National Biotechnology and Biomanufacturing Initiative

An EBRC Response to OSTP RFI; 87FR77901

January 20, 2023

Q1A:

Health

Short-term: Decentralized, agile biomanufacturing processes and facilities to reduce the costs of drugs and accelerate treatments. Distributed infrastructure will enable on-demand production of therapeutics, increase the availability of treatments and therapies for rare diseases, and harden domestic defense against emerging biothreats.
Long-term: Commercial deployment of smart, programmable biotechnologies, including therapeutic cells, probiotics for detecting and curing diseases, and platforms or organisms for disease control or eradication.

Climate and energy

Short-term: Domestic capacity to accelerate year-by-year declines in atmospheric greenhouse gas (GHG) emissions from agriculture, transportation and industry. Use biotechnology to produce value added chemicals and materials from industrial GHG.
Long-term: Eliminate use of fossil resources for energy, chemicals, fuel through implementation of engineered organisms and biosystems, providing every consumer – regardless of geography or income – with access to sustainable products.

Food and agriculture

Short-term: Economically-viable, consumer-scale processes for sustainable (plant- or cell- derived) protein and alternative meat production that quantifiably decreases the ecological and physical footprint of production.
Long-term: Widespread U.S. agriculture products and systems that leverage engineered crops and/or soils for resilience to climate change and disease.

Supply chain resilience

Short-term: Reuse and upcycling of wastes, including plastics, agricultural wastes, and GHG emissions, across the U.S. through controlled application of engineered organisms. For example, recovery of commodity chemicals in municipal waste management systems that are circled back into the supply chain.
Long-term: Net U.S. export of renewable chemicals, fuels, and materials. Biobased production, extraction, recycling, and upcycling of supply chain staples is possible and necessary for a sustainable future and healthy planet.

Q1B&C:

For R&D to support the above goals, EBRC has published four technical research roadmaps for engineering biology and biotechnology: *Engineering Biology for Climate & Sustainability* (2022); *Engineering Biology & Materials Science* (2021); *Microbiome Engineering* (2020); *Engineering Biology* (2019). These roadmaps provide expansive and detailed 20-year visions of possible engineering biology research, innovation, and application. Continued USG engagement and support for organizations that undertake such strategic assessments and planning is vital to a robust and sustainable bioeconomy. Specific R&D needs include:

Health - Fulfilling engineering biology's potential for a healthier populace will require capacity for rapid design, discovery, generation, and/or manufacturing in multiple bio-platforms (nucleic acids, proteins, and cells) and incentives (policy and financial) for physical infrastructure and workforce development. The private sector can be incentivized to develop therapeutics and treatments that are demographically equitable and affordable.

Climate and energy - Federal policies and incentives can accelerate and expand carbon capture and conversion capabilities. USG can establish and/or incentivize biorefinery networks that process regional sources of biobased and/or GHG feedstocks. USG can support R&D for sustainable bioprocesses, including fermentation and down-stream processing and feedstock-to-chemical (bio)conversion. It can incentivize the private sector (e.g., through tax breaks or subsidies) to transition to sustainable biomanufacturing in replacement of fossil fuels.

Food and agriculture - Sustainable protein production (short-term goal) at commercial scale will require cost effective scale-up processes and the development of clear, effective, yet agile standards and product regulation. Resilient agricultural systems (long-term goal) will require the translation of foundational knowledge into diverse crop systems and will require systems approaches that incorporate understanding of microbes, insects, plants, and other organisms.

Supply chain resilience - Investment in biomanufacturing could make the U.S. a forerunner in producing and exporting bio-based commodities, thereby decreasing our reliance on fragile global supply chains and enabling surge capacity during global disruptions or regional instability. Investments should support distributed manufacturing facilities and centers, agile and responsive risk assessment and regulation, and Federal incentives for sustainable processes and practices.

Q2:

Social science research has identified longstanding and pervasive misperceptions of 'the public' by scientists and policy actors, including widespread assumptions that a lack of technical knowledge underpins public distrust of new technologies. Increasing public literacy of science is important but does not correlate linearly with increased support for science. Rather, confidence in governance and regulatory structures, as well as perceptions of the underlying motivations accompanying new developments (e.g. profit vs. social justice), contribute significantly to public opinion. Working with social science partners to carefully understand the perspectives of different communities is critical for designing approaches that acknowledge and engage seriously with public concerns.

Incorporating social sciences into the research lifecycle

Education: USG should support and incentivize programs that better prepare biological scientists and engineers to understand and attend to the complex relationships between science and society, including methods of public engagement. Interdisciplinary environments, such as at the Kavli Center for Ethics, Science, and the Public, can train technical researchers to engage with the complex dynamics between science and society.

