers to post-fermentation characterization, processing and purification of biosynthetic products or cells. In order to advance bio-manufacturing, separation techniques (e.g., tangential flow filtration, distillation, etc.) need to be scalable and commercially-viable. DSP can be performed after small, medium- or large-scale fermentation, and also is essential to confirm that a desired product has been synthesized or cultivated, that it represents a certain fraction of the total products, and that desired purity has been achieved. Novel separation technologies, perhaps borrowed from the chemical engineering and/or materials science communities, may be required. Purification of unique bio-made products (e.g., intact cells) may require development of more tailored, purification tools that are designed for these types of products.

*Focus Area 2 (DSP) key areas are of interest include:*

- Novel strategies for cost-effective purification, including targeting secretion or isolation of products from cells (e.g., exosomes, inclusion bodies, and cell-surface bound products)
- Approaches for separation of inorganic/organic nanomaterial products from cell fractions and other insoluble materials
- When cells are the product (e.g., a culture for bioremediation), improved strategies for reducing final product volume while preserving viability and activity (e.g., in anaerobes, extremophiles, and photosynthetic organisms), reconstitution by customer, and controlled release/delivery.
- Environmentally-benign processes, where feasible, with renewable/reusable processing streams (eg solvents, effluent)

**C. Focus Area 3: Testing and Evaluation (T&E)** The ability to rapidly assess and characterize emergent molecules, materials, and cells across a battery of tests and evaluation procedures will be critical, and will also facilitate identification of novel defense applications for biotech-enabled products. The required evaluation platforms present major challenges, in part because of the sheer diversity of new materials, molecules, and cells that will emerge from design-build-test biotechnology platforms. Comprehensive T&E platforms that harness state-of-the-art analytical tools for characterization, assessments, and measurements of bio-produced molecules, materials, and cells will underpin successful biomanufacturing of these types of products.

*Focus Area 3 (T&E) key areas are of interest include:*

- Platform technologies for the evaluation of chemical, thermal, physical, mechanical, and optical properties of emergent molecules and materials

- Technologies for determining the suitability of molecules/materials/cells for defense applications (e.g., high energy density fuels, thermostable polymers or energetics)
- High throughput evaluation methods to support the evaluation and characterization of emergent cells (e.g., viability, stability, fitness, containment)
- High throughput evaluation methods to identify modified organisms with favorable phenotypes (e.g., product/growth yield, tolerance) or to select new chassis organisms with favorable characteristics (e.g., ability to engineer, tolerance to production conditions, safety, etc.)
- High-throughput evaluation methods to assess and sort or filter desirable properties (e.g., folded nature of biopolymers)
- Machine learning applied to T&E platforms to extract key parameters that accurately predict desired properties of end products
- Lab-pilot-full production translatable evaluation methods to assess functional properties of living cells (e.g. small molecule production) in relevant environments
- Any other methods of testing and evaluation for use in bio-manufacturing

#### **D. Questions to Address**

1. What is the current state of U.S. and global manufacturing capability associated with synthetic biology and what are the limits of current practice?
2. Does this technology area allow for pre-competitive collaboration that protects shared background intellectual property (IP) and partnership generated IP? Which technical components are likely to be shareable pre-competitively? What strategies could be employed to address IP issues?
3. What level of investment would be meaningful? What cost-sharing models could be employed to generate these levels of investment (federal government, state and local government, industry, academia), and what level of investment is possible from non-federal government sources?
4. What metrics could be used to measure progress or success annually?
5. What current industrial infrastructure, including capital equipment, is available to address the technology focus area? What infrastructure is lacking?
6. What are barriers that must be addressed in order to better enable domestic supply chains for synthetic biology (e.g. feedstocks, synthesized DNA, and other reagents essential to biomanufacturing)?
7. What strategies should be employed to address biosafety, biosecurity, bio-containment and to consider potential unintended consequences of synthetic biology?
8. Are there other focus areas or key areas of interest that may be of greater potential than those identified in this RFI?

**6. Information Requested** Responders interested in any of the suggested technology focus areas (or others) are asked to organize the information they provide around the questions in section 5.D. Any additional information deemed relevant by respondents is encouraged as well (subject to the page count and format limitations in paragraph 7).

