

Reforming Animal Research Regulations: Workshop Recommendations to Reduce Regulatory Burden

Report of an April 17, 2017 workshop organized by FASEB,
AAMC, and COGR, with assistance from NABR



Participant List

Workshop on Reforming Animal Research Regulations, April 17, 2017

Nancy Ator, PhD
*Professor, Behavioral Biology
Chair, Animal Care and
Use Committee*
Johns Hopkins School
of Medicine

Matthew Bailey
President
National Association for
Biomedical Research

**Kathryn Bayne, MS,
PhD, DVM, DACLAM,
DACAW, CAAB**
Chief Executive Officer
AAALAC International

**Taylor Bennett, DVM,
PhD, DACLAM, DACAW**
Senior Scientific Advisor
National Association for
Biomedical Research

Richard Bookman, PhD
*Senior Advisor, Program
Development & Science Policy*
University of Miami Miller
School of Medicine

Lizbet Boroughs, MSPH
*Associate Vice President,
Federal Relations*
Association of American Universities

**Cindy Buckmaster, PhD,
CMAR, RLATG**
*Director, Center for
Comparative Medicine*
Baylor College of Medicine
Chair, Board of Directors
Americans for Medical Progress

Kevin Cain
Director, Governmental Affairs
Association of American
Veterinary Medical Colleges

Anne Deschamps, PhD
Associate Director, Science Policy
Federation of American Societies for
Experimental Biology

Anurupa Dev, PhD
Senior Science Policy Analyst
Association of American
Medical Colleges

J. Crawford Downs, PhD
*Vice Chair of Research,
Department of Ophthalmology*
University of Alabama at
Birmingham School of Medicine
*Chair, ARVO Animals in
Research Committee*

Richard Eckert, PhD
*Chair, Department
of Biochemistry
and Molecular Biology*
University of Maryland
School of Medicine

Howard Garrison, PhD
Director, Office of Public Affairs
Federation of American Societies
for Experimental Biology

Molly Greene, BA, CPIA
*Advisor, Institutional Animal Care
and Use Committee*
Michigan State University

**F. Claire Hankenson,
DVM, MS, DACLAM**
*Director and Attending
Veterinarian*
Michigan State University

Joseph R. Haywood, PhD
*Assistant Vice President,
Regulatory Affairs*
Michigan State University

Steve Heinig
Director, Science Policy
Association of American
Medical Colleges

Michael Heintz, MS, JD
Director, Advocacy & Training
Society for Neuroscience

Jeffrey Henegar, PhD
*Director, Animal Care and
Quality Assurance*
University of Missouri
*Chair, APS Animal Care and
Experimentation Committee*

Kevin Kregel, PhD
Associate Provost
University of Iowa
*Chair, FASEB Animals in Research
and Education Subcommittee*

Ross McKinney, MD
Chief Scientific Officer
Association of American
Medical Colleges

Lisa Nichols, PhD
*Director, Research and
Regulatory Reform*
Council on Governmental Relations

Alexander Ommaya, DSc
*Senior Director,
Clinical Effectiveness
and Implementation Research*
Association of American
Medical Colleges

Sangeeta Panicker, PhD
Director, Research Ethics
American Psychological Association

**Stacy Pritt, DVM, MS,
MBA, CPIA, DACAW**
*Director, Institutional Animal
Care and Use Committee*
University of Texas
Southwestern Medical Center
Vice President, AVMA

Alice Ra'anan
*Director, Government
Relations and Science Policy*
American Physiological Society

Sarah Rovito, PE
*Assistant Director,
Research Policy*
Association of Public and
Land-Grant Universities

James Rowlett, PhD
*Professor, Department of
Psychiatry & Human Behavior*
University of Mississippi
Medical Center
*Chair, APA Committee on Animal
Research and Ethics*

Mar Sanchez, PhD
*Associate Professor, Psychiatry
and Behavioral Sciences*
Emory University
School of Medicine
*Chair, SfN Committee on
Animals in Research*

Yvette Seger, PhD
Director, Science Policy
Federation of American Societies
for Experimental Biology

Scott Simon, PhD
*Professor, Biomedical
Engineering*
*Vice Chair, Institutional Animal
Care and Use Committee*
University of California, Davis

Lauren Stump, DVM
*Assistant Director,
Government Relations*
American Veterinary Medical
Association

Ara Tahmassian, PhD
*Chief Research
Compliance Officer*
Harvard University

**Sally Thompson-Iritani,
DVM, PhD**
Director, Office of Animal Welfare
University of Washington

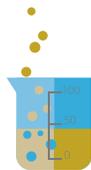
James Tomasek, PhD
Vice President for Research
University of Oklahoma
Research Park

Matt Windsor, PhD
*Senior Manager, Science
Communications*
Association for Research in Vision
and Ophthalmology

Report Reviewer
**Reginald W. Miller, DVM,
DACLAM**
*Dean, Research-Operations
and Infrastructure*
Icahn School of Medicine at
Mount Sinai

Reforming Animal Research Regulations:

Workshop Recommendations to Reduce Regulatory Burden



Executive Summary

The Federation of American Societies for Experimental Biology (FASEB), the Association of American Medical Colleges (AAMC), and the Council on Governmental Relations (COGR), with the assistance of the National Association for Biomedical Research (NABR), convened a workshop on reforming animal research regulations on April 17, 2017. The goal of the workshop was to provide actionable recommendations for **promoting regulatory efficiency, animal welfare, and sound science**. These recommendations are directed to federal agencies involved in the oversight of federally funded animal research, in particular the National Institutes of Health (NIH) and the United States Department of Agriculture (USDA).

The use of animals in research continues to be vital to our understanding of human and animal disease and the development of treatments and cures. Researchers take their commitment to the humane care and use of research animals very seriously, but there are numerous conflicting, outdated, or ineffective regulations that do not improve animal welfare. The proposed changes to regulations, policies, and guidelines outlined in this report would make research and researchers far more efficient while maintaining standards of care.

The vast amount of administrative effort necessary to comply with oversight requirements for federally funded animal research has been highlighted in a number of reports. To date, however, the majority of recommendations to reduce ineffective or redundant requirements by modifying and harmonizing federal regulations and policies have not been implemented. The focus of the April 2017 workshop was to identify requirements that demand significant administrative effort but do not enhance animal welfare. Workshop participants sought to prioritize steps that agencies and Congress can take to reduce these inefficiencies.

Highlights of the major recommendations developed by workshop participants¹ are listed here. Additional recommendations on related topics are included in the body of the report. Many of these recommendations echo those made in previous reports from other organizations. Workshop participants strongly believe that these issues can and should be addressed without delay.

¹ Participants' names are listed on Page 1. Their affiliations are provided for identification purposes only and do not represent an endorsement of these recommendations by their respective organizations.

Major Recommendations

Executive Office of the President and Congress

- The Executive Office of the President (EOP) and the Office of Management and Budget (OMB) should explore whether regulatory efficiencies could be gained, and burden reduced, by consolidating animal research oversight under a single Federal office or entity with one primary set of regulations and guidance documents. A committee of experts engaged in animal research from entities that receive federal research awards should be invited to assist with this effort. The group should include those involved with oversight responsibility at the institutional level, such as institutional administrators, Institutional Animal Care and Use (IACUC) members, veterinarians, and investigators engaged in animal research.
 - Harmonize existing federal requirements for those species currently covered by USDA and those covered by the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) to conform to the least burdensome standard while maintaining animal welfare.
 - Pilot new models and structures through the Federal Demonstration Partnership, as appropriate.
- The EOP and OMB should consider requiring at least a 60-day comment period on the merits and impact of any proposed policies, guidance documents, frequently asked questions (FAQs), or interpretive rules before they are issued. Final policies and guidance should include material changes that reflect germane comments received from the regulated community.
 - Near-final documents should be reviewed by an external advisory committee of experts engaged in animal research from the regulated community before they are disseminated for public comment or final agency review. This would help ensure that policies and guidance meet their intended objectives while maintaining or improving animal welfare without creating unnecessary administrative work and cost.
 - All guidance documents should state clearly that they do not carry legal or regulatory force.
 - Guidance documents should not be accompanied by a requirement to obtain agency approval for alternative methods and/or processes.
- Congress should amend §2143(b)(3) of the Animal Welfare Act (AWA) and §495(b)(3) of the Health Research Extension Act (HREA) to require only annual inspection by the IACUC. This will eliminate significant administrative work for investigators and IACUC members and allow staff to better focus their efforts on the daily oversight and welfare of animals. Such a change is neither intended to negate or minimize the expectation for IACUCs to assess and assure compliance with federal requirements regarding the welfare of animals used in research, teaching, and testing.

