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Q1: Identify one or more grand challenges for the bioeconomy in areas such as health, energy, the environment, and agriculture, and suggest concrete steps that would need to be taken by the Federal government, companies, non-profit organizations, foundations, and other stakeholders to achieve this goal.

Grand Challenge 1: Access to Quality Affordable Health Care

The United States has by far the most expensive health care system in the world while delivering outcomes that are well below the best. Without intervention, the cost of health care is also likely to increase as populations age over the coming decades. **The grand challenge is to reduce health care costs to no more than 12% of the gross domestic product, while increasing average life expectancy to at least 82 years, by the year 2025.**

To address this challenge, research is needed on the following topics:

Health Economics and Policy: creating the incentive structure for the efficient delivery of health care, so that providers and insurers are motivated to eliminate waste that occurs due to: (1) care that is unlikely to provide substantial benefits to the patient, (2) resources that are under-utilized, (3) inappropriate use of expensive resources when cheaper alternatives exist, (4) delays in the introduction of new cost-effective therapies caused by regulatory burden.

Health Informatics: improving the use of informatics to assess the therapeutic approaches that are best suited to each individual, based on his or her health care history, genetic factors and biomarkers, health behavior and environment and proven efficacy of alternative approaches. Informatics should be used to provide a health care assistant to the provider and the patient to help them navigate through alternative therapies and make the best choices.

Health Care Efficiency: creating mechanisms to improve productivity, offering the capacity to serve more patients in less time while improving health outcomes. This can include methodologies to mine and analyze data sets to provide meaningful performance metrics in real time, and for retrospective analysis, and to couple efficiency methods to compensation and reimbursement.

Health Communication: developing tools to effectively share information with patients in a way that motivates them to make the best health care decisions and to prevent disease based on their circumstances. Likewise, developing tools to effectively share information with health care professionals and guide their decision should also be a priority.

Grand Challenge 2: Targeted Therapies and Diagnostics for Cancer

41% of Americans born today will be diagnosed with cancer at some time in their life. Nearly 600,000 people will die this year from cancer in the United States. Cancer is the second leading global killer, accounting for 12% of all deaths, and the World Health Organization estimates that cancer will become the leading cause of death worldwide, as it already is in the United States. Despite the large investments in cancer research made in the U.S. over the last 50 years, we do not yet have the types of therapies and diagnostics that will dramatically alter cancer survival rates. **The grand challenge is to extend life expectancy by increasing the five-year survival rate among all malignancies to 90% by the year 2025, through innovative science-based therapies and diagnostics.**

The specific opportunity is to use nanomedicine and other techniques arising from chemistry and physics to precisely target therapies to disrupt the mechanisms by which malignant cells reproduce. Specific focus areas include:

Theranostics that use multifunctional nanoparticles to image the tumor, provide targeted treatment and assess in real-time the therapeutic action.

External activation of nanoparticles as a mechanism for non-invasive local delivery of drug and/or tumor ablation.

Nanoparticles, including their synthesis, genetic engineering, surface engineering and characterization that can be readily tailored for multifunctionality toward specific clinical applications.

Biomarkers that can be exploited to attach nanoparticles to specific cancer cells.
Nanoparticle delivery of DNA/RNA based therapies.

These approaches can be integrated with modeling, simulation and information technologies, so that we can better predict, and precisely target, therapies and diagnostics.

Grand Challenge 3: Healthy Environments

Worldwide, nearly two million people (many children, who would otherwise live much longer lives) die each year due to unsafe drinking water and poor sanitation or hygiene. Close to one million people die each year due to exposure to unhealthy air. These and other environmental factors cause a huge loss of life around the world, particularly in developing countries where the life expectancy can be as low as 40 years. **The grand challenge is to increase the life expectancy of all countries in the world to at least 60 years through the improvement of environmental conditions and the prevention of disease.**

The approach should be to create an integrated program that merges public health with engineering to understand the causation of disease, simultaneously developing affordable technologies to remedy environmental conditions and understanding the cultural factors that may favor one solution over another. The United States should become the world leader in innovative technologies to improve water cleanliness, reduce emissions, and remedy other environmental hazards.

Q2: Constrained Federal budgets require a focus on high-impact research and innovation opportunities. With this in mind, what should be the Federal funding priorities in research, technologies, and infrastructure to provide the foundation for the bioeconomy?

