COGR
Council On Governmental Relations

Laboratory Animal Welfare: Coordination and Harmonization of Regulations and Policies; NIH Notice and Request for Comments

Input is sought on each of the following proposed actions that the agencies are considering:

1. Allow investigators to submit protocols for continuing review using a risk-based methodology.

The Council on Governmental Relations (COGR) is an association of approximately 190 leading research universities and affiliated academic medical centers and independent research institutes. COGR concerns itself with the impact of federal regulations, policies, and practices on the performance of research conducted at its member institutions. We appreciate the opportunity to comment on proposed actions to reduce regulatory burden associated with the conduct of federally funded animal research. Many of our responses are derived from the report *Reforming Animal Research Regulations: Workshop Recommendations to Reduce Regulatory Burden*, issued on October 24, 2017. The workshop and resulting report resulted from a collaborative effort on the part of COGR, The Federation of American Societies for Experimental Biology (FASEB), the Association of American Medical Colleges (AAMC), and the National Association for Biomedical Research (NABR), which brought together university investigators, laboratory animal veterinarians, and administrators engaged in animal research or oversight; chairs and administrators of Institutional Animal Care and Use Committees (IACUCs); directors of university animal welfare programs; accreditors; and representatives of associations with members who are engaged in animal research and oversight. As indicated in the report, the focus of the workshop was to identify requirements that demand significant administrative effort but do not enhance animal welfare and to prioritize steps that agencies and Congress can take to reduce inefficiencies.

As noted in the FASEB/AAMC/COGR/NABR report, which considers and incorporates reports and recommendations from the National Academies, National Science Board, Federal Demonstration Partnership, and the National Institutes of Health, "Applying the human subjects' regulatory framework for exempt research and expedited review to animal research would mean that studies with little risk could be processed more expeditiously. Veterinarians and IACUC members could spend more time on studies with a higher risk potential." The report recommends that "NIH and USDA establish a risk-based process for review of animal research protocols similar to that for human subjects research under 45 CFR 46; §46.110. Through issuance of a Notice in the Federal Register similar to the NIH Notice issued in 2014 regarding Significant Changes (NOT-OD-14-126), USDA and OLAW could amend the protocol review requirement to define types of studies involving low-risk, noninvasive, or minimally invasive procedures. These studies could then be deemed exempt from full IACUC consideration or eligible for administrative or single member (expedited) review, without concurrence by the full IACUC." Such studies might include those that are observational and otherwise non-invasive. This risk-based methodology would be applicable and is recommended both when an IACUC

administrator/member makes an initial determination of risk and with respect to continuing protocol review (all protocols whether new or ongoing), not just for continuing review. The process could work similarly to the Veterinary Verification and Consultation process with a focus on the IACUC Administrator reviewing and triaging low risk protocols rather than the veterinarian.

The report also recommends that USDA revise §2.31(d)(5) of the AWA Regulations as follows: "The IACUC shall conduct continuing reviews of activities covered by this subchapter at appropriate intervals as determined by the IACUC, including a review as required in §2.31(d)(1-4) *at least once every three years* (emphasis added)." This would make review frequency consistent with the PHS Policy. The 1999 NIH Initiative to Reduce Regulatory Burden also recommended establishing a common protocol review frequency associated with the level of risk, but not less than every three years. We believe a risk-based approach to review would reduce administrative burden without reducing protections.

2. Allow annual reporting to OLAW and USDA on the same reporting schedule and as a single report through a shared portal.

The 2016 National Academies report, *Optimizing the Nation's Investment in Academic Research*, recommended that Congress direct OMB to convene representatives from federal agencies and the research community to assess the feasibility and utility of establishing a unified federal approach to develop, promulgate, and manage policies and regulations pertaining to the care and use of research animals, and in a related recommendation that multiple annual reports to various agencies about animal care programs be replaced by a single annual report under the proposed government-wide oversight program. Allowing annual reporting to OLAW and USDA on the same reporting schedule and as a single report through a shared portal, would be beneficial in terms of burden reduction, however, it is also less impactful than the Academies proposal.