- Congress should amend §2146 of the AWA to remove the requirement for annual USDA inspection of research facilities and allow for an inspection frequency based on compliance history, as part of the agency's Risk Based Inspection System process.

NIH and USDA

- 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 (Cures) 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.
 - The committee could be designated an “expert subcommittee” of the Research Policy Board mandated by Cures. Agencies might also consider a permanent animal research advisory group modeled after the Department of Health and Human Services Secretary's Advisory Committee on Human Research Protections.
- As part of the review mandated by Cures, all current Public Health Service (PHS) and USDA regulations, policies, guidance documents, FAQs, and interpretive rules, as well as the process for generating them, should be reviewed by an external advisory group of experts engaged in animal research from entities that receive federal research awards. This 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. The purpose of this review should be to ensure that these documents emphasize matters of core importance to animal welfare identified in HREA and AWA statutory language and are consistent with current scientific and technological knowledge and approaches.
- NIH and USDA should 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 the NIH Office of Laboratory Animal Welfare (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.

NIH

- 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.” 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. Thus, 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.
- 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.
- 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.
- Streamline the assurance for animal research. In addition, for Category 1 institutions, allow proof of accreditation in lieu of the detailed program description.

USDA

- Revise §2.31(d)(5) of the AWA Regulations (AWR) 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.
- 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.
- 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...”

Introduction

The Federation of American Societies for Experimental Biology (FASEB), the Association of American Medical Colleges (AAMC), and the Council on Governmental Relations (COGR), with the assistance of the National Association for Biomedical Research (NABR), convened a workshop on reforming animal research regulations on April 17, 2017. Workshop participants were 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.²

The goal of the workshop was to provide actionable recommendations for **promoting regulatory efficiency, animal welfare, and sound science**. These recommendations are directed to federal agencies involved in the oversight of federally funded animal research, in particular the National Institutes of Health (NIH) and the United States Department of Agriculture (USDA).

Section 2034 of the 21st Century Cures Act (Cures), signed into law on December 13, 2016 (1), directs leadership of NIH, USDA, and the Food and Drug Administration (FDA) to “complete a review of applicable regulations and policies for the care and use of laboratory animals and make revisions, as appropriate, to reduce administrative burden on investigators while maintaining the integrity and credibility of research findings and protection of research animals.” The review is to be completed within two years of the bill’s enactment. In carrying out this task, the agencies are directed to:

- Seek the input of experts, as appropriate;
- Identify ways to ensure regulations and policies are not inconsistent, overlapping, or unnecessarily duplicative, including with respect to inspection and review requirements by Federal agencies and accrediting associations;
- Take steps to eliminate or reduce identified inconsistencies, overlap, or duplication;
- Take other actions, as appropriate, to improve the coordination of regulations and policies with respect to research with laboratory animals.

The review mandated by Cures provides a ready means to pursue the recommendations in this report. Cures also establishes a Research Policy Board (RPB) comprised of federal officials and representatives of academic or other non-profit research institutions or other organizations with relevant expertise. The RPB is charged with coordinating and improving regulations and policies, discussing policy and regulatory gaps and challenges, and conducting an ongoing assessment of regulatory burden using expert subcommittees as needed.

² Participants’ names are listed on Page 1. Their affiliations are provided for identification purposes only and do not represent an endorsement of these recommendations by their respective organizations.

Background

Various reports have detailed the high levels of administrative burden associated with federal oversight of animal research. In 2012, the Federal Demonstration Partnership (FDP) conducted a survey of principal investigators (PIs) of federally funded research projects to assess the impact of federal regulations and reporting requirements. The survey included 13,453 PIs from 111 institutions with active federal grants (2). One important survey finding was that PIs estimate that 42 percent of their total time spent on federally funded research projects was consumed by administrative requirements rather than the actual conduct of research. Those researchers engaged in projects involving human or animal subjects reported that administrative tasks related to Institutional Review Boards (IRB; for human subjects) and IACUCs (for animal subjects) were “by far the most time-consuming.”

In 2014, the National Science Board (NSB) issued a request for information (RFI) on regulatory burden and received significant input from FASEB (3). Over 3,000 PIs and university administrators responded, and over 200 PIs and administrators participated in roundtable discussions conducted at institutions.

Key recommendations made by RFI respondents were for agencies to create exempt and expedited review categories for animal research similar to human subjects regulations; reduce or consolidate overlapping inspections by agencies and accreditors; avoid *de facto* regulation in the form of guidance documents and frequently asked questions (FAQs); eliminate the USDA policy requiring a literature search for alternatives to potentially painful procedures; consider a single set of guidelines across all agencies, comparable to the Common Rule regulation of human subjects research; and refrain from modifying policies and guidance without consulting the regulated community. It was also recommended that OLAW refrain from interpreting “should” statements in the *Guide for the Care and Use of Laboratory Animals (Guide)* as “must” statements (4).

Based upon this input, the NSB report, *Reducing Investigators’ Administrative Workload for Federally Funded Research*, recommended that “An evaluation of the regulations, policies, guidance, best practices, and FAQs of all regulatory, independent, and certification bodies governing animal research should be considered to identify policies and guidance that increase investigators’ administrative workload without improving the care and use of animals.” The Board also observed that “detailed regulations and policies requiring a literature search for alternatives to animals may considerably increase PIs’ workload without a realization of measurable improvement in animal care and use.”

More recently, the 2016 National Academies report, *Optimizing the Nation's Investment in Academic Research* (5), recommended that Congress direct the Office of Management and Budget (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 report back to Congress. The report also recommended that:

- Reporting, assurances, and verifications to agencies be reduced and streamlined;
- Noncompliance reports be tiered to the level of significance or impact on animals and included in annual rather than individual reports;
- Multiple annual reports to various agencies about animal care programs be replaced by a single annual report under the proposed government-wide oversight program; and,
- Research institutions assess their own regulatory processes to determine where their compliance activities can be streamlined while still complying with federal regulations.

An NIH report on reducing regulatory burden published almost two decades ago identified similar concerns to those raised in the FDP, NSB, and National Academies reports (6). This report focused on five compliance areas: conflict of interest, research integrity, human subjects protections, animal care and use, and hazardous waste disposal. Recommendations on animal care and use included:

- Establishing an advisory body comprised of institutional representatives to collaborate with agencies in the formulation and interpretation of policies and guidelines;
- Reducing the number of redundant reviews and inspections while maintaining sufficient oversight;
- Recommitting to efforts to develop a common reporting format for annual reports required by agencies and accreditors;
- Establishing a common protocol review frequency depending on the level of risk, but not less than every three years;
- 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; and,
- That Congress amend the Animal Welfare Act (AWA) to permit more than one major surgery on an animal if approved by the IACUC.

There have been some efforts to reduce burden. An example is NIH's 2014 Notice (NOT-OD-14-126) permitting certain protocol changes to be handled administratively according to IACUC-reviewed and approved policies (in consultation with a veterinarian authorized by the IACUC) and for other changes to be handled administratively without policy, consultation, or notification (7).

Nevertheless, repeated calls for animal research regulatory reform have largely gone unanswered, and recommended reforms have not been implemented. With the mandate from Cures and the current administration's focus on regulatory reform (8, 9), now is the time to act on recommendations to reduce excessive and unnecessary administrative work associated with animal research while still ensuring the highest standards of animal care.

