COUNCIL ON GOVERNMENTAL RELATIONS

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The National Academies Committee on Federal Research Regulations and Reporting Requirements (the Committee) released Part 2 of its report, *Optimizing the Nation's Investment in Academic Research; A New Regulatory Framework for the 21st Century*, on June 29. The full report includes Parts 1 and 2 and is available online. COGR has previously commented on Part 1 of the Committee's report. Here we focus on Part 2, which addresses federal regulations governing human subjects research, the "Common Rule," and proposed revisions to the rule; export controls; select agents and toxins; intellectual property and technology transfer reporting; and consideration of how to operationalize the proposed regulatory framework and Research Policy Board (RPB) recommended in Part 1.

Ethical, Legal and Regulatory Framework for Human Subjects Research

Part 2 of the report begins with an examination of the ethical, legal, and regulatory framework for human subjects research (Chapter 9). The Committee provides a history of the development of the Belmont Principles, the ethical foundation for the Common Rule, and the independent commission that established them. The report notes that questions about the application of these principles to current and evolving research questions and contexts have arisen since the publication of the Belmont Report four decades ago.

In this chapter, the Committee makes the case for a new independent national commission to examine, and update as necessary, "the ethical, legal and institutional frameworks for protecting human research subjects" and how they might be applied to research involving de-identified biospecimens; large datasets; research involving discrete and insular communities and adults with diminished decision-making capacity; comparative effectiveness, clinical innovation and quality assurance; minimal-risk sociobehavioral research; and other contexts. The report notes that a 2002 Institute of Medicine report called for the formation of an independent committee to "reassess the adequacy of the federal regulatory system overseeing human research" but that the committee was never created. The proposed commission would be authorized by Congress and modeled on the President's Commission for the Study of Ethical Problems in Medicine and Biomedical and Behavioral Research,' a successor to the commission that created the Belmont Report.

Per the report, the proposed commission would recommend regulatory approaches to unresolved questions including the scope of human research activities that should be covered by federal regulations; addressing the boundaries between research and medical care; incorporating investigator responsibility; and balancing individual rights with collective obligations to advance public health. Regarding the latter concern, the Belmont Report indicates that "Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. Such treatment falls under the principle of beneficence. The term "beneficence" is often understood to cover acts of kindness or

charity that go beyond strict obligation. In this document, beneficence is understood in a stronger sense, as an obligation. Two general rules have been formulated as complementary expressions of beneficent actions in this sense: (1) do not harm and (2) maximize possible benefits and minimize possible harms."

The report also recommends that the proposed commission be charged with addressing questions such as where in the executive branch the regulatory authority for human subjects research should lie, whether with individual agencies or with one independent agency, and whether there should be a standing advisory committee on human subjects protections. Presently, the Secretary's Advisory Committee on Human Research Protections (SACHRP) advises the Secretary of the Department of Health and Human Services (HHS). The Committee may be suggesting consideration of an advisory committee that has broader reach. With regard to a commission addressing where in the executive branch the regulatory authority for human subjects research should lie, our organization sees no harm in the proposed commission considering this question and making recommendations.

The report suggests that the volume of comments received in response to the Common Rule advanced notice of proposed rulemaking (ANPRM) and NPRM, and the concerns expressed, underscore the need to address issues that have emerged since the publication of the Belmont Report. The Committee suggests that the NPRM "could be detrimental to areas of important research" and "does not adequately or effectively address the breadth, depth, and import of unanswered questions." The report highlights the public's concerns about the NPRM as indicated by a review of NPRM comments conducted by the HHS Office for Human Research Protections (OHRP), and notes that OHRP's review aligns with a COGR-APLU analysis of the comments as well as comments made by the non-profit group Public Responsibility for Medicine in Research and others.

The Committee suggests that the NPRM is "marred by omissions, the absence of essential elements, and a lack of clarity." "In addition, important questions about the overall impact and long-term costs of the proposed regulatory changes are unresolved." It highlights concerns about the proposal to expand the definition of "human subject" to include deidentified biospecimens as an illustration of the problem of moving the NPRM forward to a final rule. Regarding biospecimens, the COGR-APLU analysis found that 76% of all comments addressed proposed changes to the treatment of biospecimens. Of these, 74% of all responses and approximately 96% of responses from patients and members of the research community (including researchers, universities, medical centers and industry) opposed the proposed changes. The report suggests that the current system may be "better served by explicit sanctions against investigators and institutions seeking to re-identify biospecimens sources…than by redefining all research with de-identified biospecimens as human subjects research subject to a revised Common Rule." SACHRP, in its response to the NPRM, also suggested that in addition to other measures such as education, notification and an opportunity to opt-out of future research, "limitations and sanctions on unauthorized re-identification are preferable in this context to a 'broad consent' mandate that would not represent meaningful consent and could substantially hamper scientific progress."

