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The American Physiological Society

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Response to Office of Science and Technology Policy
Request for Information: Building a 21st Century Bioeconomy
BIOECONOMY@OSTP.GOV

The American Physiological Society (APS) appreciates the opportunity to comment on federal efforts to foster innovative research. The APS is a professional society dedicated to fostering research and education as well as the dissemination of scientific knowledge concerning how the organs and systems of the body function. The Society was founded in 1887 and now has over 10,000 member physiologists who conduct research at colleges, universities, medical schools, and other public and private research institutions across the U.S. We offer these comments on behalf of our members. Please note that we did not address each of the 17 questions posed in the request for information.

(1) *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.*

Years of research into the molecular components of biological systems have provided the raw materials for understanding the functions of cells, tissues, organ systems, intact organisms and even whole populations. However, despite tremendous gains in biomedical research there remains a need to integrate what we know about biology on the molecular and cellular levels with the function of organisms in all their physiological complexity. Doing so will lead to a better understanding of human health and disease, and facilitate the development of new treatments and prevention strategies. The scientific community is poised to move forward into these exciting new areas, but doing so will require funding support and recognition within funding agencies of how this work is critical to translational research. Federal agencies could further these translational goals through requests for applications and other funding mechanisms. Importantly, additional support much greater than currently available will be necessary to speed progress and take advantage of scientific opportunities.

Another major challenge facing biomedical researchers is the integration and analysis of multi-dimensional data sets. Technologies developed in the last two decades have generated large amounts of different types of data. In order to take full advantage of this growing resource, the scientific community needs researchers with the necessary skills to harness the data and trained in both the biomedical and computer sciences. Research-intensive engineering and computer science universities should be encouraged to collaborate with health science partners to train researchers for work in this area.

(2) *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?*

Trying to identify "high impact research and innovation opportunities" may be counterproductive because it is difficult to identify such research in its early stages. It can often take years for the impact of a research discovery to become apparent. A narrow focus on identifying and funding high-impact research may not be an effective use of resources and could result in missed opportunities to fund research that may have unanticipated long-term impacts.

(3) *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[1])?*

The National Institutes of Health (NIH) is trying to focus on translational research with the goal of accelerating the application of basic research findings. Basic physiological research has an important role to play in this process through target validation, efficacy testing and the identification of biomarkers. For example, one area of emphasis in the plan to streamline translational research is using high throughput techniques to identify target molecules and compounds that can potentially point the way to a new drug. This approach will require further research to validate the effect of these compounds in physiological systems.

Physiologists can place data generated from high throughput techniques into the context of physiological systems and aid in the development of preclinical models. Although working with animal models is expensive, time-consuming, and challenging, this work remains an important safeguard in the drug development process. We can maximize the benefit of high throughput technologies by continually improving validation models whether they are *in vivo, in vitro,* or *in silico*.

To solve large scale problems, collaborations will be necessary to bring together scientists with the appropriate expertise. One example of fostering collaboration to address major challenges comes from the National Institute of Allergy and Infectious Disease, which is funding three major HIV/AIDS research ventures targeting eradication of the disease, each characterized by investigators at several institutions and crossing traditional boundaries. This effort, the Martin Delaney Collaboratory, aims to accelerate progress toward a cure for AIDS by facilitating research partnerships among government, academia and industry.

(4) *The speed of DNA sequencing has outstripped advances in the ability to extract information from genomes given the large number of genes of unknown function in genomes; as many as 70% of genes in a genome have poorly or unknown functions. All areas of scientific inquiry that utilize genome information could benefit from advances in this area. What new multidisciplinary funding efforts could revolutionize predictions of protein function for genes?*

As referenced in our answer to question #1, we should build on the wealth of molecular data, including genome sequences that have been generated. Physiologists are particularly well positioned to advance understanding of gene function in the context of physiological systems. This should be made a priority.

(5) *What are the barriers preventing biological research discoveries from moving from the lab to commercial markets? What specific steps can Federal agencies take to address these shortcomings? Please specify whether these changes apply to academic labs, government labs, or both.*

The APS supports efforts to promote a better exchange of ideas and materials between researchers in academia and industry. As part of the NIH effort to advance translational sciences, the agency has been trying to develop agreements giving academic scientists access to unused or underutilized compounds. These are Intellectual Property (IP)-protected compounds that pharmaceutical companies may have developed for one purpose that could serve another or else the company decided not to pursue because it did not work as expected or toxicity problems arose. The Drug Rescue and Repurposing initiative is part of the Chemical Genomics Center Pharmaceutical Collection. This effort is designed to determine whether the compounds that have been approved for market and the thousands of compounds that never made it to market might be useful for diseases other than their intended purpose. The bio-industry and universities could play a big part in bioinformatics, development of new high-throughput screens, and safety and efficacy assessment of these compounds. There are numerous issues still to be worked out, including how to deal with IP issues.

The APS also recommends that the government look carefully at financial conflict of interest policies to ensure that they are not unnecessarily inhibiting productive scientific relationships between federally-funded researchers and their colleagues in industry. It may be advantageous to look for ways to incentivize research partnerships between sectors in the “pre-IP” space.

(6) *What specific changes to Federal Small Business Innovation Research (SBIR) and Small Business Technology Transfer (STTR) programs[2] would help accelerate commercialization of federally-funded bioeconomy-related research?*

The APS recommends that SBIR and STTR programs be evaluated to assess whether they are meeting the goal of increased commercialization of research discoveries.