Recommendations

Response to the 21st Century Cures Act

Issue: Cures mandates a "complete a review of applicable regulations and policies for the care and use of laboratory animals..." As detailed in this report, over the past several years the scientific community has made recommendations, in multiple reports, suggesting much needed reform of animal research regulations, policies, and guidance. To date, however, few of these recommendations have been implemented by federal agencies.

Major Recommendation:

1. NIH and other federal agencies involved in the review of regulations and policies for the care and use of laboratory animals mandated by Cures 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.
 - a. The committee could be designated an "expert subcommittee" of the RPB mandated by Cures. Agencies might also consider a permanent animal research advisory group modeled after the Department of Health and Human Services (HHS) Secretary's Advisory Committee on Human Research Protections.

Consolidated Oversight

Issue: The AWA charges the Secretary of Agriculture with promulgating standards to govern the humane handling, care, treatment, and transportation of animals by dealers, research facilities, and exhibitors. Within USDA, APHIS is charged with fulfilling this regulatory oversight responsibility. The Health Research Extension Act (HREA) of 1985 charges the Director of NIH with establishing guidelines for the proper care of vertebrate animals in Public Health Service (PHS)-funded biomedical and behavioral research, teaching, and testing activities funded by NIH.

The Office of Laboratory Animal Welfare (OLAW) interprets the PHS Policy on Humane Care and Use of Laboratory Animals (PHS Policy); supports educational programs; and negotiates Animal Welfare Assurances (documents from institutions assuring compliance with the PHS Policy). OLAW monitors compliance with the PHS Policy by institutions receiving research funds from either the NIH or the National Science Foundation (herein referred to as “Assured institutions”) and requires Assured institutions to comply with the PHS Policy and the *Guide*, “an internationally accepted reference on animal care and use” published by the National Academies’ Institute for Laboratory Animal Research.

Although OLAW stated in its response to comments to the NSB RFI that it works with the USDA and other agencies to coordinate policies, guidance, and activities, significant inconsistencies and duplications still remain. OLAW, APHIS-Animal Care (APHIS-AC), and other agencies communicate with each other but are subject to different laws, so their regulations, policies, guidance, and reporting requirements each use different terminology.

For example, OLAW requires institutions to report serious or continuing noncompliance with the PHS Policy, serious deviations from the *Guide*, or suspensions of animal research activity by the IACUC. APHIS-AC requires institutions to report when activities are suspended by the IACUC, uncorrected significant deficiencies, the number of animals used annually, exceptions to the AWA regulations, and changes in the institution’s scope of operations. Other federal agencies that fund animal research, such as the Department of Defense and Veterans Administration, have additional and sometimes more burdensome requirements.

The National Academies report, *Optimizing the Nation’s Investment in Academic Research*, recommends an evaluation of the feasibility and utility of a simplified regulatory oversight structure that eliminates overlap and inconsistent requirements. A single Federal office could be charged with overseeing this consolidated regulatory framework, an arrangement comparable to how the Federal Policy for the Protection of Human Subjects (“Common Rule”) is overseen by the HHS Office for Human Research Protections. The structure could be based upon the *U.S. Government Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research and Training*. Such a structure could significantly reduce administrative work at the federal, institutional, and individual levels by harmonizing the requirements across all agencies and eliminating gaps in oversight.

Major Recommendation:

2. The Executive Office of the President (EOP) and OMB should explore whether regulatory efficiencies could be gained, and burden reduced, by consolidating animal research oversight under a single Federal office or entity with one primary set of regulations and guidance documents. A committee of experts engaged in animal research from entities that receive federal research awards should be invited to assist with this effort. The 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.
 - a. Harmonize existing federal requirements for those species currently covered by USDA and those covered by PHS Policy to conform to the least burdensome standard while maintaining animal welfare.
 - b. Pilot new models and structures through the FDP as appropriate.

Promulgation of New Rules and the Regulatory Process

Issue A: Agency requirements (sometimes issued as suggestions or recommendations) based upon interpretative notes, policies, procedures manuals, terms of awards, FAQs, webinars, journal articles, etc., constitute a significant driver of administrative burden associated with animal research (see Appendix A). These kinds of materials have proliferated over the past decade and have become *de facto* regulations. In most cases there is no input from the research community or adequate analyses of outcomes such as costs, actual impact on animal welfare, and scientific implications.

As of September 2017, OLAW's web page listed 84 FAQs about the PHS Policy (10), nearly a four-fold increase over the 22 OLAW FAQs from 1995. In addition, according to its website, OLAW has published 37 notices and 14 Commentaries since 2000. Prior to that year, OLAW had published only eight notices and seven Commentaries. Moreover, since 2008, OLAW has held 37 webinars and posted the transcripts as further guidance. While these kinds of guidance can be helpful in interpreting PHS Policy, it should be made clear that they do not carry the force of regulation.

In 2007, OMB released its Agency Good Guidance Practices (GGP) bulletin stating (11), "The purpose of [GGP] is to ensure that guidance documents of Executive Branch departments and agencies are: Developed with *appropriate review and public participation*, accessible and transparent to the public, of high quality, and *not improperly treated as legally binding requirements*" [emphases added]. OLAW allows for alternative approaches to guidance where statute or regulation is not cited, but it also requires agency approval for such alternatives, which is inconsistent with the GGP.³

³ Unless specific statutory or regulatory requirements are cited, the Notices should be viewed as recommendations and an institution may use an alternative approach if the approach satisfies the requirements of the Policy and is determined acceptable by OLAW (Page 21). https://grants.nih.gov/grants/olaw/100909_seminar_transcript.pdf

Major Recommendations:

3. The EOP and OMB should 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. Final policies and guidance should include material changes that reflect germane comments received from the regulated community.
 - a. Near-final documents should be reviewed by an external advisory committee of experts engaged in animal research from the regulated community before they are disseminated for public comment or final agency review. This would help ensure that policies and guidance meet their intended objectives while maintaining or improving animal welfare without creating unnecessary administrative work and cost.
 - b. All guidance documents should state clearly that they do not carry legal or regulatory force.
 - c. Guidance documents should not be accompanied by a requirement to obtain agency approval for alternative methods and/or processes.

Issue B: Sunset Review for Regulatory Guidance: Science and technology change over time. However, oversight processes as well as regulations, policies, and guidance documents are not always modified to reflect these changes. Further, agencies and accreditors sometimes encourage compliance with current practice rather than the use of innovative alternative approaches.

Major Recommendation:

4. As part of the review mandated by Cures, all current PHS and USDA regulations, policies, guidance documents, FAQs, and interpretive rules, as well as the process for generating them, should be reviewed by an external advisory group of experts engaged in animal research from entities that receive federal research awards. This 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. The purpose of this review should be to ensure that these documents emphasize matters of core importance to animal welfare identified in HREA and AWA statutory language and are consistent with current scientific and technological knowledge and approaches.

The Guide for the Care and Use of Laboratory Animals

Issue: The *Guide* is written by an independent, non-governmental organization, with the stated purpose “to assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate.” It is a combination of requirements (“must” statements) based on U.S. regulations and requirements, and effective practices and recommendations. Some of these practices have evolved to become engineering standards (e.g., specific cage space and numbers of mice per cage) that may not be consistent with current scientific findings.

PHS Policy requires institutions to use the *Guide* as the basis for developing and implementing an institutional animal care and use program. Compliance with more than 40 “must” statements in the *Guide* regarding animal care practices is required, as is compliance with several hundred “should” statements. Although there is no statutory or regulatory basis to consider advisory statements mandatory, OLAW’s FAQ C7 states: “Deviation from a ‘should’ statement with IACUC approval is a departure from the *Guide* and must be reported in the semiannual report to the IO [Institutional Official].” This requirement does not appear to be consistent with the *Guide* language that defines a “should” statement as “a strong recommendation for achieving a goal.” *Guide* authors further recognize “that individual circumstances might justify an alternative strategy.” As previously noted, OMB’s GGP Bulletin states, “given their legally nonbinding nature, significant guidance documents should not include mandatory language such as ‘shall,’ ‘must,’ ‘required’ or ‘requirement,’ unless the agency is using these words to describe a statutory or regulatory requirement.”

