Departmental Response:
Assessment of the Report of the SEAB Task Force on Biomedical Sciences

Introduction

On November 21st, 2015, Energy Secretary Ernest Moniz charged the Secretary of Energy Advisory Board (SEAB) to create a Task Force to evaluate opportunities for increased collaboration between the Department of Energy (DOE) researchers and biomedical scientists supported by other agencies, especially the National Institutes of Health (NIH). In particular, the Secretary asked that the Task Force identify "new areas of research by DOE investigators that could…significantly advance the pace of progress in biomedical sciences" and "new mechanisms for conducting research in coordination with scientists from government laboratories…universities, academic medical centers, and industry." The Secretary's request was endorsed by Francis S. Collins, Director of the National Institutes of Health.

In response to the Secretary's request, SEAB assembled the Task Force on Biomedical Sciences, composed of four SEAB members and five other prominent scientists with multidisciplinary expertise, including disciplines referenced in the Secretary's request – precision medicine, bioinformatics, and near real time imaging of biological structures and functions, among others. The Task Force was co-chaired by SEAB members Dr. Steve Koonin and Dr. Harold Varmus. In addressing the challenge, the Task Force met by conference call and organized two workshops with invited participants that included DOE and NIH program administrators, and leading scientists from DOE national laboratories, universities, and industry. The report was reviewed by the full SEAB and approved at the September 22, 2016 meeting of the Board.

The DOE commends the Task Force for its significant effort in producing this informative report. The Task Force has identified compelling opportunities where current DOE-sponsored activities could support the biomedical research enterprise, and new research challenges that could benefit from the unique expertise found within the DOE, its laboratories, and its broader community of researchers. As noted in both the Secretary's charge and in this report, the DOE and NIH have a long history of working together on mutually beneficial activities. This includes the development and application of NIH-funded beamlines at the DOE's X-ray synchrotron light sources for structural biology research, the Human Genome Project, and the use of DOE-sponsored high performance computers to the study of complex biological systems. The DOE expects that current DOE-NIH collaborations will continue to bear fruit, with new opportunities for coordination or collaboration, including but not limited to the opportunities identified in this report, developing in the future.

Summary of Task Force Report

The Task Force report concluded that multi-disciplinary progress in the biomedical sciences has crucial implications for the Nation's health, security, and competitiveness. Progress in the biomedical sciences and in public health depend not only on research in biology and patient care, but on fundamental and evolving technologies and applications of physics, chemistry, and computational and data sciences. The historical interplay of technology, physical and computational sciences, and the biomedical sciences have resulted in important developments, including imaging diagnostic tools (Magnetic Resonance Imaging, Computerized Tomography, and Positron Emission Tomography), as well as new therapeutics.

The Task Force noted that U.S. scientific goals and responsibilities and the domains of Federal Agencies are imperfectly aligned. Federal support for research in the biosciences, including in the biomedical sciences, is distributed broadly among multiple Federal agencies, including the Health and Human Services (the National Institutes of Health and the Centers for Disease Control), the Department of Energy, the National Science Foundation, Veterans Affairs, and the Department of Defense (DoD), with untapped opportunities to synergize scientific progress with enhanced coordination and collaboration.

The report calls for stronger engagement and partnership between the Department of Energy (DOE) and the National Institutes of Health (NIH). DOE’s mission-driven basic research capabilities make it an especially promising partner for increased collaboration with the NIH, the Nation’s leading agency for biomedical research. Conversely, NIH is well-positioned to expand its relationships with DOE. While NIH would gain greater access to technologies and expertise in engineering and fundamental sciences, DOE researchers would also benefit from opportunities to tackle novel questions and problems that would in turn potentially improve DOE’s approach to its diverse mission space, including national security.

The report notes that novel biomedical technologies could be developed more efficiently and strategically through increased partnership. Particular DOE capabilities of interest to the biomedical research community include instrumentation, materials, modeling and simulation, and data science. These capabilities are becoming increasingly important in many areas of biomedical research, including cancer, neuroscience, microbiology, and cell biology; applications of high-performance computing and machine learning towards the analysis of massive and complex clinical and genetic datasets; radiology and radiobiology; and biodefense.

DOE modeling and simulation capabilities, initially developed to support the Department’s nuclear weapons mission, are now routinely applied to basic sciences and to energy-related problems. These simulations integrate understanding and data at multiple levels and dimensions and provide predictions for various courses of action. With the rapid expansion of biomedical data, opportunities now exist to apply advanced simulation technologies to biomedical problems. With increasing computing capability attainable as a result of the Exascale Computing Initiative, the application of advanced computing and data analysis methods to the biomedical sciences can be expected to continue growing into the future.

