



# FASEB

Federation of American Societies  
for Experimental Biology

Representing Over 120,000 Researchers

301.634.7000  
www.faseb.org

9650 Rockville Pike  
Bethesda, MD 20814

May 9, 2014

Office of Laboratory Animal Welfare  
National Institutes of Health  
RKL 1, Suite 360, MSC 7982  
6705 Rockledge Drive  
Bethesda, MD 20892

RE: RFI: Invitation to Comment on Proposed Guidance Regarding Significant Changes to Ongoing Animal Activities (NOT-OD-14-063)

SUBMITTED VIA: <http://grants.nih.gov/grants/rfi/rfi.cfm?ID=36>

Dear Dr. Brown:

The Federation of American Societies for Experimental Biology (FASEB) appreciates the opportunity to comment on the *Request for Information: Invitation to Comment on Proposed Guidance Regarding Significant Changes to Ongoing Animal Activities*. FASEB is composed of 26 scientific societies collectively representing over 120,000 biomedical researchers, many of whom conduct animal research. We recognize the profound importance of the humane use of animals in research and support efforts to ensure it.

The Federation is concerned, however, that this proposed guidance may unnecessarily increase regulatory burden and place less significance on the professional judgment of investigators and the IACUC. In past guidance (FAQ D9), OLAW has stated that the IACUC has some discretion in determining what constitutes a significant change. The scientific community has appreciated the latitude given to use professional judgment and establishing performance based standards within an institution's animal care and use program. We believe that this proposed guidance weakens the ability of investigators and IACUCs to draw on their vast knowledge by prescribing circumstances in which certain activities must be considered significant changes. Thus, FASEB requests that OLAW reconsider the need for this additional guidance. However, should this guidance go forward, we recommend that the following significant revisions be incorporated to minimize increases in administrative burden and provide clarity.

### Significant Changes

In its response to the 2013 Request for Information issued by the National Science Board's Task Force on Administrative Burden, FASEB recommended that NIH encourage the animal research community to use designated member review instead of full committee review when appropriate.

As such, we are pleased that OLAW has restated in this guidance that significant changes can be approved by designated member review. Utilizing designated member review instead of full committee review for protocol amendments can streamline the approval process, reduce the possibility that in-progress research is halted, and reduce burden placed upon the full IACUC. All of this can occur while still ensuring the welfare of the animals.

While we commend OLAW for highlighting the use of designated member review, we are concerned that some of the language in sections A and B, which identify situations constituting significant changes, is unclear. This ambiguity may lead to increased rather than decreased administrative burden. As an example, in section B it states that a “change” in animal numbers constitutes a significant change. A change can be either a reduction or an increase, and FASEB believes that reducing the number of animals in an approved protocol should not be considered a significant change. Requiring that an IACUC consider cases where studies are concluded without using all the animals is an unnecessary regulatory burden for both investigators and IACUC members. Moreover, in this scenario, an investigator could be prompted to use more animals than minimally necessary, violating a tenet of the 3Rs principle (reduction, replacement, and refinement).

This likewise applies to the “change’ in frequency or number of procedures proposed on an animal. Only an increase in the frequency or number of procedures should be considered significant, provided that the treatment does not serve to alleviate animal pain and distress. These non-significant protocol changes should be able to be approved at the staff level.

**Therefore, we suggest the following changes to the wording of sections A and B to reduce the ambiguity, support performance based standards and professional judgment, and reduce administrative burden:**

- A. Significant changes are those changes that have or may have a direct impact on animal welfare including ~~but not limited to~~ changes:
- **changes** that have the potential to increase the level of pain or distress of the animal;
  - changes that involve anesthesia, analgesia, sedation, or euthanasia;
  - **increased** frequency or number of **invasive** procedures;
  - **changes in the type or anatomical location of invasive procedures; and**
  - **changes in frequency, interval, type, number, or anatomical location of** substances **administered** to the animal.

B. Some activities that may not have a direct impact on animal welfare are also significant.

These include ~~but are not limited to~~ changes:

- **increases** in animal numbers (see Guide for the Care and Use of Laboratory Animals, p. 25) or **change** in species;
- ~~in~~ housing **and/or** use of animals in a location that is not part of the animal program overseen by the IACUC;
- **changes in** the scope of an approved animal activity (see NIH Grants Policy Statement Part 2 8.1.2.5); and
- **changes** in Principal Investigator.

### **Non-Significant Changes**

We have two major concerns with guidance proposed in section C. First, providing all members of the IACUC with a record of non-significant changes appears to be in contradiction to the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals (Policy). Section IV.B.7 of the PHS Policy states that as an agent of the institution, the IACUC shall “review and approve, require modifications in (to secure approval), or withhold approval of proposed **significant changes** regarding the use of animals in ongoing activities.” Additionally, in section IV.E.1.c, the Policy states that the awardee shall maintain “records of applications, proposals, and proposed **significant changes** in the care and use of animals and whether IACUC approval was given or withheld.” Finally, section IV.E.2 of the Policy asserts that records relating directly to proposed **significant changes** in ongoing activities reviewed and approved by the IACUC be maintained for three years. In none of these sections does the Policy state that the IACUC is to be informed of any non-significant changes handled by the IACUC staff or that these changes need to be recorded and kept on file.

Second, we are extremely concerned with the additional regulatory burden that recording and informing the IACUC of non-significant changes would incur. While information on non-significant changes could be provided to the IACUC after the protocol has been modified and approved, and thus not interfere with the research project, it would substantially increase the workload of IACUC staff. Furthermore, the inclusion of the correction of typographical errors and grammar among items to be summarized would be so burdensome that it could result in no such corrections being submitted to the detriment of protocol clarity. In larger animal care and use programs, an IACUC staff can make many non-significant changes to their approved protocols per month. Collating a list of these non-significant administrative changes would

increase the regulatory burden and workload of staff with no perceived benefit. **Therefore, we encourage OLAW to remove the requirement that the entire IACUC is to be informed of non-significant changes handled by the IACUC staff from section C.**

As currently written, we are concerned that this guidance will cause a large increase in administrative burdens for investigators and institutions engaged in animal research and undermine the importance of professional judgment and performance based standards. However, if this guidance is to go forward, we urge OLAW to make significant revisions to the areas of the proposed guidance as noted above.

Thank you for considering FASEB's comments. Please do not hesitate to contact us if we can provide you any additional information.

Sincerely,

A handwritten signature in black ink, appearing to read "Margaret K. Offermann". The signature is written in a cursive style with a long horizontal stroke at the end.

Margaret K. Offermann, MD, PhD  
FASEB President