The *Guide* is written broadly so that its recommendations can be applied by diverse institutions and in diverse settings where animals are bred, raised, or utilized for research, teaching, and testing. This approach presumes that users—whether scientists, IACUCs, veterinarians, or breeders—will apply professional judgment in making specific decisions regarding animal care and use. The *Guide* is written in general terms because IACUCs have a key role in interpretation, implementation, oversight, and evaluation of their animal care and use programs.

The language in FAQ C7 essentially nullifies this role. If the IACUC takes a different course of action than a “should” statement, this must be reported to the IO as a departure from the *Guide*. PHS Policy IV.B.3.c further adds administrative burden by requiring that the IACUC report every six months on “departures” from the *Guide* that have been approved by the IACUC and the accompanying reasons. The OLAW guidance on its website for determining those IACUC decisions that represent “departures” in this category—in contrast to the definition of “departures” that do not need to be singled out—makes clear the arbitrary, fine grain differences.

Other guidance documents provide recommendations for the care of farm animals, wildlife, and birds. These documents are comparable to the *Guide* and are important resources in providing advice on caring for and enhancing the welfare of those species; however, they are not regulations and should not be given regulatory status.

Major Recommendation:

5. The *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.” 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. Thus, 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.

Additional Recommendations:

6. OLAW should cease using the word “deviation” in their guidance documents when referring to IACUC-approved alternative strategies to “should” statements in the *Guide*. As with USDA regulations, the meaning of words used in OLAW guidance documents not defined in legislation or the PHS Policy should be that of a standard dictionary.
7. The *Guide* should be a “living” document that continuously incorporates changes in the scientific literature. Consideration should be given to an online version of the *Guide* with periodic updates provided in partnership with an independent group such as the American Association for Laboratory Animal Science.

Protocol Review

Issue A: AWA Regulations (AWR) are inconsistent with the PHS Policy. Section 2.31(d)(5) of the AWR requires that the IACUC “conduct continuing reviews of activities...at appropriate intervals as determined by the IACUC, but *not less than annually*” (emphasis added). In contrast, section IV.C.5 of the PHS Policy requires that the IACUC “conduct continuing review of each previously approved, ongoing activity covered by this Policy *at appropriate intervals as determined by the IACUC, including a complete review in accordance with IV.C.1-4. at least once every three years*” (emphasis added).

Revising §2.31(d)(5) of the AWR as follows would significantly reduce the regulatory burden on many of those involved in animal care and use programs, especially investigators: “The IACUC shall conduct continuing reviews of activities covered by this subchapter at appropriate intervals as determined by the IACUC, including a complete review as required in §2.31(d)(1-4) at least *once every three years.*”

Workshop participants and investigators responding to the NSB report “*Reducing Investigators’ Administrative Workload for Federally Funded Research*” suggested that the USDA requirement for annual protocol review significantly increases paperwork without improving animal welfare, as IACUCs can determine whether more frequent review is appropriate on a study-by-study basis. No requirement for annual review exists in the AWA.

In webinars hosted by NABR, APHIS representatives have “clarified” that the apparent AWR annual review requirement can be met in various ways by registered institutions, and that annual review of the protocol *per se* is not required. NABR webinars do not represent a formal statement of government policy, so this guidance, while helpful, cannot be relied upon by the regulated community.

Major Recommendation:

8. Revise §2.31(d)(5) of the AWR 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.

Issue B: Greater focus on oversight in areas with a higher potential for risk could ensure animal welfare and allow investigators to devote more time to research. This concept is consistent with human research regulations. 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 AWR and PHS Policy (§2.31(d)(2) and IV.C.2, respectively) allow for review of proposed research projects through either full committee or designated member review, if no committee members object. The Common Rule, in contrast, provides greater flexibility for review of human subjects research. For example, some forms of research have been designated exempt and others qualify for expedited review by a single member of the IRB, with no requirement to secure agreement from other members. This risk-based approach is more administratively efficient than the current animal regulatory framework and still maintains necessary protections.

Major Recommendation:

9. NIH and USDA should 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.

Issue C: Currently researchers cannot perform major multiple survival operative procedures on the same animal in an unrelated study, even when multiple years have elapsed between procedures or when multiple protocols are involved. This limitation, which is specific to the U.S., conflicts with efforts to replace, reduce, and refine animal research; it increases the number of animals used.

Presentations and reports at laboratory animal science meetings indicate many instances where repeated procedures have minimal or negligible animal welfare implications, and would be the best option under a 3Rs (Replace, Reduce, Refine) analysis. Better outcomes for animals, such as transfer to a facility with an adoption program, might even be achieved. We believe IACUCs should have better access to these options so long as animal welfare takes priority.

As written, USDA Animal Care Policy #14—Major Survival Procedures—prohibits the use of animals in more than one proposal involving a major operative procedure. This prohibition exceeds the statutory authority provided in the AWA and AWR. The current regulations, AWR §2.31(d)(1)(x)(A-C), leave approval of multiple survival surgery at the discretion of the IACUC if justified for scientific and animal welfare reasons, with a provision that the Secretary may approve that usage for other special circumstances.

AWA §2143(a)(6) prohibits the Secretary from promulgating “rules, regulations, or orders with regard to the design, outlines, or guidelines of actual research or experimentation by a research facility as determined by such research facility” with certain exception as provided in subparagraphs (C)(ii)-(v) and (7). Therefore, this guidance document should be revised to be consistent with existing statutory and regulatory authority. Both the AWA and AWR require that such usage be scientifically justified, but there is no requirement limiting that use to one activity. As currently written, Policy #14 would appear to be in violation of AWA §2143 requirements.

Major Recommendation:

10. 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.

Issue D: 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 was only needed when increased risk to animals would result, the administrative burden for both investigators and IACUCs could be reduced.

Additional Recommendation:

11. 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.*”

Literature Search

Issue: AWA §2143(a)(3)(B) states that the principal investigator must consider “alternatives to any procedure likely to produce pain to or distress in an experimental animal.” Section 2143(e)(3) authorizes the establishment of information services at the National Agricultural Library to provide (inter alia) “information on improved methods of experimentation which could reduce or replace animal use; and minimize pain and distress to animals.”

Section 2.31(d)(1)(ii) of the AWR requires the IACUC to determine whether proposed animal use activities meet various requirements, including verification 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, e.g., the Animal Welfare Information Center, used to determine that alternatives were not available.”

In 1989 when the final rule on §2.31 of the AWR was published, USDA explained it as follows (12):

“We have modified the requirement concerning consideration of alternative procedures to allow research facilities greater flexibility in devising internal procedures for their principal investigators to follow, which simplify their task of indicating what sources were consulted. The principal investigator must provide a written narrative of the sources consulted, such as biological abstracts, *Index Medicus*, the Current Research Information Service (CRIS), and the Animal Welfare Information Center that is operated by the National Agricultural Library. We believe that in fulfilling this requirement, Committee members will discuss these efforts with the principal investigator in reviewing the proposed activity. We also believe that consideration of alternatives will be discussed during Committee meetings where proposed activities are presented for approval, and made part of the meeting minutes. If the Committee determines that the written narrative prepared by the principal investigator provides adequate assurance that alternatives were considered, the Committee’s meeting minutes need only reflect this determination.”

USDA’s Animal Care Policy #12 (Issued March 25, 2011) states that “APHIS continues to recommend a *database search* as the most effective and efficient method for demonstrating compliance with the requirement to consider alternatives to painful/distressful procedures” (emphasis added). This is not consistent with USDA language in the final rule, namely, “If the [IACUC] determines that the written narrative prepared by the principal investigator provides adequate assurance that alternatives were considered, the Committee’s meeting minutes need only reflect this determination.”