Similarly, cancer research involves a wide variety of questions about biological systems—ranging from structural and cell biology to genetics and microbiology—and about medical practices—including radiological diagnoses, detection of early cancers, measurements of tumor response and relapse, and improvements in drug delivery. Pursuit of these many topics involves methodologies that are especially well studied in DOE laboratories. Among them are nanotechnology and other materials sciences; radiation physics, radiochemistry, and radiobiology; imaging technologies; and computational tools. Many of these capabilities at DOE laboratories offer powerful incentives for interagency collaboration, as demonstrated by the ongoing DOE collaboration with the NIH's National Cancer Institute and other partners as part of the Vice President's Cancer Moonshot Initiative.

DOE Response to Task Force Recommendations

The Task Force identified four recommendations to improve the substance and mechanisms of DOE-NIH interactions in the relatively near future and to enhance the potential for greater interaction in the long term.

Recommendation 1: ***Define Joint Research Programs in the Most Fertile Areas of Biomedical Research and Applicable Technologies****. DOE and NIH leadership should jointly charge panels of DOE and NIH researchers to explore and document opportunities for increased collaboration in both problem-oriented (e.g. cancer and neuroscience) and technology-oriented (e.g. imaging, materials, modeling and simulation) topic areas.*

There are many productive areas of scientific inquiry and technology development for researchers from both the NIH and the DOE. The DOE strongly supports the use of DOE, NIH, or joint DOE-NIH sponsored principal investigator-driven scientific workshops to define the research needs for these communities and identify mutually beneficial priority areas of collaboration. Past experience has demonstrated that this process can yield productive and synergistic ideas for broad participation by the scientific research community. As these activities reveal new research needs that are best tackled through joint DOE-NIH support, opportunities to address them through the mechanisms described by the Task Force, including jointly funded research programs, multi-disciplinary research centers, and user facilities, will be explored.

There are several workshops currently planned for the next 12-18 months that can serve as venues for greater engagement among DOE and NIH-supported researchers. The Office of Science scientific user facilities and their annual user meetings are a strategic opportunity to introduce the broader NIH research community to the tools and approaches available, as well as to encourage productive new collaborations. DOE's open science user facilities currently support users from across the Federally-funded research community, including the NIH. In 2015, 15 Office of Science user facilities hosted more than 2700 NIH-funded users working on nearly 1200 unique projects. Over the next year and a half, the DOE Office of Science will work with the NIH to identify opportunities to further engage the biomedical research community in annual users meetings at DOE user facilities.

The Office of Science user facilities provide researchers with the most advanced tools of modern science, including: high performance scientific computing; nanoscale synthesis, fabrication and characterization tools; and X-ray light and neutron sources for characterization of materials, chemistries, and biologicals. These facilities are provided to the scientific community based on merit review of the proposed work and at no cost for work intended for publication in the peer reviewed literature. Each of these facilities supports a formal user organization to represent the users and facilitate the sharing of information, the formation of collaborations, and the organization of research efforts among the user community. To support these efforts, the facilities sponsor annual users meetings that include invited speakers and talks featuring recent science highlights as well as focused workshops.

Several new instrumentation projects recently developed at the X-ray light sources have demonstrated the potential of facility-based DOE-NIH engagement. For example, the NIH-funded Bionanoprobe at the Advanced Photon Source (APS) was developed based on a workshop held at the APS that identified the need for a high-resolution X-ray instrument capable of imaging the elemental and chemical state of trace metals in biological systems. More recently, two workshops held at the joint Stanford Synchrotron Radiation Light-source (SSRL) and Linac Coherent Light Source user meeting in October 2016 introduced newly developed capabilities specifically to the bioresearch community: 1) instruments for faster data measurements in macromolecular crystallography, the key X-ray technique for 3D atomic-level resolution of protein structure; and 2) integration of coherent imaging with electron microscopy to study dynamics of structural sub-states of macromolecules.

The DOE anticipates that the NIH will also identify opportunities to broaden participation in relevant NIH principal investigator meetings as well as engage the DOE research community in biomedical workshops. Such efforts are already underway: the *NIH Workshop on X-ray free electron laser and application for biomedical research* was held in November 2016, and the *Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative Investigators Meeting* was held in December 2016. Similarly, the DOE will look for new opportunities to engage NIH-supported researchers in DOE principal investigator meetings where there is a clear mutual benefit.

