EPA STAR Request For Applications

Assessment Tools for Synthetic Biology Products

Informational Webinar for Applicants

May 28, 2020

2 PM EDT

Webinar Objectives

- Go over application Information in the EPA STAR RFA ***Assessment Tools for Synthetic Biology Products*** (Technical, Eligibility, Submission).
- This an overview of what is provided in the RFA.

Webinar Ground Rules

- Please hold your audio questions until all EPA presentations have been made. We prefer that you pose questions in the chat box, which you can do at any time.
- No specific research proposal can be discussed, but clarifying questions regarding what is written in the RFA announcement may be answered.

ORD's Chemical Safety for Sustainability Research Program

This RFA is supported by EPA's Chemical Safety for Sustainable Research Program (CSS).

CSS provides methods, data, information and tools to EPA partners and stakeholders enabling more informed, timely decisions about chemicals, many of which have not been thoroughly evaluated for potential risks to human or ecological health.

https://www.epa.gov/aboutepa/about-chemical-safety-sustainability-research-program

Award Information

Estimated Number of Awards:

Approximately 7 awards

Anticipated Funding Amount:

Approximately $4.4 million for all awards

Potential Funding per Award:

- Up to a total of $750,000 per regular award, including direct and indirect costs, with a maximum duration of 3 years
- Up to a total of $453,333 for early career awards, including direct and indirect costs, with a maximum duration of 3 years.

Background

- Transformational synthetic biology tools and techniques are enabling the fabrication of a wide range of biotechnology products.
- To realize the potential benefits of synthetic biology while avoiding unintended consequences that may adversely impact public health and the environment, it is crucial to better comprehend the underpinning science and to develop appropriate assessment technologies.
- The manufacturing and agricultural benefits of these varied products will depend on robust evaluation approaches and monitoring capabilities to ensure their safety and to assure public trust.

Background

- Oversight of biotech products is shared between the EPA, the U.S. Department of Agriculture (USDA), and the U.S. Food and Drug Administration (FDA).
- Novel techniques, such as CRISPR-Cas9 and other genome editing, and metabolic engineering technologies, have transformed and accelerated the creation and production of the next generation of agricultural (e.g., genetically engineered products that qualify as pesticides under the Federal Insecticide, Fungicide, and Rodenticide Act-FIFRA) and industrial materials (e.g., microbial biotechnology-derived substances considered new chemicals under the Toxic Substances Control Act-TSCA).
- US law mandates that risk assessment of a product is based on its end use, including biotechnology products.

Introduction

Research solicited in this RFA will support the development of improved science-based human health and environmental risk assessments of new biotech products

Information and effective tools are needed to evaluate and monitor parameters such as long-term stability, persistence, efficacy, and reliability of biotech products in order to assess any possible unintended public health and ecological impacts

Better understanding of how novel biotech products interact at the cellular and systems levels will allow for more informed decisions on their safety and efficacy

- Some examples of appropriate risk assessment tools include models, bioinformatic systems, and field-based and i*n vitro* methods
- Biotech products of interest include, but are not limited to: industrial or consumer chemicals; pesticides (including intermediates); and new microbes used in biomass conversion for chemical production, microbial fuel cells, mining and resource extraction, building materials, waste remediation and pollution control, and non-pesticidal agriculture applications.

Research Areas of Interest

- **Research Area 1: Long-term stability, persistence, efficacy, and reliability of microbial biocontainment strategies, synthetic microbial genetic constructs, or microbial genetic restriction technologies:**
  a. Long-term stability, persistence, and reliability of synbio microbial biocontainment strategies (e.g., xenonucleic acids, noncanonical amino acids, recoded microorganisms) for **synbio microorganisms**.
     - For the purposes of this RFA, 'biocontainment methodologies' are those that prevent unintended proliferation of genetically modified organisms in the environment.

Applications must address at least 1 of the 3 Research Areas

Areas of Interest

Research Area 1, continued: Long-term stability, persistence, efficacy, and reliability of:

b. Stability and persistence of synthetic genetic constructs in microbes (e.g., are synthetic transgenes eliminated from viral, bacterial, algal or fungal genomes over time?).
   - "Synthetic genetic constructs" are defined as new biological entities, not directly derived from extant organisms, such as enzymes, genetic circuits, and cells or the redesign of existing biological systems for useful purposes.

Areas of Interest

Research Area 1, continued: Long-term stability, persistence, efficacy, and reliability of:

c. Efficacy of genetic restriction technologies or orthogonal gene constructs in precluding horizontal gene transfer from synthetic microorganisms. Horizontal gene transfer is a process in which organisms exchange genetic material with other species.

- "Genetic restriction technologies" are defined as methods that impede transgene movement. Particularly with self-replicating microbial systems, re-engineered cells may produce undesired consequences if they escape or overwhelm their intended host environment.

Research Area of Interest

Research Area #2: Ecological effects/impacts of synbio organisms or by-products that are released into the environment.

a. Survival, persistence, and unintended ecological effects of synbio microorganisms, plants and animals.

b. Unintended environmental effects/potential impacts of synthetic microorganisms, plants and animals such as: bacteriophages, plant viruses, entomopathogens, bacterial or fungal colonizers, (e.g., rhizobia, other nitrogen-fixing bacteria, mycorrhizae), higher plants, mosquitoes, or rodents.