3. Harmonize the guidance from NIH and USDA to reduce duplicative considerations of alternatives to painful and distressful procedures.

The FASEB/AAMC/COGR/NABR report makes the following recommendation: "Amend the language in USDA Animal Care Policy #12 with respect to literature searches to be consistent with AWR §2.31(d)(1)(ii), which charges the IACUC to determine "that the principal investigator has considered alternatives to procedures that may cause more than momentary or slight pain or distress to the animals, and has provided a written narrative description of the methods and sources…" A 1999 NIH initiative and report on reducing regulatory burden made a similar recommendation: "That USDA revise Policy #12 in the Animal and Plant Health Inspection Service (APHIS) Animal Care Policy Manual to charge the IACUC with final responsibility for determining the documentation required to assure that the principal investigator has considered alternatives to any potentially painful procedure." As noted in the FASEB/AAMC/COGR/NABR report, "keyword/literature searches are not required by either the AWA or AWR" and "have been shown to be ineffective." We suggest that if an IACUC has determined that the investigator has adequately considered alternative procedures and

provided a narrative description of methods and sources this will not weaken protections but represents an improvement over the current process.

USDA could harmonize to Section IV.C.1 of the PHS Policy which indicates that "In order to approve proposed research projects or proposed significant changes in ongoing research projects, the IACUC shall conduct a review of those components related to the care and use of animals and determine that the proposed research projects are in accordance with this Policy. In making this determination, the IACUC shall confirm that the research project will be conducted in accordance with the Animal Welfare Act insofar as it applies to the research project, and that the research project is consistent with the Guide unless acceptable justification for a departure is presented. Further, the IACUC shall determine that the research project conforms with the institution's Assurance and meets the following requirements: a. Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design…"

4. Provide a minimum 60-day comment period for new OLAW policy guidance.

Allowing adequate time for response and input from the research community is critical to developing effective and balanced guidance. As recommended in the FASEB-AAMC-COGR-NABR report, "…consider requiring at least a 60-day comment period on the merits and impact of any proposed policies, guidance documents, FAQs, or interpretive rules before they are issued." The report also recommends that: (1) Final policies and guidance include material changes that reflect germane comments received from the regulated community; (2) "near-final" documents be "reviewed by an external advisory committee of experts from the regulated community engaged in animal research before they are disseminated for public comment or final agency review"; (3) guidance documents clearly state that they do not carry legal or regulatory force; and (4) guidance documents not be accompanied by a requirement to obtain agency approval for alternative methods or processes.

Consistent with items 3 and 4, as noted in the FASEB-AAMC-COGR-NABR report "The Guide for the Care and Use of Laboratory Animals (Guide) is not a regulatory document. Given that, OLAW should use the Guide as it was intended, namely, 'to assist institutions in caring for and using laboratory animals in ways judged to be professionally and humanely appropriate." "OLAW should revise FAQ C7 and PHS Policy IV.B.3.c to ensure that IACUC-approved alternative strategies from 'should' statements in the Guide are not deemed departures or deviations and are not required to be included in the semiannual report to the Institutional Official. This would be consistent with OMB's Agency Good Guidance Practices Bulletin and would significantly reduce administrative burden without compromising animal welfare." As indicated in the report "The Guide allows facilities to produce welfare outcomes for animals in diverse and innovative ways by permitting alternative strategies to 'should' statements upon approval by the IACUC."

As noted recently by Office of Information and Regulatory Affairs Administrator and in a hearing by the House Committee on Oversight and Government Reform, agencies routinely fail to comply with the Office of Management and Budget's 2007 "Good Guidance" Bulletin and agency guidance and FAQs often function as a "backdoor" to regulation. In conducting its review of applicable regulation, policy and guidance with the goal of

reducing administrative burden, NIH, USDA and FDA should review all pertinent guidance documents to ensure that guidance does not carry, or have the appearance of carrying, regulatory force or requirements. We suggest that in addition to being publicly vetted, guidance documents should be used sparingly.