(7) *What high-value data might the government release in the spirit of its open government agenda that could spur the development of new products and services in the bioeconomy?*
Are there data and/or drugs sitting in government labs, which have not been made publically available? The pressure to publish is less if you are in the NIH intramural community and as such there may be valuable data that in inaccessible to the broader community. Could we suggest some sort of data sharing for unpublished data from government research labs?

The APS recommends encouraging interactions between intramural and extramural scientists by incentivizing intramural scientists.

(9) *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?*

This topic was recently addressed in a request for information (RFI) from the NIH (NOT-OD-11-106). The comments below were submitted on behalf of the APS in response to that RFI:

> One approach as outlined below, would be to change the nature of the PhD training process, which could provide added flexibility and will be more readily adaptable to shifts in demand for qualified biomedical researchers.
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> Consideration should also be given to ensuring balance between disciplines. Some fields of research may have too many students entering training programs for the available number of post-graduate career opportunities, while others have too few students entering the pipeline.
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> *Characteristics of PhD training in biomedical research*
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> Graduate training (at the pre- and post-doctoral levels) should be focused on trainees developing the skills and knowledge required to solve our nation's biomedical and health problems and become productive members of the biomedical workforce. Trainees should be provided with career development resources designed to match the needs of the marketplace.
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> Currently PhD training programs do an excellent job of preparing students for careers in academic science. But biomedicine needs a broader diversity of professionals to be successful, and PhD programs are not designed to prepare students for these careers. One way to achieve this goal would be to alter pre-doctoral graduate training such that the first two years provide a broad base of knowledge and skills, including program curriculum, research experience and career development. Career development should include the skills necessary to run a successful research program including business skills, project and lab management, as well as resources to prepare students for careers in fields beyond academic bench research. This two year training program may culminate in the award of a Master of Science degree, followed by entry into a PhD program. Given the prior two years of training we would anticipate that the PhD program would be more focused on research with reduced emphasis on course work.
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> Clearly, new mechanisms of support will need to be developed for the Master's degree portion of training, including scholarships, loans and teaching assistantships; such funding mechanisms will be especially important to ensure that under served minority groups continue to enter the biomedical research work force. Once a student moves to the PhD program we would anticipate that federal support would be available from training grants and other similar mechanisms.
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> We anticipate that this approach will provide graduate students an additional set of basic skills to expand their career opportunities, as well as result in a more flexible pipeline for biomedical research by effectively increasing the scientific workforce while at the same time providing for increased career opportunities.

(10) *What roles should community colleges play in training the bioeconomy workforce of the future?*

The APS recommends improving the quality of science education at community colleges and aligning science curricula with the needs of four year colleges and universities. This will allow community college students to make a fluid transition to programs in biological, biomedical and bioengineering programs.

There are a large number of qualified individuals graduating from high school who cannot afford the costs of a four year education at leading colleges and universities. Thus, by creating cutting edge science programs at the community college level, which are inherently more affordable compared to the four-year college and university setting, it will be possible to enable more qualified individuals to move through the pipe line to meet future needs for scientists and physicians. This system is in place in the state of California where certain community colleges have been aligned with the University of California campuses to create such a feeder system.

(11) *What role should the private sector play in training future bioeconomy scientists and engineers?*

As referenced in our response to question # 9, the APS supports the idea of offering career training to pre-doctoral students. To ensure that the next generation of scientists has the skills to meet the needs of the workplace, it would be advantageous to encourage the development of training programs that involve partnerships between industry and academia. It is especially important for graduate students and faculty to be informed of what industry is looking for in science. The drive for translational research as well as academia's growing involvement in the drug discovery process requires that university scientists gain a solid understanding of the important questions that need to be addressed, for example, target validation, target engagement, develop ability and selectivity of drug candidates, biomarkers, potential companion diagnostics etc.

Many graduate programs bring in scientists from the pharmaceutical industry to speak with students about the drug discovery process, working in industry and interviewing for industry jobs. These efforts should be encouraged and expanded.

(12) *What role might government, industry, and academia play in encouraging successful entrepreneurship by faculty, graduate students, and postdocs?*

Please see our response to question #11.

(13) *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.*

Currently federal public health service (PHS) regulations require review of animal protocols every three years. However, most research grants provide support for four years. Harmonizing the review cycles for federal grants and animal research protocols would substantially reduce regulatory burden and free up resources at the level of the individual investigator, institutional administration and federal agencies.

(14) *What specific steps can Federal agencies take to improve the predictability and transparency of the regulatory system? (Please specify the relevant agency.)*

Federally-funded researchers are typically subject to regulatory requirements from more than one federal agency. It would be advantageous to harmonize the regulations between agencies to reduce burden on individual investigators.

In addition, oversight agencies such as the USDA should take a constructive approach with respect to enforcing the Animal Welfare Act. Research institutions monitor their own compliance with the AWA through an Institutional Animal Care and Use Committee (IACUC) that reports to a designated Institutional Official. This often results in the prompt identification and correction of problems. We strongly urge that the USDA avoid taking a punitive stance when an IACUC does its job. In other words, a self-identified and self-corrected problem that is documented by the institution should not result in a USDA citation unless it represents serious and continuing noncompliance.

(17) *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?*

NIH could and should facilitate cross-institutional collaborations. It can be very difficult to collaborate with research partners at other institutions, when jurisdictional responsibilities between regulatory committees in different institutions are not clear. It is redundant and wasteful for committees at two institutions to review all aspects of collaborative projects.

In conclusion, we would like to reiterate that maintaining a first rate biomedical research enterprise now and in the future is critical to the health and welfare of Americans and economic competitiveness. Thank you for considering our comments.

Sincerely,

Joey P. Granger, Ph.D.
President
American Physiological Society