Applications must address at least 1 of the 3 Research Areas

Research Area of Interest

Research Area 3: Risks to human health from novel biomolecules produced using metabolic or genetic pathways by organisms used, in essence, as bioreactors.

Methods and models are needed to determine potential physiological responses to biomolecules made by synbio organisms, such as:

a. Adverse responses, including protein toxicity/allergenicity, to biosynthetically produced proteins, atypical nucleotides, or noncanonical amino acids (i.e., non-standard amino acids)

b. Predictive toxicity motif detection in instances where noncanonical amino acids are incorporated into peptides/proteins,

c. Synbio microorganism colonization of the human microbiome.

Applications must address at least 1 of the 3 Research Areas

Potential Expected Outputs

- Tools & Methods able to assess and monitor the effects of synthetic biotechnology products.
- Methods & models to ID & quantify probable outcomes, sources of uncertainty, & to trace cause and effect pathways.
- New or redesigned systems able to generate information on synthetic biology products and components that help determine potential adverse human and ecological effects.
- Advanced, useful evaluation and monitoring methods to assess risk to human health and the environment of beneficial synthetic biology products.

Potential Expected Outcomes

- Improved understanding of risks to human health and the environment from synthetic biotechnology production processes.

- Better identification of key connections in the continuum between the production of synthetic biotechnology products and intermediate substances with potential adverse outcomes in humans.

Eligibility Information

- Public and private nonprofit institutions / organizations, public and private institutions of higher education, and hospitals located in the U.S., state and local governments, Federally Recognized Indian Tribal Governments, and U.S. territories or possessions are eligible to apply.
- Profit-making firms and individuals are not eligible to apply.

Application Materials

- To apply under this solicitation, use the application package available at Grants.gov (for further submission information see Section IV.F. Submission Instructions and other Submission Requirements).
- Note: With the exception of the current and pending support form (available at Research Funding Opportunities: How to Apply and Required Forms), all necessary forms are included in the electronic application package. Make sure to include the current and pending support form in your Grants.gov submission.

Other Information

- Please refer to Section IV. Application And Submission Information.
- Please refer to Section V. Application Review Information.

- **Solicitation Closing Date**:

  Wednesday, July 15th, 11:59:59 pm Eastern Time

Further Reading

- USDA, FDA, EPA (2020) The Unified Website for Biotechnology Regulation; https://www.usda.gov/media/press-releases/2020/01/09/usda-fda-epa-launch-website-biotechnology-regulation
- EPA (2019) Regulation of Biotechnology under TSCA and FIFRA
- Modernizing the Regulatory System for Biotechnology ProductsExecutive Order on Modernizing the Regulatory Framework for Agricultural Biotechnology Products. June 2019; https://www.whitehouse.gov/presidential-actions/executive-order-modernizing-regulatory-framework-agricultural-biotechnology-products/
- Wozniak CA, McClung G, Gagliardi J, Segal M, Matthews K. Regulation of genetically engineered microorganisms under FIFRA, FFDCA and TSCA
- FIFRA Scientific Advisory Panel Meetings Related to Biopesticides
- Previous EPA STAR supported research on biotech-derived substances; Approaches to Assessing Potential Food Allergy from Genetically Engineered Plants.

Definitions

for the purposes of this RFA

- Synthetic biology is an interdisciplinary area that applies bioengineering tools to biology in order to fabricate a wide range of biotechnology products;
- Synbio organisms are whole organisms that have been engineered using synthetic biology;
- Synbio components are synthetic biology constructs that may be used or deployed outside of a living organism;
- Synthetic biology constructs and by-products are new or redesigned biological entities or novel biomolecules not derived from extant organisms (e.g., enzymes, genetic circuits, atypical nucleotides, noncanonical amino acids, and cells);
- Biocontainment methodologies are those that prevent unintended proliferation of genetically modified organisms in the environment;
- Synthetic genetic constructs are new biological entities, not directly derived from extant organisms, such as enzymes, genetic circuits, and cells or the redesign of existing biological systems for useful purposes;
- Genetic restriction technologies are methods that impede transgene movement. Particularly with self-replicating microbial systems, re-engineered cells may produce undesired consequences if they escape or overwhelm their intended host environment.
- Biotechnology products of interest include: industrial or consumer chemicals; pesticides (including pesticide intermediates); and new microbes used in biomass conversion for chemical production, microbial fuel cells, mining and resource extraction, building materials, waste remediation and pollution control, and non-pesticidal agriculture applications (e.g., biofertilizers, weather and climate modification).”

Agency Contacts

- **Technical Contact:**
  Barbara Klieforth, Project Officer
  klieforth.barbara@epa.gov
  202-564-7723

- **Eligibility Contact:**
  Ron Josephson, Eligibility & Peer Review Officer
  josephson.ron@epa.gov
  202-564-7823

- **Electronic Submissions Contact:**
  Debra M. Jones, Administrative Officer
  jones.debram@epa.gov
  202-564-7839