Research design: Incorporating social science expertise into research design can lead to the development of well-crafted problem statements attuned to the needs of core users/stakeholders. Frameworks for successful collaboration between social and technical scientists should be built that account for funding streams, a balanced "power dynamic," and opportunities and timelines for the integration of social findings back into technical approaches. On a broader scale, deliberative discussions can be used by USG to help prioritize research thrusts, e.g. NASA's work with the Expert and Citizen Assessment of Science & Technology (ECAST) network.

Research funding: Funding processes should better incorporate expertise from the social sciences. Doing so will promote attention to the needs of, and accountability to, the public meant to benefit from biotechnology solutions. For example, as ARPA-H becomes established, it should implement and/or fund bold strategies to incorporate social sciences into research funding.

Conduct of research and development: Public engagement and social science data should be integrated with technical data to inform the refinement of research directions throughout a project.

Public engagement and accountability: To ensure public trust, policies and governance frameworks must align with and incorporate public input on key risks and concerns. Technical researchers would benefit from viewing public engagement as an opportunity to fine-tune research approaches for greater impact, rather than a threat to research progress. For example, the deliberative public consultation processes followed by the UK's Human Fertilization and Embryology Authority were effective in the British context.

Q3:

- **Publicly-accessible databases of genomic and other -omic data for non-model organisms** are lacking. Supporting the development and accessibility of such data from a broader array of species can reduce duplicative efforts in industry, diversify feedstock and supply chains, and hasten discovery. Organisms of interest might include those that use gases or wastes as feedstocks, those that exhibit high tolerance to extreme pH, salts, etc., and, in the future, synthetic cells. Additionally, USG could support a feasibility study for standardization of genomic nomenclature across species, along with a software tool to convert legacy names to modern ones and "spot check" nomenclature.
- As in other research fields, reproducibility can be a challenge in engineering biology. The **development of common benchmarks, standards, and measurements would enable comparisons between researchers** and help ensure reproducibility across laboratories.

Q4:

Creation and maintenance of databases: USG has a crucial role to play in curating, annotating, storing, and integrating data in high quality public databases. The NIH has recently cut back drastically on their support of scientific databases, such as the Saccharomyces Genome Database. Widely used databases reduce redundancy, promote consistency, and enable the dissemination of the highest quality information.

Data repositories: USG should support the maintenance of data repositories. Such repositories should be cross-compatible, broadly shared, and *maintained*. They enable research efficiency by diminishing the need for redundant data collection, give all researchers access to cutting edge data, and enable the sharing and transfer of data.

Improved user interfaces: USG will see a greater return on its investments in databases if researchers are better able to access and use that data. Enhanced accessibility and usability can be achieved through support for updated genome browsers and other data-viewing platforms.

Bioinformatic workforce development: In our response to Q10, we highlight the importance of interdisciplinary education. A particular need is the training of software engineers and data scientists to understand biological data challenges and opportunities. Likewise, engineering biology students/trainees should minimally have access to bioinformatic training.

Q10:

USG should undertake research to better understand future workforce needs and guide investments toward meeting those needs. Simultaneously, USG can take steps to develop and deploy educational and training opportunities across the various skill levels to meet current needs for a thriving bioeconomy:

High-School:

USG must **advance strategic and coordinated educational initiatives that integrate biotechnology and engineering biology education and opportunities into public high-school education**. Community college and university faculty have reported low enrollment in classes related to biotechnology, perhaps due to student unawareness of bioeconomic opportunities. Thus earlier introduction may be valuable.

- USG must articulate national and state-level goals that require the adoption of effective biotechnology curricula, spotlighting its importance for sustainability, a robust economy, and national security.
- The Departments of Education, Labor, and Commerce can i) support teacher training and umbrella organizations that advance industry-relevant pedagogy and ii) incentivize industrial partners to work directly with schools to hire candidates for meaningful professions in the bioeconomy without post-secondary schooling.

Undergraduate:

USG can **provide more opportunities for undergraduates to gain industry skills and experience by**:

- Providing funding and access to undergraduate research opportunities, particularly for those who may not have many research opportunities at their home institutions.
- Directing funding, structural support, or incentives for the development of internship or apprenticeship programs with industry, particularly at community colleges, PUIs, HBCUs, and other MSIs. Through such programs, students can gain the hands-on experience they need to supplement course-learning and be prepared to enter the workforce.
- Supporting the establishment of certificate programs for specialized positions within the bioeconomy workforce, for example a certificate program for community college students to gain specialized skills in fermentation engineering.

USG can **facilitate interdisciplinary programs and curricula** to: i) train future workers to embrace interdisciplinary, collaborative approaches; ii) bring relevant expertise from other disciplines to bare on engineering biology; and iii) support the incorporation of public engagement and social science into the technical research lifecycle. (This also applies to doctoral and postdoctoral training.)

Masters:

Masters programs that give students experience in applying conceptual knowledge of biology to biomanufacturing processes could rapidly increase the availability of a skilled workforce.