**DISCLAIMER:** This RFI is issued solely for information and planning purposes and does not constitute a solicitation. The Government does not intend to award a contract based on this RFI, nor is the Government obligated to issue a solicitation based on responses received. The Government does not consider responses to this notice to be offers nor can they accept responses to form a binding contract.

Respondents are advised that the Government is under no obligation to acknowledge receipt of the information received, or provide feedback to respondents with respect to any information submitted under this RFI. Neither proprietary nor classified information should be included in the submittal. It is the respondent's responsibility to ensure that the information owner has approved the submitted materials for public release. Respondents are solely responsible for all expenses associated with responding to this RFI. The Government will not provide reimbursement for costs incurred in responding to this RFI.

The information submitted in response to this RFI may be used to help the Government further define its requirements and business approach. Input on technical aspects of the responses may be solicited by the Government from non-Government consultants/experts who are bound by appropriate non-disclosure requirements. If the Government develops a program that addresses any submitted or similar topic, the resulting procurement will address technology and business specific requirements as defined by the Government. Responders to this RFI will have no competitive advantage in receiving any awards related to the submitted topic area.

**7. Required Responses** Responses to this RFI are limited to 5 double-spaced pages with one inch margins using standard letter-size 8½” x 11” paper. The page count includes any title page. The font for text should be Times New Roman 12-point or larger. Responses must be unclassified and should not contain company proprietary information. Please pay attention to any company templates that automatically create a “company proprietary” or similar type statement. Those must be removed from the response. Separate responses should be submitted for each technology area. Multiple responses from a firm are acceptable. Marketing information is NOT desired in the response. Endorsements from elected officials are NOT desired in the response.

**8. Request for Clarification** A responder may request clarification, in writing, from the Contracting Office for any aspect of this RFI that is unclear by sending an e-mail to: [mary.sharits@us.af.mil](mailto:mary.sharits@us.af.mil). Any requests for clarification must be received no later than seven (7) business days prior to the close of this RFI in order to receive a timely response. Technical questions regarding this RFI should be directed to the contracting focal point, Mary Ann Sharits [mary.sharits@us.af.mil](mailto:mary.sharits@us.af.mil) who will direct them to the appropriate technical focal point.

**9. Submission of Documentation** Responses to this RFI are due to the Contracting Office identified below by **3:00 PM Local Time, 8 Nov 2019**. Any late responses will NOT be reviewed. Responders shall provide one (1) electronic copy (in Microsoft Word) of their response on a CD or DVD. USBs will NOT be accepted. DO NOT send via email, and DO NOT send any hard copies. Please ensure your response does not have any markings stating the information is proprietary or it will not be considered. Submission of existing commercial

documentation and product literature is NOT an acceptable response. Documentation shall be sent to the following Contracting Office address:

AFRL/RXKMC  
ATTN: Mary Ann Sharits  
2130 Eighth Street, Building 45  
Wright-Patterson AFB, OH 45433-7541

**10. Additional Information** While MIIs are expected to have a non-profit entity as prime contractor, all responsible sources may submit information. All routine communications regarding this announcement should be directed to the contractual or technical points of contact listed above. The Government may or may not use any responses to this RFI as a basis for a subsequent project. If projects developed in part from the RFI responses become the subject of a subsequent acquisition; any such acquisition will be posted in FedBizOpps.gov and grants.gov. Responses to this RFI will not be returned. The Government is under no obligation to acknowledge receipt of the information received, or give feedback to respondents with respect to information submitted under this RFI.

**11. Submission Checklist**

- Maximum of 5 double-spaced pages including any title page
- 8 ½” x 11” paper
- One inch margins
- Times New Roman 12-point font or larger
- Unclassified
- No proprietary information or markings (failure to comply will disqualify the submission)
- No marketing information, commercial documentation, or product literature
- No endorsements from elected officials at the federal, state, and/or local level
- Microsoft Word format, NOT PDF!
- Submitted on a CD or DVD, NOT USB, NOT via email, NO hard copies
- Due date 3:00 PM Local Time, 8 Nov 2019.** (Late responses will not be considered)