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National Institutes of Health
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Submitted electronically to: <http://grants.nih.gov/grants/rfi/rfi.cfm?ID=36>

Re: NOT-OD-14-063: Invitation to Comment on Proposed Guidance Regarding Significant Changes to Ongoing Animal Activities

The National Association for Biomedical Research (NABR) represents more than 360 public and private universities, medical and veterinary schools, teaching hospitals, voluntary health organizations, professional societies, pharmaceutical and biotechnology companies and advocates sound public policy for the humane care and use of laboratory animals in biomedical research. On behalf of its member institutions, NABR thanks OLAW for the opportunity to provide comments regarding the proposed Guidance Regarding Significant Changes to Ongoing Animal Activities.

We applaud OLAW's stated purpose for proposing the subject guidance, the dual objectives of supporting the use of performance standards and professional judgment by Institutional Animal Care and Use Committees (IACUC) in following the Public Health Service (PHS) Policy for the Care and Use of Laboratory Animals (Policy) and reducing the burden on investigators and institutions by facilitating greater autonomy within local IACUCs. The recently released National Science Board Report, [Reducing Investigators' Administrative Workload for Federally Funded Research](#), identifies animal research and IACUC requirements as making a significant contribution to administrative burden. The report highlights the requirement for making changes in research protocols as one considered a particular problem by investigators. OLAW is positioned to help remedy the situation with improved guidance on the subject. NABR hopes this opportunity is taken.

To accomplish its stated purpose and minimize regulatory burdens, NABR agrees with the proposal's introductory statements about the responsibilities, authority and discretion of IACUCs. However, after emphasizing IACUC autonomy in determining what is a significant change in animal activities as provided in the Policy (IV.B.7), detailed lists of what is and is not significant are provided. This approach undermines the IACUC's performance, negates its professional judgment and defeats the purpose of this OLAW guidance. Given the diversity of PHS grant awardees' laboratory animal programs, it is inherently difficult to list examples that will apply and be understood by all. Some of the proposed guidance as written will be misinterpreted and, therefore, more burdensome on

institutions. Further, and of greater concern, some of the listed examples go beyond the current requirements of PHS Policy.

In keeping with the Office of Management and Budget publication, Final Bulletin for Agency Good Guidance Practices (January 2007), this proposed guidance is intended to offer OLAW's advice concerning the subject issue, but should not establish additional regulatory requirements. NABR recommends the nature of the document be made clear in the introduction. It is intended as a guide for following the PHS Policy. The reference to "meeting the standards of the PHS Policy" in the statement of purpose is imprecise. The Health Research Extension Act of 1985 authorized the Secretary of Health and Human Services, through the Director of the National Institutes of Health, to establish "guidelines."

NABR's specific comments to illustrate the points made above are as follows:

1. The tone of the document is rigid and undermines the spirit, intent and purpose of a "guideline." To wit, labeling significant changes as "... including but not limited to" those listed in Section A. and B., or as not significant in Section C., is more than a guideline.
2. Defining "all changes that involve anesthesia, analgesia, sedation, or euthanasia" as significant may not be appropriate for many institutions.

Many IACUCs have developed and approved guidance documents that include drugs, dosages and/or methods for specific species in use at the institution. Under these circumstances, changes between approved agents and methods consistent with IACUC-approved guidelines should not be considered significant, allowing them to be handled administratively.

3. It is important to state PHS Policy affords an IACUC the authority "to approve ranges of variables, as long as the range does not interfere with the welfare of the animal or the range is scientifically justified." In this instance, some examples of such ranges would be instructive, because action is in the hands of IACUCs. A good one to show would be the idea of IACUCs allowing investigators to show a range in the animals to be used in their applications/proposals. Equally important is reminding IACUCs of their responsibility to clearly define and communicate to investigators their policy for determining significance.
4. In view of institutional diversity as well as autonomy, an IACUC must establish its own process for allowing administrative approval of non-significant changes. Limiting approval to "IACUC staff," as proposed in Section C, is inconsistent with this stated purpose. NABR recommends that this section be revised and shortened to read: C. Changes that are not significant may be handled administratively without advance IACUC review and approval.

5. The IACUC being informed of minor changes, routinely handled administratively, is not a current PHS Policy requirement. A variety of institutional standard operating procedures may provide the information an IACUC needs to function properly. References to IACUC notification in Section C. should be deleted.
6. Most examples on the list of minor changes eligible for administrative approval raise questions, rather than provide guidance. Implying that IACUC notification is needed for typographical or grammatical errors is excessive. NABR believes the focus of the PHS Policy and IACUC decision making is on significant changes affecting animal welfare. This list should be dropped.
7. One important issue not adequately addressed is change in the number of animals approved for an activity. Investigators told the National Science Board that obtaining IACUC approval for animal number changes caused unnecessary effort and delays. Predicting exact needs several years ahead often is problematic. OLAW's proposed guidance suggests a 10% change in the number of animals not regulated by USDA is not considered significant. NABR thinks the more helpful suggestion to give IACUCs would be to establish what levels of change or range are deemed not significant at their institution. The PHS Policy (IV.D.1.a) specifies that applications and proposals identify the "approximate number of animals to be used."

NABR members are anxious to meet their obligations to protect animal welfare in accordance with PHS Policy. In these times of declining financial resources, it will greatly benefit all PHS assured institutions and their laboratory animals, if administrative time and costs are minimized. We appreciate OLAW's assistance in these endeavors.

Thank you for your consideration of our comments and please contact me if you have any questions.

Sincerely,

Matthew R. Bailey
Vice President