Priorities should include research structured around these principles:

- Creation of new informatic tools for the storage, sharing, visualization and analysis of large biological data sets. These tools should be built on a platform of technology that includes high performance computing, high-speed networking and mobile devices. Advanced informatics should be used throughout all research in the bioeconomy.
- Encouragement of "open science" models of research, whereby data sets and other research products are freely shared among research communities.
- Collaborative science, whereby emphasis is placed on the creation of centers of excellence that bring together researchers, patients, students and industry within integrated environments, along the lines of NSF's Science and Technology Centers and Engineering System Centers.
- Completion of fundamental research that is informed by real problems.

Q3: What are the critical technical challenges that prevent high throughput approaches from accelerating bioeconomy-related research? What specific research priorities could address those challenges? Are there particular goals that the research community and industry could rally behind (e.g., NIH $1,000 genome initiative)?

The critical technical challenge needed to advance high throughput approaches will be the management, sharing, integration and analysis of greatly expanded data sets originating from these technology. Research on the science of **informatics enabled discovery** should be the highest priority. Programs of research should focus on the creations of systems that allow for the expedited analysis of massive new data sets, and the presentation of results directly and immediately to the health care provider or researcher.

Q9: The majority of doctorate recipients will accept jobs outside of academia. What modifications should be made to professional training programs to better prepare scientists and engineers for private-sector bioeconomy jobs?

The pathway to an academic career in the life sciences, combining doctoral and post-doctoral training, has become much too long and much too unpredictable. The NIH should consider limiting support for post-doctoral training for each recipient to no more than two years, and reinvesting the savings in support of additional research projects through other award mechanisms, such as the RO1. In addition, greater emphasis should be placed on the creation of professional education at the masters degree level. Seed funding for the creation of professional masters degrees should be a priority.

Q11: What role should the private sector play in training future bioeconomy scientists and engineers?

Private research universities play a critical role in the education of scientists and engineers. The University of Southern California alone awards more than 10,000 degrees each year, including more than 6,000 advanced degrees. It is critical for the federal government to continue supporting the research and educational endeavors of private research universities.

In addition, the private companies can contribute more in the future through the creation of internships and through cooperation in the dissertation portion of doctoral education. Support for industry research experiences whereby students would spend periods from 6 to 18 months at an industrial laboratory while completing their dissertations would be highly valuable. This might be enabled through grant supplements.

Q13: What specific regulations are unnecessarily slowing or preventing bioinnovation? Please cite evidence that the identified regulation(s) are a) slowing innovation, and b) could be reformed or streamlined while protecting public health, safety, and the environment.

The recently enacted rules on Responsibility of Applicants for Promoting Objectivity in Research will be a major burden on universities and likely impede progress in the bioeconomy. The direct cost of this regulation will exceed $1.5 million at our university over the next five years, not including the time burden imposed on investigators in the disclosure process. The regulation creates a new burden on universities to assess the relevance of investigators' financial interests to their research. The regulation will add to the length of time required to submit proposals to the NIH, and will inhibit investigators from participation in HHS due to the added regulatory burden associated with HHS funding. At the same time, the regulations do not address the most critical issue in conflict of interest: that of biomedical companies providing personal payments to investigators who simultaneously act as evaluators of biomedical products and promoters of the very same products.

In addition, with so many Federal funding opportunities requiring collaboration between multiple partners, sub-recipient regulations can be streamlined to reduce burdens and allow research teams to get to the research, rather than spend time and resources on paperwork. Regulations should be aimed at making collaborations easier to execute.

Last, the added reporting requirements associated with ARRA funding have been costly to our university. A reduction in such regulations would be beneficial.

Q16: What are the highest impact opportunities for public-private partnerships related to the bioeconomy? What shared goals would these partnerships pursue, which stakeholders might participate, and what mutually reinforcing commitments might they make to support the partnership?

The bioeconomy lacks the agility of the software, computer and communication industries. The time to market is far slower, and the competitive pressures are much smaller. The highest priority should be to make the bioeconomy more entrepreneurial and competitive by streamlining the regulatory process underlying

Q17: What are the highest impact opportunities for pre-competitive collaboration in the life sciences, and what role should the government play in developing them? What can be learned from existing models for pre-competitive collaboration both inside and outside the life-sciences sector? What are the barriers to such collaborations and how might they be removed or overcome?

It would be beneficial to create a DARPA-like model for advanced research in the life sciences. Through this approach, program officers would be empowered to build research communities to formulate new solicitations, and would have expedited mechanism to select proposals that are particularly innovative. The current NIH model that separates scientific review from the scientific programs inhibits the ability of NIH to implement creative research programs.