5. Other approaches not previously mentioned.

It is our hope that, consistent with the spirit and language of the 21st Century Cures Act, NIH, USDA and FDA review and consider reform measures related to all applicable regulations, policies and guidance. In addition to the proposed actions outlined above, we ask that NIH, USDA and FDA consider the following recommendations made in the FASEB-AAMC-COGR-NABR report, many of which were previously made in the 1999 NIH Initiative to Reduce Regulatory Burden and other reports:

- "NIH and other federal agencies involved in the review of regulations and policies for the care and use of laboratory animals mandated by the 21st Century Cures Act should appoint an external advisory group of experts engaged in animal research from entities that receive federal research awards to serve as advisors. The advisory group should include those involved with oversight responsibility at the institutional level, such as institutional administrators, IACUC members, veterinarians, and investigators engaged in animal research. This will foster progress and impartiality in the conduct of this review, which should take into account relevant regulations, policies, and guidance, along with the recommendations of this and other reports that have addressed regulatory burden associated with animal research." We believe active engagement of grantees in the review and reform process would be mutually beneficial with respect to improving efficiencies while maintaining protections. As the FASEB/AAMC/COGR/NABR report notes, the 1999 report on regulatory reform commissioned by NIH recommended the establishment of an advisory body on animal care and use comprised of institutional representatives to collaborate with agencies in the reformulation and interpretation of policies and guidance.

- "Eliminate the requirement for verification of protocol and grant congruency in NIH Grants Policy 4.1.1.2 to allow for reasonable advances, discoveries, and other developments in the overall research objectives." This would be consistent with revised human subjects regulations. As indicated in the FASEB-AAMC-CGR-NABR report, "The preamble of the Common Rule states, 'the final rule eliminates the requirement in the pre-2018 rule at §.103(f) that grant applications undergo IRB review and approval for the purposes of certification. The grant application is often outdated by the time the research study is submitted for IRB review and contains detailed information about the costs of a study, personnel, and administrative issues that go beyond the mission of the IRB to protect human subjects. Therefore, experience suggests that review and approval of the grant application is not a productive use of IRB time." "Through amendments of and modifications to protocols over the lifetime of a study, all work conducted under PHS-funded mechanisms is covered by an approved protocol. These changes must be within the scope of the proposed work, but may not have been conceived at the time of proposal submission or initial funding."

- "Revise the NIH guidance in NOT-OD-05-034 regarding prompt reporting to include only those incidents that jeopardized the health or well-being of animals. OLAW specifies that the grant number be included in these reports, but this is not required in PHS Policy (IV.F.3). Grant numbers should not be required on noncompliance reports in order to protect investigators and study teams from harassment by parties seeking to disrupt animal research." This is not an effort to reduce transparency, but to improve safety for NIH-funded investigators targeted for their use of animals in research.

- "Revise USDA Animal Care Policy #14 to reflect the language in AWA §2143 and AWR §2.31(d)(1)(x)(A-C), allowing approval of multiple survival operative procedures at the discretion of the IACUC and as justified for scientific and animal welfare reasons." This will enhance the community's efforts to reduce the number of animals involved in research. The 1999 NIH report on reducing regulatory burden similarly recommended that the Animal Welfare Act be amended to permit more than one major surgery on an animal if approved by the IACUC, however, the FASEB/AAMC/COGR/NABR report suggests that this can be addressed through revisions to policy 14.

- Amend the third bullet in section 8.1.2.5 of NIH Grants Policy to read "Change from the approved use of live vertebrate animals that would result in an increased risk." As noted in the FASEB/AAMC/COGR/NABR report, "for human subjects research, prior approval for a change in scope is required for "change from the approved involvement of human subjects that would result in an *increased* risk" (emphasis added)." "If prior approval for a change in the research scope for NIH studies were only needed when increased risk to animals would result, the administrative burden for both investigators and IACUCs could be reduced."

