February 14, 2020

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Director, Division of Comparative Medicine
and Malgorzata M. Klosek, PhD
Director, Division of Construction and Instruments
Office of Research Infrastructure Programs (ORIP)
Office of the Director, National Institutes of Health
Bethesda, MD

Submitted electronically

Re: NOT-OD-20-050 - Request for Information (RFI): FY 2021-2025 Strategic Plan for the Office of Research Infrastructure Programs: Division of Comparative Medicine and Division of Construction and Instruments Programs.

Dear Dr. Murphy and Dr. Klosek:

The Association of American Medical Colleges (AAMC) and the Association of American Veterinary Medical Colleges (AAVMC) are grateful for this opportunity to provide our perspectives on objectives for the next five-year strategic plan of the Office of Research Infrastructure Programs (ORIP).

The AAMC is a not-for-profit association representing all 154 accredited U.S. medical schools, nearly 400 major teaching hospitals and health systems, and more than 80 academic and scientific societies. Through these institutions and organizations, the AAMC represents nearly 173,000 faculty members, 89,000 medical students, 129,000 resident physicians, and more than 60,000 graduate students and postdoctoral researchers in the biomedical sciences.

The AAVMC is a not-for-profit association representing all 32 accredited U.S. veterinary medical schools. 4000 faculty members, 13,000 veterinary medical students, and 3000 graduate students.

Our member institutions collectively perform more than half of all the extramural research funded by NIH and manage many ORIP-supported animal resources, shared instrument cores and research facilities. The ORIP plays a uniquely important role for the extramural research community. While other NIH institutes and centers may support instrumentation, infrastructure, and animal research within the context of their specific missions, the ORIP's programs advance these resources more broadly and extensively, across disciplines, with an emphasis on developing shared resources. Competitive, merit-reviewed awards from these programs help advance state-of-art technology for biomedical research and support a diverse range of institutions. The ORIP provides opportunities for construction and renovation of major research facilities (when appropriated funds are available) and support for nonhuman primate and other animal resources.

The following comments respond to specific topic areas invited in the Request for Information, and outline objectives or elements for ORIP's strategic planning. These comments are based in part on discussions and input from members of AAMC's Group on Research Advancement and Development for research deans, Group on Business Affairs, and Group on Institutional Planning,[1] and AAVMC's Research Committee leadership, as well as from individual investigators.

Animal Resources and Biomaterials

Gaps, challenges, and opportunities that can be effectively addressed by the development of new animal models and related biomaterials and "omics" tools for characterization and understanding of disease-related biological processes.

- The next strategic plan should include support for research programs that more completely characterize the complexity of animal models in relation to human disease or physiological states. Investigators on individual research project grants often understandably focus on a single principal phenotype in addressing the effect of specific factors under study. Many diseases are complex and multifactorial. In research into those diseases, animal models should reflect the multiple traits observed in humans as much as possible. Future programing through ORIP should help more fully characterize those models and traits and should support studies of animal model development and validation. Also, corresponding to the "omics" tools noted in the question, much more study is needed of environmental factors in the laboratory that affect animals as appropriate models for disease (for example, variations in animal habitat). Better understanding of these factors should also aid in improving the rigor and reproducibility of studies with animal models.

- The strategic plan should dedicate more resources for automation. Funding for automation in animal facilities has not kept pace with the technological advances employed in other industries that involve work with animals. Some limited adoption has occurred in animal husbandry such as automatic watering, and ventilated rodent caging. This automation has become so commonplace that many do not conceive of it as an advanced technology. Robotics (cage changers, bottle handlers, bedding dispensers, etc.) have evolved significantly over the past twenty years. Funding mechanisms for animal resources should evolve as well to support these advances.

- ORIP should address varying needs for access to nonhuman primates (NHPs). Historically, the demand for nonhuman primates has fluctuated significantly. Due to the long gestation and maturation time for NHPs, changes in breeding production do not affect the availability of animals for research until four to five years later. This results in a cycle of shortages and unsupported oversupply. To prevent this, ORIP should provide basic support for a reserve supply of NHP species commonly used in research to act as a

[1] AAMC GRAND is a professional development group for research deans and deans of clinical and translational research within medical schools and teaching hospitals. The GBA advances administrative and fiscal management in academic medical institutions to support medical education, research, and health care. The GIP advances the discipline of planning in academic medicine by enhancing the skills and knowledge of professional planners and promotes the value of planning.

buffer during shortages. In addition, investigators using NHPs increasingly need animals with specific characteristics, and this reserve could facilitate maintaining enough animals to meet those needs. Such characteristics may include aged animals, females, or primates exhibiting certain temperaments or behaviors.