Doctorate and postdoctoral:

USG should **improve financial support for graduate students and postdoctoral researchers**, potentially through higher fellowship stipends or dedicated supplemental funds for PIs. To ensure that talented individuals do not self-select out of advanced degree programs based on financial necessity, graduate students and postdoctoral researchers need to make a livable wage *that accounts for regional cost-of-living*. The availability of supplemental needs-based funds could be particularly enabling to those with dependents.

Retraining and upskilling:

USG should **provide formal and informal opportunities tailored to those from sunsetting industries to develop skills and abilities that align with regional bioeconomy jobs**. It can also catalog and provide incentives for companies to enroll their employees in short, effective programs that are specific for current and potential bioeconomy workers.

Q11:

Long-standing inequities limit the diversity of our nation's skilled workforce; **USG support is needed to broaden access to biotechnology education**. Agencies like NSF have impactfully placed an emphasis on broadening participation in STEM, institutions serving underrepresented communities (MSIs, HBCUs, etc.) are generally under-resourced in emerging areas like the bioeconomy. Further, **education and training needs to extend beyond traditional academic institutions to all points of entry**, with programs and resources for non-traditional communities outside the educational pipeline.

USG should:

- Provide support to MSIs to introduce students to engineering biology and biomanufacturing, teach industry-relevant skills, and support programs and activities that expose students to biotechnology career opportunities.
- Catalyze the training of talent at all educational levels through skills-oriented training programs that offer a credential or certificate to teenagers in poor and/or immigrant communities; veteran-serving community programs that provide after-hours training with wrap-around support for active service military spouses and under-employed service-men and -women; and informal education centers with coordinated public programming that can familiarize residents of non-traditional STEM hubs with the career opportunities and required technical skills to meet regional needs in biomanufacturing.

- Offer financial support for universally accessible laboratory design or accommodations, enabling participation and contributions of Disabled people.

Q12:

USG should establish an interagency group to coordinate applied biosafety research and biosecurity innovation across agencies involved in life sciences research, innovation, regulation, and commercialization. This interagency group should **assess the current state of safety and security practice in the life sciences, identifying effective frameworks and approaches**. It should **seek stakeholder input** on i) likely future safety and security needs through horizon scanning activities; ii) the prioritization of safety and security research and innovation needs; iii) potential research approaches to address those needs; iv) strategies to incentivize (or mandate, if/when appropriate) broad implementation of best practices, including by private research laboratories and/or within industry; and v) approaches to stakeholder engagement—as opposed to only compliance—with safety and security practices.

These activities will enable USG to make strategic investments in supporting and enhancing applied biosafety research and biosecurity innovation. The interagency group must have representation across agencies to avoid redundancy and invest via agencies with the appropriate funds, program managers, and outlook. USG should be attentive to both technical (e.g., biocontainment approaches, DNA synthesis screening) and nontechnical (e.g., building a security culture) research needs. Such activities require consistent funding for iteration and implementation.

USG may consider needs such as: i) the development of technical biosecurity tools that can be embedded in bioenabled products (e.g., kill switches and other biocontainment methods); ii) machine learning that predicts the function of an engineered sequence or organism in an operational context; iii) risk estimation tools at multiple scales and cellular contexts; iv) social science research on strategies for fostering innovation and overcoming obstacles to the adoption of biosafety and biosecurity tools and practices by stakeholders; and v) strategies to minimize economic barriers/hurdles to implementing safety and security best practices in the bioeconomy.

Q13:

Enhance:

Some stakeholders in the bioeconomy need additional information or clarity from USG to implement best safety or security practices. For example, DNA synthesis companies have no means of objectively measuring the true efficacy of their screening systems. Information provided to USG elsewhere contains details on the kinds of government actions that may enhance security practices for DNA synthesis screening, for example sets of test sequences designed to probe screening efficacy to help companies strike the right balance between catching sequences of concern and minimizing false positives.

USG should also consider which other suppliers of biotechnology research materials (e.g. protein synthesis companies, plasmid repositories, and other producers of “biological parts”) may benefit from safety and/or security guidance. Some have developed in-house practices that could be validated against guidance, and all would benefit from understanding the risk landscape and mitigating approaches. Importantly, safety and security measures have to be economically viable. Explicit guidance coordinated between agencies on best practices helps companies efficiently implement suggested measures.

Incentivize:

Funders could incentivize researchers to incorporate safety and security activities and consideration into their work by directing them to do so in requests for proposals, incorporating engagement with these topics into scoring criteria, including safety and security experts on review panels, and requiring grantees to report on security and safety activities. Funders should include information to grantees on what this engagement looks like and be wary of building a “compliance culture” with boilerplate answers.

