FASEB
Federation of American Societies for Experimental Biology

Representing Over 130,000 Researchers

301.634.7000
www.faseb.org

9650 Rockville Pike
Bethesda, MD 20814

November 9, 2017

Ms. Rebeckah Adcock
Regulatory Reform Officer
Senior Advisor to the Secretary, Office of the Secretary
Office of Budget and Program Analysis, USDA
Jamie L. Whitten Building, Room 101–A
1400 Independence Ave. SW
Washington, DC 20250

Re: Request for Information: Identifying Regulatory Reform Initiatives

Dear Ms. Adcock:

On behalf of the Federation of American Societies for Experimental Biology (FASEB), we offer comments in response to the Request for Information (RFI): Identifying Regulatory Reform Initiatives. FASEB comprises 31 scientific societies collectively representing over 130,000 scientists and engineers, many of whom use United States Department of Agriculture (USDA) regulated animals in biological and biomedical research. The role of animals remains critical to the understanding of fundamental processes of life and in developing treatments for injury and disease for both humans and animals. We are pleased to see USDA interested in reforming regulations so as to ease regulatory burdens. The topic of excess regulatory burden is one that is extremely important to FASEB and its member societies.

In April 2017, FASEB, in coordination with the Association of American Medical Colleges, the Council on Governmental Relations, and the National Association for Biomedical Research, hosted a workshop that brought together experts in animal research regulatory compliance. The goal of the workshop was to develop recommendations that federal agencies and Congress could take to reform animal research regulations and ultimately reduce burden for institutions, institutional animal care and use committees (IACUC), and individual scientists. We anticipate that the recommendations resulting from discussions at the workshop will be helpful to USDA in their goal of identifying regulatory reform initiatives.

Recommendations specific to USDA included:

1. Establishing a risk-based approach for review of animal research protocols similar to that for human subjects research
2. Revising §2.31(d)(5) of the Animal Welfare Regulations (AWR) to allow for review of activities every three years to align with the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy)

3. Revise USDA Animal Care Policy #14 to reflect the language in Animal Welfare Act (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
4. Revising USDA Animal Care Policy #12 to eliminate the requirement for keyword/literature searches when evaluating alternatives to potentially painful or distressful research

Reasoning for each of the recommendations is presented below.

1. Establishing a risk-based approach for review of animal research protocols similar to that for human subjects research

Greater focus on oversight in areas with a higher potential for risk could ensure animal welfare and allow investigators to reduce administrative burden thereby devoting more time to research. This concept is consistent with human subject research regulations, which provide a regulatory structure allowing for exempt research and expedited review of research protocols. 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. Extending this framework to animal research would mean that studies with little risk could be processed more expeditiously, and veterinarians and IACUC members could spend more time on studies with a higher risk potential.

Section 2.31 (d)(2) of the Animal Welfare Regulations (AWR) and section IV.C.2 of the Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) allow for review of proposed research projects through either the full IACUC 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. Establishing this risk-based approach for review would need to be harmonized with PHS Policy.

2. Revising §2.31(d)(5) of the AWR to allow for review of activities every three years to align with PHS Policy

The AWR is inconsistent with 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).

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 Animal Welfare Act (AWA). Therefore, we recommend that USDA revise §2.31(d)(5) of the AWR as follows to 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*."

3. 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.

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.

4. Revising USDA Animal Care Policy #12 to eliminate the requirement for keyword/literature searches when evaluating alternatives to potentially painful or distressful research

The AWA requires that a "principal investigator considers alternatives to any procedure likely to produce pain to or distress in an experimental animal." 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[1]:

> "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."

Keyword and literature searches for identifying alternatives to research that may cause more than slight or momentary pain or distress are not required by the AWA or AWR; however, they have been strongly encouraged in Policy #12 of the APHIS *Animal Care Resource Guide*. Policy #12 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

[1] https://www.nal.usda.gov/awic/final-rules-animal-welfare-9-cfr-parts-2-and-3

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. For example, Silverman *et al.* published an article with results from a survey describing responses from IACUC members, the aim of which was to evaluate strengths, weaknesses, and effectiveness of IACUCs within the United States[2]. According to this study, fewer than half of the respondents indicated that literature searches were useful in finding alternatives to procedures in which there was more than slight or momentary pain or distress. 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.

Therefore, to reduce the burden placed upon research investigators and IACUC staff, we urge USDA to amend the language in USDA Animal Care Policy #12 with respect to database searches to be consistent with AWR §2.31(d)(1)(ii).

FASEB commends USDA for identifying reform initiatives in an effort to ease regulatory burdens. The Federation appreciates the need for regulations; however, we want to make sure that the effort expended meeting the requirements achieves the outcomes as initially envisioned. We thank you for considering FASEB's comments. Please do not hesitate to contact us if we can provide you any additional information.

Sincerely,

Thomas O. Baldwin, PhD
FASEB President

[2] Silverman et al. A self-assessment survey of the Institutional Animal Care and Use Committee, Part 1: animal welfare and protocol compliance. *Lab Animal*. 41(8), pp 230-235, 2012.