*Recommendation 2: **Define and Create Organizational and Funding Mechanisms that Bring Diverse Researchers Together and Cross-Train Junior People**. With a focus on early-career scientists, such methods include, but are not limited to, cross-agency assignments, summer gatherings, NIH-grant supplements, and training programs.*

Scientific user facilities that were historically developed to address fundamental questions in the physical sciences have become critical tools for the biomedical research community, as noted above. However, the grand challenges in the biomedical sciences are beginning to play a role in determining how these capabilities evolve in the future. This is clearly evident in the DOE’s advanced computing capabilities and the Exascale Computing Initiative. As part of the Vice President’s Cancer Moonshot, the DOE and its national laboratories are partnering with the National Cancer Institute (NCI) to support development of the next generation of computing tools that will significantly accelerate discovery in cancer research.

The major advantage to DOE of this partnership is to gain a deeper understanding of the architectural requirements for integrating simulation, scalable data analytics, and machine learning in the next generation of DOE supercomputers. The cancer community has the richness of data necessary to fully explore this opportunity and drive development of new computing architectures. Memoranda of Understanding (MOU) signed by the Secretary with the NCI and with Veterans Affairs, which hold some of the richest sets of medical histories in the world, will provide developers with access to the data necessary to develop integrated advanced computing systems.

The use cases in the three DOE-NCI pilot projects will be used to evaluate the next generation CORAL supercomputers that will be available over the next couple of years at three DOE national laboratories, and will provide feedback to the designers of future exascale computing systems. DOE’s National Nuclear Security Administration and Office of Science, several DOE laboratories, and the NCI have already invested funding in the current fiscal year for this project, and additional matching funds were requested by both agencies in the FY2017 President's Budget.

This partnership in advanced computing for precision oncology extends beyond the confines of Federal agency collaboration. In 2016, Secretary Moniz, NCI Director Douglas Lowy, and Glaxo-Smith-Kline (GSK) CEO Andrew Witty signed a Statement of Principles and a MOU for Accelerating Therapeutics for Opportunities in Medicine (ATOM), a new public-private partnership between DOE, NCI, and GSK that will attempt to reduce the time from pharmaceutical target to first human trials to a single year or less. The partnership seeks to bring together expertise in modeling and simulation, data analytics, and high performance computing with oncologists and pharmaceutical chemists in an agile innovation environment. The agreement aims to have GSK share its wealth of pre-competitive data to use in evaluation and validation of new predictive cancer models designed for use on the next generation of high performance computers. Throughout the process, the participants will be pushing towards the most open data sharing possible for each data type and dataset. This partnership will be open to additional participants that agree to the requirements, aims, goals, and culture of ATOM.

Agency partnerships like the DOE-NCI pilot projects and the workshops described above enhance collaboration and dialogue between the DOE and NIH research communities. These activities begin to address the Task Force's recommendation for more opportunities to bring diverse researchers together. The DOE strongly agrees with this recommendation. Such opportunities can result in cross-fertilization of ideas from diverse scientific disciplines, as well as the cross-training and cross-mentoring of early career scientists. The DOE will work with the NIH, scientific professional societies, and other research community groups to identify a broad suite of mechanisms to support interdisciplinary training and mentorship.

Recommendation 3: ***Define and Secure Funding for One or More Joint Research Units and/or User Facilities****. The DOE and the NIH should continually look for opportunities that are uniquely suited to the creation of facilities that serve multiple users or focus on multi-investigator, multi-disciplinary team science.*

The DOE-NCI pilot projects described above are one example in a growing DOE-NIH collaboration ecosystem. For cancer research, the DOE-NCI collaboration can grow to include other relevant science-based questions, for example a new jointly funded research program targeting the relationship between low dose radiation exposure and the onset of cancer. The recent report from the Biological and Environmental Research Advisory Committee (BERAC), a response to an Office of Science charge to provide advice on a SEAB-recommended low dose research program identified compelling science-based areas of inquiry that would be of interest to the NCI and would leverage current research activities supported by the Office of Biological and Environmental Research in both "omics" and bio-imaging technology. Furthermore, capabilities in data-mining that will be developed from the DOE-NCI pilot project could be applied to new low dose radiation epidemiological studies in order to provide the basis for revisiting existing regulations.

The NIH and the biomedical research community have traditionally been important partners of the DOE's Isotope Development and Production for Research and Applications Program, managed by the Office of Science's Office of Nuclear Physics. The Isotope Program supports production, and the development of production techniques, of radioactive and stable isotopes that are in short supply and of critical importance to the Nation. The NIH serves both as customer for the available isotopes – used by the medical community for both diagnostics and therapeutics, including for clinical trials of promising isotope-based cancer treatments – and as a driver for new isotope research. This latter contribution is evidenced by NIH engagement in the development of the 2015 Long Range Plan for the DOE-NP Isotope Program. The DOE and the NIH will undoubtedly continue to work closely to develop new isotope-based tools and treatments. DOE is currently working on developing large-scale production capabilities for alpha emitters, a class of radioisotopes with high priority for the medical community due to their promise for highly localized cancer treatment, and opportunity exists for more research in the development of theranostic agents that combine the properties of diagnostic agents with those of therapeutic agents in a single platform.