- Revise §2.31(c)(3) of the AWR to state: "The IACUC may, at its discretion, determine the best means of conducting an evaluation of the institution's programs and facilities that includes all members wishing to participate in the process. The IACUC may invite ad hoc consultants to assist in conducting the evaluation. However, the IACUC remains responsible for the evaluation and report." Per the FASEB/AAMC/COGR/NABR report, "Consistent with the HREA requirement, section IV.B.1-3 of the PHS Policy charges the IACUC with this review, but allows flexibility in who conducts it. Experienced reviewers who are not committee members could lend greater focus and efficiency to the process and, if managed well, free up IACUC members to focus on other aspects of IACUC activity. This would not diminish the expectation for the IACUC members to review and approve the report and address or correct any findings."

- "USDA should consider including AAALAC International accreditation as a factor in their risk assessment." Accreditation could be recognized as an important self-evaluation process that is conducted every 3 years to consider or reconsider how the animal research program is working. This would be one factor among many.

Feedback is sought on whether the following tools and resources are or would be helpful for reducing burden on investigators:

1. **Encourage the use of sections of the AAALAC International program description in applicable parts of the OLAW Animal Welfare Assurance, for institutions accredited by AAALAC International.**

The FASEB-AAMC-COGR-NABR report recommended that NIH "streamline the assurance for animal research." "In addition, for Category 1 institutions, allow proof of accreditation in lieu of the detailed program description." As noted in the report, the assurance for human subjects is much more streamlined. Using sections of the AAALAC program description in applicable parts of the assurance would appear, at least in part, to address this recommendation. Having greater harmonization between the AAALAC program description and the PHS Assurance sections would also be beneficial. Allowing proof of accreditation in lieu of the detailed program description would lead to even greater burden reduction.

2. **Encourage the use of the FDP Compliance Unit Standard Procedures as a repository of best practices for standard procedures used for research with animals.**

COGR supports the promotion of resources that aim to streamline requirements and reduce administrative burden, including the Federal Demonstration Partnership's Compliance Unit Standard Procedures for research with animals provided those Standard Procedures and best practices are understood to be suggestions. Individual institutions must determine if they apply under local circumstances. We also caution that CUSP is still being developed and piloted.

3. **Encourage the use of the IACUC Administrators Association repository of best practices by IACUCs.**

COGR supports the promotion of resources such as effective practices that aim to streamline requirements and reduce administrative burden provided those best practices are understood merely to be suggestions and individual institutions can decide if they apply under local circumstances. NIH support for this resource might allow for open access and regular maintenance.

4. **Encourage the use of new or existing tools to streamline protocol review through use of designated member review (DMR), DMR subsequent to full committee review, and/or Veterinary Verification and Consultation.**

COGR agrees that it would be helpful for NIH and USDA to encourage use of designated member review, DMR subsequent to full committee review, and/or Veterinary Verification and Consultation, as well as any new "tools" or mechanisms as adopted that would streamline review. NIH might also consider expanding the use of VVC. For example, rather than limit the veterinarian to confirm conformance to an IACUC policy, give the veterinarian the authority to approve changes/modifications that the veterinarian has the authority to oversee such as treatments, anesthetics, analgesics, and euthanasia. This could be expanded with the authority of the

IACUC to other procedures as well. COGR supports FASEB's suggestion that OLAW simplify the VVC process and trust the professional judgement of veterinarians to determine what significant changes can and cannot be approved.

5. **Expanded IACUC training activities that focus on reducing burden on investigators.**

Encouraging the use of resources that aim to streamline requirements and of new and existing tools to streamline protocol review as outlined in the questions and responses above will aid in the reduction of administrative burden. Highlighting the non-binding nature of guidance and the flexibility provided in regulation and policy would also be very beneficial.

We would also recommend grants to the community for developing and sharing materials that promote efficient practices, similar to those provided in relation to the NIH Single IRB Policy, and to address concerns about reproducibility. OLAW might also consider highlighting existing efforts as a means of raising awareness. COGR has published a checklist of actions that member institutions have taken to reduce institutional burden associated with animal research. More recently we have expanded the checklist and distributed it to our members and are working cooperatively with the Association of American Medical Colleges to further reduce burden on investigators.