Policy #12 is problematic for four reasons. First, keyword/literature searches *are not required* by either the AWA or AWR. Second, such searches have been shown to be ineffective. Third, the requirement to perform unproductive literature searches represents unnecessary regulatory burden. Finally, USDA admits, when pressed, that its Animal Care Policies have no regulatory standing but continues to refer to those policies as enforceable.

Major Recommendation:

12. 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...”

Congruency and Consistency between Grants and Protocols

Issue: The language in NIH Grants Policy 4.1.1.2, Verification of IACUC Approval, states, “It is an institutional responsibility to ensure that the research described in the application is congruent with any corresponding protocols approved by the IACUC.” While differences appear to rarely occur, the requirement places emphasis on the comparison of two documents written at different times, potentially up to nine months apart; it does not account for changes in technology and advances in science during the interim period, or throughout the funding period of the grant.

This disconnect has been recognized in the revised Common Rule for human subjects research. The preamble of the Common Rule (13) 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*” (emphasis added).

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.

Thus, in the context of the award, the congruency of grants and proposed protocols makes little sense. Furthermore, many “if/then” procedural descriptions in grant proposals are for years four and five, which is beyond the current three-year life of the IACUC-approved protocol. When procedures using animals are contingency-based in terms of the experiments’ outcomes, time is spent writing and reviewing procedures that will not be needed.

Major Recommendation:

13. 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.

IACUC Inspection and Program Review

Issue A: Both the AWA and HREA require semiannual inspections of animal facilities and study areas, but they do not contain program review provisions required by the AWR and PHS Policy. In general, semiannual inspections/program reviews rarely identify “programmatic” concerns that would not have already been identified by animal care or veterinary staff during routine daily checks. A review of the 19-page OLAW checklist used by most institutions shows how onerous this task is.⁴ Semiannual inspections are a considerable time commitment for IACUC members, the majority of whom are faculty; they are required to visit all animal study areas and animal facilities as part of the inspection. For some large research institutions, weeks are involved to schedule and complete the inspections, and significant hours of effort to review the program and finalize the report—typically with minimal findings.

Reports are then reviewed at a committee meeting, approved, and issued as a final report. The process then starts over again. This process is carried out for multiple entities, including agencies and accreditors, contributing to the sense that institutions are continually undergoing inspection. A change to annual inspections would eliminate significant administrative work and allow staff to better focus their efforts on the daily oversight and welfare of animals.

Major Recommendation:

14. Congress should amend §2143(b)(3) of the AWA and §495(b)(3) of the HREA to require only an annual inspection by the IACUC. This will eliminate significant administrative work for investigators and IACUC members and allow staff to better focus their efforts on the daily oversight and welfare of animals. Such a change is not intended to negate or minimize the expectation for IACUCs to assess and assure compliance with federal requirements regarding the welfare of animals used in research, teaching, and testing.

⁴ Retrieved from: <https://grants.nih.gov/grants/olaw/sampledoc/checklist.pdf>

Issue B: AWA §2143(b)(3) requires semiannual IACUC inspection of animal facilities but does not prescribe how this should be accomplished. AWR §2.31(c)(3) says “the IACUC may determine the best means of conducting evaluations” but then goes on to require that “at least two Committee members” participate. HREA §495(b)(3)(A) also requires a “review...in all animal study areas and facilities” but does not prescribe how that is accomplished.

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.

Additional Recommendation:

15. 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.”*

USDA Inspection of Research Facilities

Issue: AWA §2146 requires the Secretary to “inspect each research facility at least once a year” and more often if necessary until all deficiencies or deviations from the standards are corrected. Since the enactment of this legislation, the research community has shown a commitment to compliance with the AWA requirements. In fact, in FY 2016, of the 1,339 inspection reports posted in the Animal Care Inspection Service database, only 21 percent of the research facility inspections resulted in a citation, and almost two-thirds of those had only one citation.⁵

The majority of citations issued to research facilities involve administrative issues and not issues involving animal care. A comparison of the FY 2006 inspection results with those for FY 2016 show the number of citations with research facility-specific issues has declined by 87 percent. A review of FY 2016 citations also finds that 1.5 percent of facilities accounted for 30 percent of total citations, suggesting that a risk-based inspection process incorporating compliance history would significantly improve inspection process efficiency and overall compliance with the AWR.

⁵ http://www.aphis.usda.gov/animal_welfare/downloads/violations/2006violations.pdf

Major Recommendation:

16. Congress should amend §2146 of the AWA to remove the requirement for annual USDA inspection of research facilities and allow for an inspection frequency based on compliance history, as part of the agency's Risk Based Inspection System process.

Additional Recommendation:

17. USDA should consider including AAALAC International accreditation as a factor in their risk assessment.

Reporting Noncompliance and Deviations from the *Guide*

Issue: In 2005, NIH released guidance (NOT-OD-05-034) outlining when noncompliance must be promptly reported (14). This was intended to replace previous guidance issued January 12, 1994, which contained criteria for what constitutes serious or continuing noncompliance with the PHS Policy and serious deviation from the *Guide*. The 2005 guidance did not specifically include these criteria but rather a list of examples starting with “conditions that jeopardize the health or well-being of animals, including natural disasters, accidents and mechanical failures, resulting in actual harm to the animals.” Many of the remaining examples may or may not have an impact on the health and well-being of animal colonies that would appear to warrant prompt reporting.

In the 2005 guidance, dual purposes are identified for prompt reporting: 1) to ensure that issues affecting animal welfare are addressed and corrected, which is consistent with the language cited above, and 2) monitoring institutions’ animal care and use program oversight under the PHS Policy, evaluating allegations of noncompliance, and assessing effectiveness of the PHS policies and procedures. Since the issuance of this guidance, institutions have been required to routinely submit noncompliance reports even where there was no negative impact on animal welfare. Examples described in the second purpose for prompt reporting should address issues that directly affect animal health and well-being.

Major Recommendation:

18. 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.

Additional Recommendation:

19. OLAW specifies that the grant number be included in these reports,⁶ 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.

Assurance

Issue: As a non-regulatory agency, NIH ensures compliance with its Grants Policy and the PHS Policy through a voluntary assurance system. Multiple assurances must be made between the institution and NIH, in investigator interactions with the IACUC, and between the IACUC/IO and NIH. Judging by the number of employees that institutions and NIH have assigned to the assurance process, it has become redundant and burdensome for all parties.

The assurance for human subjects is less than five pages, and parties agree to the Terms of the Federal-wide Assurance; the OLAW Domestic Assurance Sample Document is 13 pages long (15). A 2016 survey on the IACUC-Admin listserv found that the average institutional assurance document is 24 pages long. This could be streamlined significantly, particularly for OLAW's Category-1 Institutions, defined as accredited by AAALAC International.⁷

Major Recommendation:

20. Streamline the assurance for animal research. In addition, for Category 1 institutions, allow proof of accreditation in lieu of the detailed program description.

⁶ https://grants.nih.gov/grants/olaw/reporting_noncompliance.htm

⁷ <https://grants.nih.gov/grants/olaw/references/phspol.htm#Definitions>

Conclusion

Providing exceptional welfare is paramount when conducting animal research, and regulatory requirements are vital to ensuring that research is executed safely, ethically, and humanely. However, excessive regulations, policies, guidance documents, and FAQs add to investigators' and universities' administrative workloads without benefit to animal welfare. In addition to faculty burden, fewer resources are available, and scientific progress is slowed.

Many reports dating back nearly two decades have called for animal research regulatory reform, yet few if any improvements have been made. While a number of recommendations are made in this report, they are not meant to be exhaustive, but rather to represent a starting point in a broader discussion between the regulated community and regulators on reducing excessive and unnecessary administrative effort and cost.

With the enactment of Cures, now is the time for action. Workshop participants—scientific investigators, laboratory animal veterinarians, IACUC members, accreditors, and representatives of associations with members engaged in animal research and oversight—are calling on the Administration, Congress, and leadership at NIH and USDA to implement the recommendations presented in this report. Doing so would allow more time to be spent directly caring for animals and assuring good stewardship of federal funds by conducting science in an efficient and productive manner.