The success of facilities projects or of jointly funded major facility upgrades like SPEAR3 at the SSRL, which was led by DOE in 2004 with significant financial support from NIH, can be attributed in large part to the DOE's continued application of the cooperative stewardship model for its scientific user facilities. The model, derived from a series of workshops in the late 1990's that culminated in the seminal Cooperative Stewardship report from the National Research Council, puts responsibility for design, construction, operation, maintenance, and upgrading of a facility core with a single clearly identified federal agency—the steward. This provides freedom for other interested parties to work with facilities on new capabilities that serve unique research communities. The explosive growth in life science users at the scientific user facilities during the last two decades is a testament to the success of this model. Going forward, future collaborations on mutually beneficial facilities and capabilities, for example cryo-electron microscopy or advanced imaging technologies at the X-ray light sources, identified through community-based scientific workshops, will benefit from continuing to utilize this highly successful model.

In general, joint planning workshops that engage the research community will be necessary if the scope of DOE-NIH collaborations expands into experimentation and instrumentation, including new user facilities, which benefit both the DOE and the multitude of biomedical research communities supported by the 27 NIH Institutes and Centers.

Recommendation 4: ***Better Inform OMB, Congress, and the Public about the Importance of and Potential for Enhanced Interagency Collaboration****. Joint presentations to the Office of Management and Budget and Congressional committees that explain the mutual benefits of greater DOE-NIH collaboration can help overcome organizational and budgetary silos that inhibit cross-agency collaboration.*

The DOE recognizes the importance of open lines of communication with the Office of Management and Budget (OMB), with Congress, and with the Public about the importance of cross-agency collaboration in meeting our Nation's biggest science and technology challenges. As part of the DOE-NCI collaboration, both agencies have worked to keep OMB and Congress abreast of developments. A subset of the new research collaborations that are born from the engagement opportunities presented above can reasonably be expected to grow into important new opportunities that are both mutually beneficial for the collaborating agencies and beneficial for the public, akin to the DOE-NCI partnership. When this happens, the DOE will work with its interagency partners and the relevant research communities to make the case for federal funding, and to socialize the benefits of the opportunity with the public. The Cancer Moonshot can be viewed as an exemplar for this type of effort, and one that could be modeled for future collaborative efforts.

Conclusion

The DOE anticipates that the efforts described above will build upon past successes and continue the strong DOE-NIH partnership built on open dialogue and with mutual benefit to the physical, biological, and biomedical sciences. The examples provided above highlight several activities that the DOE is currently pursuing, or will pursue in the near future, that can strengthen the collaborative relationship between the DOE and the NIH. The Task Force report highlighted many other areas of opportunity for joint research that are not directly addressed above, but are still compelling areas for future consideration.

The DOE has extensive experience and a strong track record of success in stewarding the development of and ensuring productivity from multi-institutional, multi-disciplinary research centers, including Energy Frontier Research Centers, Bioenergy Research Centers, and manufacturing institutes. The DOE is ideally suited to partnering with the NIH to support the development of novel co-funding mechanisms such as “foundries”, as described in the report, be it through joint funding or through sharing of best practices. As discussed above, such foundries addressing topics of mutual interest – DNA synthesis, soft matter, nanomaterials, electrodes, and others – should be jointly determined by the DOE and NIH and based on a well-defined need from the research communities. Furthermore, the specific scientific and technological goals of any foundry must be developed through carefully designed workshops, studies, or other mechanisms that directly engage the DOE and NIH communities the facilities would support.

The NIH should also be encouraged to take advantage of existing mechanisms that enable collaboration with the DOE’s network of national laboratories. Strategic Partnership Projects (SPP) provide a ready method for other federal agencies to leverage the breadth of scientific and technical expertise within the DOE national laboratories to meet their mission needs. In fiscal year 2015, the agencies within the Department of Health and Human Services supported more than $83M of SPP at 11 laboratories. This and other methods for providing non-DOE federal funding to the laboratories can be used to support many of the activities described in the report, including development of new experimental techniques in biological electron microscopy and in biodefense, where both experimental and computational research at the laboratories is already being supported by several agencies.