Ways in which ORIP can identify the need for and then implement methods to improve the viability, utility, and access to new and existing animal models, related biomaterials resources, and services.

- ORIP should promote development of centralized databases and data sharing. Such databases can provide researchers with a full understanding of the traits and characteristics of human disease as well as the known characteristics of different animal models in different species that have been identified over decades of NIH-funded research. Establishing this information will also provide a guide for the development of new animal models and their characteristics. Access to comprehensive data resources should also aid in improving the rigor and reproducibility of NIH research by helping researchers select the most effective models for human diseases. ORIP's initiatives on data sharing and data policy should be coordinated with NIH-wide initiatives.

- ORIP should revise its website and on-line information to help investigators better navigate the types of resources available. Researchers have noted to us that much information about valuable resources--for example, for invertebrate models--are contained in different "fact sheets" on different parts of the site, and information about those resources is difficult to retrieve and compare directly.

Approaches to improve the rigor and reproducibility of animal models of human health and disease, including how those models should be validated.

- ORIP can help standardize operating procedures for research techniques. Veterinarians and surgeons at research facilities are developing and optimizing surgical and other procedures in support of research projects. A central repository of practices with associated data, perhaps including videos, would be valuable. Panels of investigators could be convened around the "best" or optimal procedures and techniques, to the degree that consensus is possible. Access to such information would reduce development and training time for investigators who are adopting these procedures to their research projects, and should improve consistency among investigators, increasing reproducibility.

- Several comments above on data resources also underscored potential to improve rigor and reproducibility. Our colleagues at the American College of Laboratory Animal Medicine (ACLAM) underscore the importance of fully characterizing phenotype in animal models, conducting research that identifies gender-related differences in animals, and incentivizing data sharing.

Veterinary Training

Challenges and opportunities that should be considered for research training and career development programs targeting veterinarians or veterinary students wishing to pursue biomedical research careers.

- Veterinary scientists are essential to advancing biomedical research, as investigators, members of research teams, and as leaders in developing and sustaining valuable animal resources. NIH should continue efforts to encourage careers for veterinary medical scientists, paralleling concerted efforts on physician scientists. Research faculty have commented that veterinary medical school graduates should be more actively recruited into PhD programs at academic medical centers, and thus to train veterinary scientists alongside physician scientists and basic scientists.

Challenges and opportunities related to the integration and retention of veterinary scientists into the biomedical research enterprise.

- The majority of veterinary medical school graduates, like most graduates of AAMC member medical schools, are women. Integration and retention of veterinary scientists in academic careers hopefully will be aided by institutions' efforts to improve equitable hiring and to advance, promote, and retain women faculty and researchers. Promoting greater inclusiveness alone may not be sufficient to bring or retain more veterinarians in biomedical research, and other career development programs will also be needed. But we believe demographics and inclusiveness are often overlooked in discussions about attracting physician and veterinary scientists into academic careers. ORIP should coordinate on veterinary medical scientist training with other NIH offices advancing physician and clinician scientist career development.

Instrumentation

Up-and-coming instrumentation technologies for biomedical research and instrumentation needs of emerging scientific fields.

- The strategic planning RFI asks separately for input on instrumentation programs and for facilities construction, as these are separately managed programs. However, a theme from AAMC's discussion with constituents is how often the acquisition of new, shared instruments and cores are obstructed by demands for space and other physical infrastructure. Often, the renovation or refitting of facility space exceeds the cost of the instrument being purchased (not counting training and other human capital demands for utilizing the instrument). Although institutions are responsible for supporting the required infrastructure for awarded equipment (space, renovations, maintenance, etc.), shared instrumentation grant applications are often independently submitted. Once awarded, institutions are faced with significant infrastructure costs, sometimes greater than the cost of the equipment. Applicants should be required to provide a letter of commitment specifically stating that the infrastructure needs have been evaluated and commitments made by the institution to provide such. A detailed cost analysis is not practical at the application stage. However, basic information (site location, room number, cost estimates for renovations, and service contract costs) should be included in the application.