Summary of Recommendations

Executive Office of the President & Congress				
Corresponding Recommendation		Statutory or Regulatory Action Required	Reduction of Burden for	Report Page
2	<p>The Executive Office of the President (EOP) and the Office of Management and Budget (OMB) should explore whether regulatory efficiencies could be gained, and burden reduced, by consolidating animal research oversight under a single Federal office or entity with one primary set of regulations and guidance documents.</p> <ul style="list-style-type: none"> An advisory group of experts engaged in animal research from entities that receive federal research awards should be invited to assist with this effort. 	EOP and OMB should perform exploratory study using an advisory group of experts engaged in animal research from the regulated community	<ul style="list-style-type: none"> Investigator IACUC Institution 	10–11
2a	<ul style="list-style-type: none"> Harmonize existing federal requirements for those species currently covered by USDA and those covered by the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) to conform to the least burdensome standard while maintaining animal welfare. 		<ul style="list-style-type: none"> Investigator IACUC Institution 	10–11
2b	<ul style="list-style-type: none"> Pilot new models and structures through the Federal Demonstration Partnership (FDP), as appropriate. 		<ul style="list-style-type: none"> Investigator IACUC 	10–11
3	<p>The EOP and OMB should consider requiring at least a 60-day comment period on the merits and impact of any proposed policies, guidance documents, frequently asked questions (FAQs), or interpretive rules before they are issued.</p> <ul style="list-style-type: none"> Final policies and guidance should include material changes that reflect germane comments received from the regulated community. 	EOP and OMB should institute policy		11–12
3a	<ul style="list-style-type: none"> Near-final documents should be reviewed by an external advisory committee of experts engaged in animal research from the regulated community before they are disseminated for public comment or final agency review. 	The advisory group mentioned above (2) could assist with this review	<ul style="list-style-type: none"> Investigator IACUC Institution 	11–12
3b	<ul style="list-style-type: none"> All guidance documents should state clearly that they do not carry legal or regulatory force. 	State on all guidance documents	<ul style="list-style-type: none"> Investigator IACUC 	11–12
3c	<ul style="list-style-type: none"> Guidance documents should not be accompanied by a requirement to obtain agency approval for alternative methods and/or processes. 	State on all guidance documents	<ul style="list-style-type: none"> Investigator IACUC 	11–12
14	Congress should amend §2143(b)(3) of the Animal Welfare Act (AWA) and §495(b)(3) of the Health Research Extension Act (HREA) to require only annual inspection by the IACUC.	Amend §2143(b)(3) of the AWA and §495(b)(3) of the HREA	<ul style="list-style-type: none"> Investigator IACUC 	20
16	Congress should amend §2146 of the AWA to remove the requirement for annual USDA inspection of research facilities and allow for an inspection frequency based on compliance history, as part of the agency's Risk Based Inspection System process.	Amend §2146 of the AWA	<ul style="list-style-type: none"> Investigator IACUC Institution 	21–22

National Institutes of Health & United States Department of Agriculture

Corresponding Recommendation		Statutory or Regulatory Action Required	Reduction of Burden for	Report Page
1	<p>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 (Cures) 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.</p>	<p>Establish a review committee of experts engaged in animal research from the regulated community to assist with implementation of Cures mandates</p>		9
	<ul style="list-style-type: none"> 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. 			
1a	<ul style="list-style-type: none"> The committee could be designated an “expert subcommittee” of the Research Policy Board mandated by Cures. Agencies might also consider a permanent animal research advisory group modeled after the Department of Health and Human Services Secretary’s Advisory Committee on Human Research Protections. 	<p>Designate the review committee as an “expert subcommittee” of the Research Policy Board mandated by Cures</p>		9
4	<p>As part of the review mandated by Cures, all current Public Health Service (PHS) and USDA regulations, policies, guidance documents, FAQs, and interpretive rules, as well as the process for generating them, should be reviewed by an external advisory group of experts engaged in animal research from entities that receive federal research awards. 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.</p>	<p>The advisory group mentioned above (1a) could assist with this review</p>	<ul style="list-style-type: none"> Investigator IACUC Institution 	12
	<ul style="list-style-type: none"> This review would ensure that these documents emphasize matters of core importance to animal welfare identified in the statutory language of the HREA and AWA, and are consistent with current scientific and technological knowledge and approaches. 			
9	<p>NIH and USDA should establish a risk-based process for review of animal research protocols similar to that for human subjects research under 45 CFR 56; §46.110. Studies deemed low-risk, noninvasive, or minimally invasive could be exempt from full IACUC review or eligible for administrative review without concurrence by the full IACUC.</p>	<p>NIH and USDA should issue a Notice in the Federal Register amending protocol review requirements to define types of studies involving low-risk, noninvasive, or minimally invasive procedures</p>	<ul style="list-style-type: none"> Investigator IACUC Institution 	16

National Institutes of Health

Corresponding Recommendation		Statutory or Regulatory Action Required	Reduction of Burden for	Report Page
5	<p>The <i>Guide for the Care and Use of Laboratory Animals (Guide)</i> is not a regulatory document. Given that, OLAW should use the <i>Guide</i> as it was intended, namely, “to assist institutions in caring for and using laboratory animals in ways judged to be professionally and humanely appropriate.” The <i>Guide</i> 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.</p> <ul style="list-style-type: none"> OLAW should not consider IACUC-approved alternative strategies from “should” statements in the <i>Guide</i> as departures or deviations nor should they be 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. 	Amend NIH FAQ C7, PHS Policy IV.B.3.c, and NIH website: https://grants.nih.gov/grants/olaw/departures.htm	<ul style="list-style-type: none"> Investigator IACUC Institution 	13–14
6	OLAW should cease using the word “deviation” in their guidance documents when referring to IACUC-approved alternative strategies to “should” statements in the <i>Guide</i> . As with USDA regulations, the meaning of words used in OLAW guidance documents not defined in legislation or the PHS Policy should be that of a standard dictionary.		<ul style="list-style-type: none"> Investigator IACUC 	13–14
7	The <i>Guide</i> should be a “living” document that continuously incorporates changes in the scientific literature. Consideration should be given to an online version of the <i>Guide</i> with periodic updates provided in partnership with an independent group such as the American Association for Laboratory Animal Science.		<ul style="list-style-type: none"> Investigator IACUC 	13–14
11	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 <i>that would result in an increased risk.</i> ”	Amend third bullet in section 8.1.2.5 of the NIH Grants Policy	<ul style="list-style-type: none"> Investigator IACUC 	17
13	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 of the overall research objectives.	“Delete section 4.1.1.2 “Verification of IACUC Approval” from the NIH Grants Policy	<ul style="list-style-type: none"> Investigator IACUC Institution 	19–20
18	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.	Delete all other examples of reportable situations except “conditions that jeopardize the health or well-being of animals, including natural disasters, accidents, and mechanical failures, resulting in actual harm or death to animals” in NOT-OD-05-034	<ul style="list-style-type: none"> Investigator IACUC Institution 	22–23
19	OLAW specifies that the grant number be included in noncompliance 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.	Delete second bullet under “Information to Be Reported” in NOT-OD-05-034	<ul style="list-style-type: none"> Investigator Institution 	22–23
20	Streamline the assurance for animal research. In addition, for Category 1 institutions, allow proof of accreditation in lieu of the detailed program description.	Using the Federalwide Assurance for Human Subjects Research as a guide, streamline the Animal Welfare Assurance	<ul style="list-style-type: none"> IACUC Institution 	23