COGR, in its response to the Common Rule NPRM, suggested that risk to donors is addressed by removing identifiers, and through the use of institutions' security safeguards, and can be further mitigated by prohibiting unauthorized re-identification and imposing sanctions if it were to occur. COGR believes that a forum for addressing the issue of biospecimens that includes experts in the field, representatives from stakeholder groups and a full review of existing literature, including gaps and limitations, is needed to consider how to facilitate biospecimen research while addressing privacy and other concerns. Would limitations and sanctions on unauthorized re-identification provide the appropriate balance between the principle of respect for persons and that of beneficence? What is the true financial impact of broad consent to the healthcare system? What impact would broad consent have on medical discovery and innovation? Would the use of broad consent have a disproportionate negative impact on traditionally underrepresented groups? Is opt-out, as proposed by SACHRP, necessary or desirable from a public health perspective? Could it be effectively implemented in the absence of infrastructure and funding, and without hindering scientific exploration and discovery that benefits the public? Should opt-out be revisited at a later date as technology progresses and electronic health records improve? The commission recommended in this report may be the appropriate vehicle for addressing these and other critical questions.

With respect to the NPRM, the Committee recommends that the executive branch withdraw the proposed rule and that the regulatory structure "not be revised until the national commission has issued its report" and stakeholders have had an opportunity to respond. COGR, many of its member institutions and advisory groups such as SACHRP have also called for the NPRM to be withdrawn and we commend the Committee for making this bold and critically important recommendation. SACHRP has recommended that "HHS conduct a comprehensive re-write of the NPRM through a concerted effort to simplify the proposed changes and to focus efforts on selected issues for which there is broad support by the public, investigators, IRB professionals, sponsors and other experts." COGR believes that moving forward with a final rule at this time would be unfortunate as HHS could not address the myriad issues and shortcomings highlighted in such a short time-frame. Greater stakeholder input and consideration is needed. To the extent HHS does move forward, our organization is hopeful that they will heed SACHRP's recommendation to focus efforts on selected issues for which there is broad support.

Intellectual Property and Technology Transfer

Chapter 10 on reporting of intellectual property (IP) and technology transfer highlights the role of the Bayh-Dole Act in the management of IP derived from federally funded research and the role of agencies in overseeing university management of intellectual property via the Interagency Edison (iEdison) invention reporting system. The report suggests that iEdison is cumbersome to use, is not used by all agencies, requires extensive reporting beyond what is required by Bayh-Dole and is inadequately staffed and maintained. The report recommends that Congress transfer responsibility for the operation of iEdison to the Department of Commerce and allocate resources to upgrade and improve the system; that Commerce, in consultation with universities via the proposed Research Policy Board, develop a uniform set of requirements regarding the frequency and type of data to be submitted that does not exceed the requirements of Bayh-Dole; and that Congress authorize Commerce to ensure that individual agencies adhere to these uniform requirements.

COGR fully supports the recommendation to develop a uniform set of requirements for reporting of invention data applicable to all agencies. COGR also strongly urges that any such uniform requirements be streamlined to minimize burdens placed on universities while preserving the core principles of Bayh-Dole. With regard to excessive reporting requirements, NIH has Congressionally-driven requirements that exceed those of other agencies, including reports on invention utilization. Bayh-Dole provides for agencies to require utilization reports at their discretion.

While our organization agrees with many of the concerns discussed in the report, we believe that a lack of adequate resources and dedicated funding for the iEdison system is more the issue than the agency placement of iEdison. NIH should be given credit for managing the system under difficult constraints. COGR also acknowledges the recent improvements made by NIH in providing additional staffing and resources.

Additional funding and resources (optimally directly appropriated), and a directive that all agencies make use of the system, would allow for substantial improvements regardless of agency placement. It is therefore not clear that transferring responsibility for the operation of iEdison to the National Institute of Standards and Technology, which currently has oversight over Bayh-Dole, or another part of Commerce, would provide more than marginal improvement in government-wide reporting of IP. iEdison is a legacy system; in the long-term a gradual transition to a new, more modern and streamlined system is likely to better serve the purpose.

Select Agents and Toxins

Chapter 11 of the report focuses primarily on research with select agents and toxins. The Select Agents and Toxins List currently contains 65 agents and toxins "having the potential to pose a severe threat to human, animal or plant health" and is maintained by the Centers for Disease Control and Prevention and the U.S. Department of Agriculture (USDA). The report notes concerns that the regulations may impede research that could protect against threats, including research involving less pathogenic organisms; have raised the cost of conducting research with these agents; and have led to a decline in available specimens. The report also suggests that the lengthy clearance process may affect the number of researchers conducting this research; that there is a lack of consensus on which agents warrant placement on the list; that strains with lower virulence could be excluded from the list; and that institutions can be subject to inspections by multiple agencies. The Committee recommends that the President assign responsibility for regulating select agents and toxins to a single agency; that the Federal Select Agent Program develop an inventory management system that takes into account the self-replicating nature of biological agents; and that the regulations be amended to increase researcher access during public health emergencies, increase the number of low-virulence strains available to researchers, and make the process by which materials are added and removed from the list more transparent. COGR supports these recommendations. However, our organization believes the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 may have to be amended to assign responsibility for regulating select agents and toxins to a single agency.

