



American College of Laboratory Animal Medicine

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Re: Invitation to Comment on Proposed Guidance Regarding Significant Changes to Ongoing Animal Activities

The American College of Laboratory Animal Medicine (ACLAM), a specialty board recognized by the American Veterinary Medical Association (AVMA) as the certifying organization for laboratory animal medicine and a recognized specialty within the veterinary medical profession, was founded in 1957 to encourage education, training, and research in laboratory animal medicine and establish standards of training and experience for veterinarians professionally involved with the care and health of laboratory animals. On behalf of our 907 Active Diplomates we appreciate the opportunity to provide comments and suggestions on the proposed Guidance Regarding Significant Changes to Ongoing Animal Activities. The following includes comments on sections for which clarifications are required, modifications are proposed or as we believe changes are warranted.

"Meeting the Standards of the PHS Policy"

The Health Research Extension Act of 1985 authorizes the Secretary, acting through the Director of the NIH, to establish guidelines for the proper treatment of animals being used in biomedical and behavioral research, not to promulgate standards. The reference to "meeting the standards of the PHS policy" seems to imply otherwise. However, ACLAM appreciates that this proposed guidance document does not establish regulatory requirements, but is intended to clarify previous guidance on the issue of significant changes.

Ranges of Variables vs. a Single Value

ACLAM members recognize that the IACUC has the authority to approve ranges of variables, as long as it has determined that the ranges do not interfere with the welfare of the animal or if the range is scientifically justified. We seek clarification regarding whether the ranges of variables include anesthetics, analgesics and sedatives and the methods of euthanasia used by an investigators, if the IACUC has determined that the ranges do not interfere with the welfare of the animal or the range is scientifically justified.

OLAW states that "if the investigator chooses to use a single value rather than a range, he or she is required to adhere to this standard". If the investigator realizes during the conduct of the experiment that the single value would endanger the welfare of the animal(s) and, with veterinary consultation, reduces the dosage (or value) to protect the wellbeing of the animal(s), especially when it involves any drugs such as anesthetics/analgesics or investigational compounds, would this be interpreted as a major change? Would this change require IACUC review and approval (either by DMR or FCR) or could this be handled administratively? We suggest that administrative review with veterinary consultation would certainly reduce the burden on investigators and secure animal well-being.

Usage of IACUC Developed and Approved Guidelines

Many IACUCs, often supported by ACLAM board certified veterinarians, have developed and approved guidance documents that include drugs, dosages and/or methods for specific species in use at the institution. If an investigator's protocol states that they will use the drugs, dosages and/or methods listed in the IACUC-approved guidance document, ACLAM does not believe that changes from one approved agent to another approved agent should be considered a significant change requiring DMR or FCR. We request clarification on this topic recognizing that such changes may be handled administratively with veterinary consultation. This clarification would significantly reduce the burden on investigators.

Although we agree with the language in Part A that changes that have or may have a direct impact on animal welfare are significant changes we believe that significant reductions in the burden on investigators could be achieved if they were able to work within IACUC-approved guidelines for the use of anesthetics, analgesics, sedatives and euthanasia methods. And therefore, a change made within those guidelines with veterinary consultation would not be considered significant allowing them to be handled administratively.

Animal Numbers

ACLAM agrees that increases in animal numbers are a significant change to the IACUC protocol if it exceeds 10% of the number reviewed in USDA and non-USDA regulated species. We are aware of no statutory language which would require that USDA regulated animals be treated differently than those covered by the PHS Policy and therefore would suggest treating those alike in this regards. Furthermore, we would like to clarify whether the use of animal numbers less than reviewed by the IACUC is also seen as a significant change that needs to be indicated and justified in an amendment to the original protocol. Would this require IACUC review and approval or could this be handled administratively? The recently published document by the National Science Board summarizing a survey on "Reducing Investigators Administrative Workload For Federally Funded Research" states "that all experiments have to be predetermined and that exact animal numbers have to be statistically justified forces researchers to project these quantities years into the future, and then continually file amendments for any deviation". Researchers suggested in the survey that it is often impossible to predict the direction of their research for the length of the grant and/or IACUC protocol. ACLAM would support the notion that reducing the originally proposed number of animals would not impart a significant change nor should it require an amendment to the protocol. The development of a new method that would render the use of animals obsolete, as an example, should rather be classified as an alternative to animal use and replacement in light of the 3R's, which is commendable. This should not burden the investigator with having to write an amendment.

Administratively vs. IACUC Staff

ACLAM is concerned with the proposed language in part C indicating that changes which are not significant may be handled by the IACUC staff, as opposed to the more generic terminology "may be handled administratively". Limiting such approval to the IACUC staff would not facilitate the institutional autonomy referred to in the Purpose section of the notice. We recommend that the language in section C be changed to read "changes that are not significant may be handled administratively without IACUC review and approval".

Information Submitted to the IACUC

ACLAM is also concerned about the requirement that IACUC is to be informed of changes handled administratively. Requiring this notification adds to the administrative burden of those individuals who have been approved by the IACUC to grant administrative approval for changes that are not significant. In addition, it would take away from the valuable time IACUC's meet to discuss protocols, develop institutional policies or any other important function of the committee that pertain to the humane and ethical use of animals. To ensure institutional autonomy, the IACUC must be able to establish its own process for granting this administrative approval.

We are concerned that the language contained in the fourth bullet point, pertaining to housing, will increase the administrative burden on those managing the animal care facilities within an institution. Changes in where animals are housed within a centrally managed animal care program, and especially within a specific facility, are usually made by those who manage the facility, not by the investigators, and thus should not require a change in the information in the protocol. In some instances, institutions may require that changes from one facility (building) to another be documented in the protocol file, for purposes of the semiannual review process. However, the same institution may not require that minor administrative changes, such as room assignments within a facility, be documented in the protocol file. ACLAM believes that such changes should be handled administratively, but the process should be left to institution and the bullet point should be deleted from the examples.

Finally, ACLAM is concerned that corrections to address typographical errors, grammar and contact information would have to be tracked at all. This would add an unnecessary administrative burden to the management of the IACUC and not impact animal welfare in any way. We recommend deleting the final three bullet points.

ACLAM welcomes the opportunity to provide professional input. We believe, especially in light of the efforts to reduce administrative burden on investigators, allowing research entities to exercise professional judgment and IACUC's to self-regulate is in the spirit of the regulations governing animals in research, teaching and testing. Thank you for considering our comments and please contact me if you have any questions.

Sincerely,



Sue VandeWoude, DVM, DACLAM
ACLAM President