Minor recommendations are not color-highlighted

United States Department of Agriculture

Corresponding Recommendation		Statutory or Regulatory Action Required	Reduction of Burden for	Report Page
8	Revise §2.31(d)(5) of the AWA Regulations (AWR) 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.	Amend §2.31(d)(5) of the AWR	<ul style="list-style-type: none"> Investigator IACUC Institution 	15
10	Revise USDA Animal Care Policy #14 to reflect the language in the 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.	Amend USDA Animal Care Policy #14	<ul style="list-style-type: none"> Investigator IACUC 	16–17
12	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...”	Amend USDA Animal Care Policy #12	<ul style="list-style-type: none"> Investigator 	18–19
15	Revise §2.31(c)(3) of AWR to state: “ <i>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.</i> ”	Amend §2.31(c)(3) of the AWR	<ul style="list-style-type: none"> Investigator IACUC Institution 	21
17	With respect to inspection frequency based upon historical compliance, USDA should consider including AAALAC International accreditation as a factor.	Include AAALAC International accreditation as a criteria on the APHIS website: https://www.aphis.usda.gov/aphis/ourfocus/animalwelfare/sa_awa/ct_awa_risk_based_inspection_system	<ul style="list-style-type: none"> Investigator IACUC Institution 	21–22

Minor recommendations are not color-highlighted

1. 21st Century Cures Act. January 2017. Retrieved from: <https://www.congress.gov/114/bills/hr34/BILLS-114hr34enr.pdf>
2. Federal Demonstration Partnership. 2012. Faculty Workload Survey Research Report. Retrieved from: http://sites.nationalacademies.org/cs/groups/pgasite/documents/webpage/pga_087667.pdf
3. National Science Board. 2015. Reducing Investigators' Administrative Workload for Federally Funded Research. Retrieved from: <https://www.nsf.gov/pubs/2014/nsb1418/nsb1418.pdf>
4. National Research Council Institute for Laboratory Animal Research. 2011. Guide to the Care and Use of Animals Eighth Edition. Retrieved from: <https://www.nap.edu/catalog/12910/guide-for-the-care-and-use-of-laboratory-animals-eighth>
5. National Academy of Sciences. 2016. Optimizing the Nation's Investment in Academic Research: A New Regulatory Framework for the 21st Century. Retrieved from: <https://www.nap.edu/catalog/21824/optimizing-the-nations-investment-in-academic-research-a-new-regulatory>
6. NIH Initiative to Reduce Regulatory Burden. 1999. Retrieved from: <https://archives.nih.gov/asites/grants/06-17-2015/archive/grants/policy/regulatoryburden/index.htm>
7. National Institutes of Health. Guidance on Significant Changes to Animal Activities. Retrieved from: <https://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-126.html>
8. Executive Order 13777. "Enforcing the Regulatory Reform Agenda." *Federal Register* 12285-12287. March 1, 2017. V. 82, No. 39. <https://www.federalregister.gov/documents/2017/03/01/2017-04107/enforcing-the-regulatory-reform-agenda>
9. Executive Order 13771. "Reducing Regulation and Controlling Regulatory Costs." *Federal Register* 9339-9340. January 30, 2017. V. 82, No. 22 <https://www.federalregister.gov/documents/2017/02/03/2017-02451/reducing-regulation-and-controlling-regulatory-costs>
10. Office of Laboratory Animal Welfare web page. <https://grants.nih.gov/grants/olaw/faqs.htm>
11. OMB Agency Good Guidance Practices. <https://www.gpo.gov/fdsys/pkg/FR-2007-01-25/pdf/E7-1066.pdf>
12. Final Rules Animal Welfare: 9 CFR Parts 2 and 3. Retrieved from: <https://www.nal.usda.gov/awic/final-rules-animal-welfare-9-cfr-parts-2-and-3>
13. U.S. Department of Health and Human Services, Federal Policy for the Protection of Human Subjects; Final Rule. Fed. Reg. 82, 7149;7181 (2017). <https://www.federalregister.gov/documents/2017/01/19/2017-01058/federal-policy-for-the-protection-of-human-subjects>
14. Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals. February 24, 2005. <https://grants.nih.gov/grants/guide/notice-files/not-od-05-034.html>
15. OLAW Assurance Sample Document. <https://grants.nih.gov/grants/olaw/sampledoc/assursmp.htm>

A. Regulations, Policies, Guidance Documents, and FAQs, referenced by OLAW

<https://grants.nih.gov/grants/olaw/olaw.htm>

1. Office of Laboratory Animal Welfare—Public Health Service Policy on Humane Care and Use of Laboratory Animals
2. *OLAW Adopted:*
 - a. Guide for the Care and Use of Laboratory Animals: Eighth Edition (Guide)
 - b. American Veterinary Medical Association (AVMA) Panel on Euthanasia released the AVMA Guidelines for the Euthanasia of Animals: 2013 Edition (Guidelines)
3. Health Research Extension Act of 1985, Public Law 99-158, “Animals in Research”
4. U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training (Principles)
5. Animal Welfare Act
6. NIH Revitalization Act Of 1993; Plan For Use Of Animals In Research
7. Current list of OLAW Notices (Updated November 2016)

<https://grants.nih.gov/grants/olaw/references/notices.htm>

This document contains NIH Guide for Grants and Contracts Notices and Dear Colleague letters. Additional information and guidance is available in OLAW’s [Frequently Asked Questions](#).

1. NIH Guide for Grants and Contracts

- i. **October 25, 2016**—NIH Guide Notice NOT-OD-17-010; Reports on Site Visits to the National Primate Research Centers and the Federally Supported Chimpanzee Sanctuary
- ii. **August 2, 2016**—NIH Guide Notice NOT-OD-16-125; Notice of Change in Animal Welfare Assurance Numbering System

- iii. **October 13, 2015**—NIH Guide Notice NOT-OD-16-006; Simplification of the Vertebrate Animals Section of NIH Grant Applications and Contract Proposals
- iv. **August 10, 2015**—NIH Guide Notice NOT-OD-15-139; Notice of Memorandum of Understanding Between NIH and NSF Concerning Laboratory Animal Welfare
- v. **June 9, 2015**—NIH Guide Notice NOT-OD-15-109; Guidance on Qualifications of IACUC Nonscientific and Nonaffiliated Members
- vi. **March 17, 2015**—NIH Guide Notice NOT-OD-15-079; Notice of Update to the Public Health Service Policy on Humane Care and Use of Laboratory Animals
- vii. **December 1, 2014**—NIH Guide Notice NOT-OD-15-028; Notice of Office of Laboratory Animal Welfare Policy on Shared Animal Welfare Concerns
- viii. **August 26, 2014**—NIH Guide Notice NOT-OD-14-126; Guidance on Significant Changes to Animal Activities
- ix. **May 29, 2014**—NIH Guide Notice NOT-OD-14-099; Notice of Change in Criteria for Renewal of Domestic Animal Welfare Assurances
- x. **August 7, 2013**—NIH Guide Notice NOT-OD-13-098; Grant and Contract Submission Requirements Regarding the AVMA Guidelines for the Euthanasia of Animals: 2013 Edition
- xi. **August 2, 2013**—NIH Guide Notice NOT-OD-13-096; Implementation of the Revised International Guiding Principles for Biomedical Research Involving Animals
- xii. **March 1, 2013**—NIH Guide Notice NOT-OD-13-048; Implementation of the Updated AVMA Guidelines for the Euthanasia of Animals: 2013 Edition
- xiii. **February 21, 2013**—NIH Guide Notice NOT-OD-13-044; Notice of Change to Electronic Submission of Final Noncompliance Reports to the Office of Laboratory Animal Welfare