Export Controls

Chapter 12 of the report provides background on export controls and the administration of controls via the Departments of State and Commerce and the International Traffic in Arms Regulations (ITAR) and Export Administration Regulations (EAR) respectively. The report highlights the 1985 National Security Decision Directive 189 (NSDD 189) which established the principle that the products of fundamental research remain unrestricted to the maximum extent possible; a principle that is operationalized through fundamental research exclusions in ITAR and EAR. The report notes that ongoing efforts began in 2009 to reform export controls, which are viewed as cumbersome and having impeded university research in a number of areas, but suggests that proposed modifications to ITAR would undermine the fundamental research exclusion and that the exclusion doesn't apply to tools and instrumentation used to conduct research or construct research apparatus, thus negatively affecting the pace and quality of research. Among the Committee's recommendations are that Congress and the Administration "support a robust continuation and renewal of the Export Control Initiative" and that this initiative seek university and other stakeholder input at all stages of the process, in particular with respect to deemed export provisions, and "vigorously support the spirit and letter of the fundamental research exclusion." COGR agrees overall that these reform activities should continue, although we do not necessarily agree with all the recommendations of the cited 2007 report on deemed exports.

State and Commerce have engaged stakeholders, but universities remain concerned about the State Department's final definition of fundamental research and that this exclusion has not necessarily been applied to research conduct as well as reporting. A revised ITAR definition is expected to be published as a proposed rule early in 2017. The revised EAR definition confirmed institutions' understanding of fundamental research and NSDD 189. COGR supports an ITAR definition that further affirms NSDD 189 and that is consistent with the EAR.

Operationalizing the Proposed Regulatory Framework and Research Policy Board (RPB)

The final chapter of the report, chapter 13, includes the Committee's thoughts on operationalizing the Research Policy Board recommended in Part 1. The Committee also articulates a set of "Principles to Guide the Regulatory Framework" for the future development of federal research regulations.

The Committee suggests that the RPB would provide stakeholders with an opportunity to consider issues, policies, regulations, and new and emerging fields of research in an anticipatory way, including providing input on advanced notices of proposed rulemaking prior to publication for comment, and that unnecessary regulation could potentially be avoided by addressing agency concerns at an early stage. The Committee also proposes that the RPB evaluate the effects of existing guidance, policies and regulations and assess the cost and benefit of regulations through the development of metrics; review and discuss proposed legislative action, new research trends and implications for the governance of research; and recommend rulemaking to correct existing regulatory problems.

The Committee advocates for dedicated staff to support the RPB which it suggests could be the vehicle for assembling and analyzing data to inform policy changes or new regulations. As

indicated in our review of Part 1 of the report, COGR supports the Committee's recommendation that Congress create a new mechanism, to include an active public-private forum and a designated official within government, to foster more effective conceptualization, development, and harmonization of research regulations. Our organization would note that an infrastructure of expertise and support exists within university-based associations such as COGR, the Association of American Universities, the Association of Public and Land-grant Universities and the Association of American Medical Colleges, and optimally would be fully utilized and not duplicated, and that Congress has been reticent to create a board that would incur any cost or be permanent.

Efforts are underway to create a Research Policy Board and COGR has endorsed House and Senate bills. The *University Regulations Streamlining and Harmonization Act of 2016*, introduced by Congressman Dan Lipinski, would implement a number of recommendations put forward in the National Academies report and, like the Senate's *Promoting Biomedical Research and Public Health for Patients Act*, would create a research policy board. The House bill proposes that the board be composed of federal officials from research funding agencies, administrators from research institutions, non-profit associations representing research institutions and stakeholders from the scientific and engineering research community. It describes a board that would advise on actions to create a more efficient and less burdensome enterprise; promote a comprehensive approach to regulation; coordinate new and existing regulations, policies, guidance and reporting efforts; modify or eliminate unnecessary regulation or policy; identify counterproductive legislative mandates; develop ad hoc groups with the expertise to review and address proposed or existing regulations and policies; maximize consultation with stakeholders; review agency regulatory plans and cost estimates, including draft regulatory actions, policies and guidance; and submit annual progress reports to Congress.

The *Promoting Biomedical Research and Public Health for Patients Act*, introduced by Senator's Alexander and Murray, includes a research policy board that would likewise make recommendations on harmonizing regulations and policies of similar purpose; identify adverse consequences of existing regulations and policies and make recommendations; seek to improve coordination among agencies; develop metrics to assess burden and identify process improvements; provide a forum for discussion of research policy, regulatory gaps, challenges and best practices; and develop expert subcommittees as needed to analyze pressing issues and anticipate regulatory challenges.

Conclusions

COGR appreciates the work of the National Academies Committee on Federal Research Regulations and Reporting Requirements and the efforts of Senator's Alexander and Murray, Representative Lipinski, and other legislators in both seeking to identify regulatory challenges to the research enterprise and to implement, via pending legislation, many of the Committee's recommendations for reducing or eliminating these challenges and fostering a robust environment for federally funded research.