USG could develop or invest in certification or credentialing efforts such as: i) recognizing the comprehensive incorporation of safety and security practices into an organization; ii) recognizing the training and competency of a researcher or student in biosafety and biosecurity; iii) training opportunities for future biosafety and/or biosecurity leaders; and/or, iv) training opportunities for early-stage (undergraduate or graduate) technical researchers. To incentivize participation, relevant government career track positions could require certification. As the value of such training becomes recognized across research and the bioeconomy, individuals with such a certificate might receive higher pay or be permitted to work on certain projects.

Q14:

Biotechnologies are dispersed through economic segments such as food and agriculture, energy, and materials. Aggregating the contributions of biotechnologies to the economy would bring much needed clarity to the size and growth areas of the bioeconomy. Indicators should include GDP and other traditional measures of economic activity while capturing unique properties of the bioeconomy. For example, one indicator could represent absolute and relative levels of recycled carbon in food and product manufacturing. Though challenging to measure, such indicators would be meaningful to researchers, industry, investors, and consumers, and would motivate continued attention to developing a *sustainable* bioeconomy.

A first step toward developing indicators is establishing definitions, as recently completed by NIST. Starting from NIST's broad definition of the bioeconomy, bioeconomic activity could be divided between that which is driven by *engineering* biology (e.g., fermentation of an engineered organism) and that which is not (e.g., lumber production). This may be cumbersome in areas of the bioeconomy that support both biotech and non-biotech based outputs, such as agriculture. Furthermore, regulatory frameworks in the US are product-, not process-, based, meaning that some organisms developed with gene editing techniques are exempt from regulation and are indistinguishable from similar or even the same products developed without biotechnology. Establishing more clear and comprehensive regulations and definitions around products in the bioeconomy will inform what is and should be measured.

USG could also measure the translation of government-sponsored research into commercial biotechnologies. Capturing this data could involve aligning the US Patent Public Search database with innovations resulting from government support and tracking the licensing of those patents . Tracking the distribution of patents across segments of the bioeconomy over time could highlight areas on the cusp of significant growth.

These indicators and metrics will clearly be challenging to develop, thus it is essential that they are developed with the expertise of NIST and the input of private sector organizations and other stakeholders. They should be developed with an eye toward international relevance to facilitate a healthy global bioeconomy.

Q16:

USG should support international cooperation in the bioeconomy by supporting efforts, initiatives, and/or fora that bring together policymakers and practitioners from around the world (Dixon et al., 2022). In such spaces, bioeconomy plans, priorities, opportunities for collaboration, lessons-learned, etc. can be exchanged enabling trust and relationships to grow. Such fora can expose policymakers to the opportunities of biotechnology and consider their own nations' bioeconomic potential and strengths. International sharing and adoption of standards can enable trade and technology sharing. And shared values of safety, security, and service to people and the planet can be established, codified, and committed to. EBRC is hosting its second Global Forum, which serves these purposes, in February 2023 in Singapore. While interest in attending the forum is widespread, eight countries with invited delegates will not be represented due to lack of travel funding, including some from under-resourced nations with nascent and burgeoning bioeconomies. USG could play a leading role in making future Global Fora more wide-reaching by enabling the participation of additional delegations.

The US should also undertake horizon scanning activities, domestically and with international partners, to better position itself to anticipate both the positive outcomes and negative consequences stemming from biotechnology developments. Such activities would enable the US to identify areas for technical and/or regulatory partnership and break down international silos. Horizon scanning also enables biosafety and biosecurity preparedness, identifying coming dual-use technologies and informing US funding decisions for safety and security research.

Q17:

As more individuals around the world understand and gain technical training in the field, the potential for the accidental or deliberate misuse of biotechnologies grows. As more engineered biotechnologies are deployed in the environment, the likelihood of a loss of biocontainment grows, potentially negatively impacting ecosystems.

The United States *must* provide leadership that sets standards and norms for how biotechnology development can proceed safely and securely. Widespread buy-in and adoption of such standards is also critical to their successful implementation; this can only be achieved by international coordination and cooperation (see Q16). Priority areas for leadership include:

- Regularly updating Guidance for DNA synthesis providers with community input and encouraging counterparts in other countries to provide similar guidance;
- Updated ePPP and DURC policies (as are currently being worked on by NSABB) that may serve as templates for other countries to build similar risk-based policies;
- Support for organizations working to build a robust culture of biosafety and security within the field both domestically and internationally;
- Support for an international body that articulates international standards for the safe and secure advancement of research (e.g., standards for operating BSL-3 and BSL-4 laboratories) and serves as a neutral body able to respond to requests from countries in making their biological research more safe and secure.
- Setting a standard for a functional, effective, and streamlined regulatory environment that considers and weighs both the benefits and hazards associated with given products.
- Developing frameworks for communicating and reaching agreement on biocontainment measures for environmentally deployed engineered biotechnologies near international borders.