- xiv. **September 10, 2012**—NIH Guide Notice NOT-OD-12-148; Guidance on Departures from the Provisions of the Guide for the Care and Use of Laboratory Animals
- xv. **March 8, 2012**—NIH Guide Notice NOT-OD-12-081; Change in Criteria for Renewal of Animal Welfare Assurances for Foreign Institutions
- xvi. **December 2, 2011**—NIH Guide Notice NOT-OD-12-020; Adoption and Implementation of the *Guide for the Care and Use of Laboratory Animals: Eighth Edition*
- xvii. **December 1, 2011**—NIH Guide Notice NOT-OD-12-021; Update of Sample Interinstitutional Assurance
- xviii. **March 18, 2011**—NIH Guide Notice NOT-OD-11-053; Guidance to Reduce Regulatory Burden for IACUC Administration Regarding Alternate Members and Approval Dates
- xix. **September 1, 2010**—NIH Guide Notice NOT-OD-10-128; Clarification on the Roles of NIH Scientific Review Groups (SRG) and Institutional Animal Care and Use Committees (IACUC) in the Review of Vertebrate Animal Research
- xx. **August 6, 2010**—NIH Guide Notice NOT-OD-10-121; Report on Site Visits to Chimpanzee Facilities and Associated Resources to Aid Grantee Institutions
- xxi. **July 14, 2010**—NIH Guide Notice NOT-OD-10-114; Update on Applicability of the Shelf Life Extension Program (SLEP)
- xxii. **June 4, 2010**—NIH Guide Notice NOT-OD-10-102; Update of the Guide for the Care and Use of Laboratory Animals
- xxiii. **April 19, 2010**—NIH Guide Notice NOT-OD-10-049; Instructions for Completion and Technical Evaluation of the Vertebrate Animal Section (VAS) in NIH Contract Proposals
- xxiv. **April 16, 2010**—NIH Guide Notice NOT-OD-10-083; Update of Sample Animal Welfare Assurance for Foreign Institutions
- xxv. **April 15, 2010**—NIH Guide Notice NOT-OD-10-081; Guidance on Confirming Appropriate Charges to NIH Awards during Periods of Noncompliance for Activities Involving Animals

- xxvi. **March 17, 2010**—NIH Guide Notice NOT-OD-10-027; Instructions for Completion and Peer Review of the Vertebrate Animal Section (VAS) in NIH Grant Applications and Cooperative Agreements
- xxvii. **January 8, 2009**—NIH Guide Notice NOT-OD-09-035; Guidance to IACUCs Regarding Use of Designated Member Review (DMR) for Animal Study Proposal Review Subsequent to Full Committee Review (FCR)
- xxviii. **February 15, 2008**—NIH Guide Notice NOT-OD-08-049; Update of Sample Animal Welfare Assurance
- xxix. **October 12, 2007**—NIH Guide Notice NOT-OD-08-05; Implementation of the Revised American Veterinary Medical Association Guidelines on Euthanasia
- xxx. **January 26, 2007**—NIH Guide Notice NOT-OD-07-044; NIH Policy on Allowable Costs for Grant Activities Involving Animals when Terms and Conditions are not Upheld
- xxxi. **March 24, 2006**—NIH Guide Notice NOT-OD-06-052; Guidance on Use of Telecommunications for IACUC Meetings under the PHS Policy on Humane Care and Use of Laboratory Animals
- xxxii. **February 24, 2005**—NIH Guide Notice NOT-OD-05-034; Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals
- xxxiii. **July 13, 2004**—NIH Guide Notice NOT-OD-04-052; Office of Extramural Research Guidance Regarding Animal Welfare Documents Submitted to the Office of Laboratory Animal Welfare
- xxxiv. **June 6, 2003**—NIH Guide Notice NOT-OD-03-046; Revised Guidance Regarding IACUC Approval of Changes in Personnel Involved In Animal Activities
- xxxv. **July 17, 2002**—NIH Guide Notice NOT-OD-02-062; PHS Policy Clarification Regarding Use of Carbon Dioxide for Euthanasia of Small Laboratory Animals
- xxxvi. **February 12, 2001**—NIH Guide Notice NOTOD01017; Office of Extramural Research Guidance Regarding Administrative IACUC Issues and Efforts to Reduce Regulatory Burden

xxxvii. **February 3, 2000**—NIH Guide Notice NOT-OD-00019; Office of Extramural Research Guidance Concerning the Production of Monoclonal Antibodies in Animals

xxxviii. **December 21, 1999**—NIH Guide Notice NOT-OD-00007; Office of Extramural Research Guidance Regarding Reduction of Regulatory Burden in Laboratory Animal Welfare

2. Dear Colleague Letters

- i. **November 17, 1997**—OPRR Reports Dear Colleague Letter No. 98-01; Subject: Production of Monoclonal Antibodies Using Mouse Ascites Method
- ii. **June 2, 1997**—OPRR Reports Dear Colleague Letter No. 97-03; Subject: Maintenance of Properly Constituted IACUCs
- iii. **May 30, 1997**—NASA Principles for the Ethical Care and Use of Animals
- iv. **March 8, 1995**—OPRR Reports Dear Colleague Letter No. 95-02; Subject: Sources of Custom Antibody Production
- v. **January 14, 1994**—OPRR Reports Dear Colleague Letter; Subject: Requirements for Annual Reporting to OPRR
- vi. **January 11, 1994**—OPRR Reports Dear Colleague Letter; Subject: Internal Distribution of Your Animal Welfare Assurance
- vii. **May 21, 1990**—OPRR Reports Dear Colleague Letter; Subject: Use of Expedited Protocol Review Procedures by IACUCs

3. Frequently Asked Questions: PHS Policy on Humane Care and Use of Laboratory Animals (Last Revised: December 6, 2016) [84 FAQs] <https://grants.nih.gov/grants/olaw/faqs.htm>

4. Office of Laboratory Animal Welfare—Vertebrate Animals Section [If live vertebrate animals are to be used, applicants must address the following criteria] https://grants.nih.gov/grants/olaw/vertebrate_animal_section.htm

B. Regulations, Policies, Guidance Documents, FAQ, referenced by USDA

1. Animal Welfare Act
2. Animal Care Policy Manual (May 23, 2016) https://www.aphis.usda.gov/animal_welfare/downloads/Animal%20Care%20Policy%20Manual.pdf
3. Animal Welfare Act and Regulations [The “Blue Book”] https://www.aphis.usda.gov/animal_welfare/downloads/AC_BlueBook_AWA_FINAL_2017_508comp.pdf
4. Animal Welfare Inspection Guide https://www.aphis.usda.gov/animal_welfare/downloads/Animal-Care-Inspection-Guide.pdf
5. The Reporting of Adverse Events at Research Facilities on USDA Inspection Reports (November 2014) https://www.aphis.usda.gov/animal_welfare/downloads/Adverse-Events-on-Inspection-Reports-Tech-Note.pdf

C. Regulations, Policies, Guidance Documents, FAQ, referenced by FDA

1. Federal Food, Drug, and Cosmetic Act (FD&C Act)
2. Animal Welfare Act
3. Public Health Service Policy of Humane Care and Use of Laboratory Animals
4. Good Laboratory Practice for Nonclinical Laboratory Studies (21 CFR Part 58)
5. Various “Guidance Documents”

D. Regulations, Policies, Guidance Documents, FAQ, referenced by DOD

1. Regulations, Standards & Requirements
http://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.acuro_regulations
2. Animal Welfare Act
3. Army Regulation 40-33: The Care and Use of Laboratory Animals in DOD Programs

4. Department of Defense Instruction 3216.01 Use of Animals in DOD Programs
5. Defense Federal Acquisition Regulation: Animal Welfare Clause
6. The Guide for the Care and Use of Laboratory Animals
7. U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training
8. AVMA Guidelines on Euthanasia
9. ACRO Animal Appendix (requiring submittal of IACUC approved protocol for their review) http://mrmc.amedd.army.mil/index.cfm?pageid=Research_Protections.acuro_Animalappendix

E. Regulations, Policies, Guidance Documents, FAQ, referenced by VA

1. Animal Welfare Act
2. VHA Handbook 1200.07—Use of Animals in Research—
https://www.va.gov/vhapublications/ViewPublication.asp?pub_ID=2464
3. U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training
4. Guide for the Care and Use of Laboratory Animals
5. AVMA Guidelines on Euthanasia
6. PHS Policy
7. Health Research Extension Act

F. Regulations, Policies, Guidance Documents, FAQ, referenced by EPA

7. EPA Solicitation Clauses—<https://www.epa.gov/grants/epa-solicitation-clauses#animal>
8. Animal Welfare Act
9. U.S. Government Principles for the Utilization and Care of Vertebrate Animals used in Testing, Research, and Training