- Related, advances in technology have put new, high-powered instruments within reach of more academic institutions, but ORIP program funding is limited to the purchase of one instrument or the infrastructure to house the instrument. For example, one institution considered ways that three individual instruments could be purchased and linked together in ways that would support innovative research and data collection. But the requirement for each instrument to be a stand-alone core prevented that approach. There is a need for support for integrated technologies that bring together instruments into one core for high impact analysis and with support for infrastructure.

- Consistent with the theme of the comments above, several academic institutions see an advantage in co-locating multiple cores and instruments, a so-called "core floor." The ORIP's current shared instrumentation programs have understandably focused on single instruments, and these programs have been important and successful, especially in promoting more integrated science (as teams organize to use shared facilities) and, AAMC believes, better stewardship of resources (at the very least, avoiding unnecessary duplication of instruments and facilities in proximate labs). As part of the next strategic plan, the ORIP should consider convening a working group to consider integrated approaches for supporting multiple instruments within facilities. The working group should consider other instrumentation needs and the potential for coordination with other NIH programs. For example, the National Institute of General Medical Sciences has undertaken an initiative to support Cryo-EM (electron microscopy) regional cores, a highly sought-after technology. (Another technique identified as important by our research deans is single cell RNA sequencing.) The rules of the Shared Instrumentation Program (SIG) program indicate that SIG grants do not support "multiple instruments bundled together." The wording strongly discourages the inclusion of ancillary equipment required for full functioning. For example, purchase of a light sheet microscope from one vendor, will also require the purchase of advanced software (typically costing $30,000) from a different vendor. This second purchase is not forbidden but appears to be highly discouraged and should be clarified in future ORIP guidance.

- The SIG RFA appears to discourage building your own instrument. While Cores will typically buy out-of-the-box instruments, cutting edge science sometimes requires cutting edge instruments, and there is no current funding mechanism for actively solving this problem. A funding mechanism for exploratory development of instrumentation is recommended.

- The volume and complexity of data is an increasingly difficult problem for institutions. It would be worthwhile for ORIP to institute a program complementary to the SIG program, to assist with data storage, i.e., a Cloud based system. The new NIH STRIDES program may allow for such development.

- The S10 Instrumentation Program Award guidelines make clear that although NIH helps to fund the purchase of the instrument, "post-award service contracts" are excluded from funding. However, a better approach would be to consider Total Cost of Ownership in funding decisions. While the upfront cost to purchase an instrument is certainly a burden

to most institutions (hence, the need for the SIG), NIH funded research would be better served if ORIP allowed inclusion of service contracts in the purchase price for the first 1-2 years. Thereafter, these costs could shift to the institution, presumably after the instrument was fully operationalized.

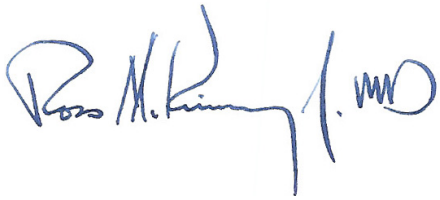
Construction

Specialized laboratory environments and other building infrastructure needs driven by emerging scientific fields and novel experimental approaches.

- Cryopreservation of biological samples and reagents are a significant institutional cost. Storage of these materials is an essential component of the biomedical research enterprise. Yet, adequate storage sites are lacking, and many researchers are using outdated, unreliable equipment (e.g., 20-year-old minus-80-degree freezers). The NIH could become the leader in advancing energy efficiency by financing institutional equipment replacement grants. These grants would be a combination of the SIG mechanism and the G20/C06 to build out adequate storage rooms (proper HVAC, floor weights, central temperature monitoring, etc.). Many institutions relegate these decisions to individual researchers or departments. This approach renders the output from NIH investments in research (specimens/data), vulnerable.

The AAMC and AAVMC would be pleased to provide any additional information or clarification on these comments. Please feel free to contact us directly or Stephen Heinig, AAMC Director for Science Policy, at sheinig@aamc.org

Sincerely,



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