

**Report on the Review of Responses to**  
**and**  
**Recommendations concerning (the)**  
**Request for Information (RFI):**  
**Standards for the Care and Use of Laboratory Animals**  
**Notice Number: NOT-OD-06-011**

## Background

The Public Health Service Policy on Humane Care and Use of Laboratory Animals (PHS Policy) incorporates by reference the latest edition of the Institute for Laboratory Animal Research (ILAR) *Guide for the Care and Use of Laboratory Animals (Guide)*. The *Guide* was initially published in 1963 and has been revised several times, most recently in 1996. The purpose of the *Guide*, as indicated in the Preface of the 1996 edition, is to assist institutions in caring for and using animals in ways judged to be scientifically, technically, and humanely appropriate. Further, recommendations of the *Guide* are based on published data, scientific principles, expert opinion, and experience with methods and practices that have proved to be consistent with high-quality humane care and use. All domestic National Institutes of Health (NIH) awardee institutions are required by the PHS Policy to use the *Guide* as a basis for developing an institutional animal care and use program for activities involving animals. Serious deviation from the provisions of the *Guide* must be promptly reported to the NIH's Office of Laboratory Animal Welfare (OLAW).

On November 9, 2005 the NIH issued a Request for Information (RFI): Standards for the Care and Use of Laboratory Animals – Notice Number: NOT-OD-06-011 (<http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-06-011.html>). The intent of this RFI was to solicit new scientifically valid information, methods or practices, published data or other advances in the humane care and use of laboratory animals, in order to assess the need for updating the standards in the current 1996 *Guide*. As noted in the RFI, NIH was interested in new information and knowledge related to the four chapters of the 1996 *Guide*: institutional policies and responsibilities; animal environment, housing, and management; veterinary medical care; and physical plant. Interested parties, individuals, or organizations could submit information in a variety of formats in response to this request. The deadline for the submission of the information was extended to March 31, 2006 <http://grants2.nih.gov/grants/guide/notice-files/NOT-OD-06-040.html>.

### Submissions

The NIH received 132 items for evaluation from 39 submitters (i.e. individuals, multiple individuals, scientific professional societies, animal protection organizations, and laboratory animal science organizations). The materials received reflected a variety of genre including: memos and letters, annotated discussions, bibliographies, review articles and scientific publications, both single articles and collections of articles.

The submissions received in response to the RFI were divided into five Topic Areas: General comments regarding revision of the *Guide*; Institutional/IACUC matters, training (*Guide* Chapter 1); Neurosciences, pain and distress; behavioral consideration (*Guide* Chapters 2 & 3); Laboratory animal medicine; analgesia, anesthesia and euthanasia; and toxicology (*Guide* Chapter 3), and Laboratory animal management/husbandry and field studies (*Guide* Chapters 2 and 4).

## Review

An expert Committee of 12 scientists and veterinarians from Public Health Service agencies (Centers for Disease Control and Prevention – two; Food and Drug Administration – four, and National Institutes of Health – six) were asked to participate in a critical review of the submissions. The Committee included:

- Laboratory animal medicine veterinarians, including diplomates of the American College of Laboratory Animal Medicine.
- Individuals involved in the development or implementation of US policies that directly and indirectly impact the use of laboratory animals within their respective agency.
- Individuals with scientific expertise in biomedical engineering-radiation biology, neurobiology of pain, animal behavior, immunology, pharmacology, pathology and physiology.
- Ten members who are or have been members (including chair and attending veterinarian) of Institutional Animal Care and Use Committees (IACUC).

All reviewers' portfolios contained Topic Area 1 (General Comments). The twelve reviewers were grouped into four subcommittees of three reviewers and each subcommittee was instructed to critically review one of the remaining four topics (2-5). A primary reviewer was designated for each submission for Topic Areas 2-5. Additionally one person was designated as a coordinator for each subcommittee.

Reviewers were instructed to factor into their review the following non-exclusive list of considerations: Was the information published (especially post 1996) in a peer-reviewed journal? When a scientific/technical paper or preliminary data was submitted, was the author considered an expert on the topic discussed? Consider the validity/merits of the submission. Where data were provided, has the research been subject to validation by another laboratory? Was the sample size reasonable? Were variables controlled as necessary? Did the author's recommendation or conclusion drawn from the paper constitute new information? Would implementation of the recommendation or conclusion require a change in the performance standards of the *Guide*? Reviewers were instructed to share their comments and determinations for all items in their portfolio with the primary reviewer. Additionally reviewers were instructed to examine all other submissions outside of their assigned portfolios, and note any impressions or knowledge they may have regarding any submission that may not have been obvious to other members of the Committee.

At the convened meeting of the Committee, a review was conducted by Topic Area. Each primary reviewer discussed the submission(s) within their portfolios and provided their opinions. As necessary, this was followed by discussion by the subcommittee and full Committee, respectively. At the conclusion of the discussion of all submissions within a Topic Area, the subcommittee was asked to recommend whether any single submission or a cluster of submissions provided new information that documented a need for a revision of the performance standards found in the *Guide*.

## **Findings**

Following its in-depth review, the Committee unanimously determined that the information provided in response to the RFI contained no scientific evidence that would warrant revising the associated performance standards of the 1996 *Guide*. The Committee determined that the performance standards contained in the current *Guide* continue to be relevant and support the Public Health Service commitment to animal welfare in PHS-supported scientific endeavors. It also noted that utilization of performance standards, rather than engineering standards, has allowed individual institutions to adapt policies and procedures to their own institutional environments (e.g. research subject emphasis, selected animal models, climatic conditions). Many of the submissions, in fact, reflected a diversity of approaches to achieving the performance standards found within the *Guide*.

However, the Committee recognized that, owing to the evolution of improved institutional practices and procedures since 1996, many of the references contained in the *Guide* are out-of-date. In this regard, the Committee considered that a number of the submissions provided in response to the RFI might be helpful to institutions by providing ideas on how to achieve the standards described in the *Guide*, particularly in connection with the conduct of institutional program reviews and the development of institutional positions and guidance for investigators. The Committee determined that there is a need for an updated Appendix A of the *Guide*. Additionally, some submissions (e.g. #6 Dauchy *et al*, Effects of light on oncology research; #1 Nadon, Maintaining rodents for gerontology research) were considered highly significant for a limited scientific audience.

The Committee observed that the research described in a number of the publications submitted in response to this RFI were supported by the National Center for Research Resources (NCR), and noted that hypothesis driven research on topics of laboratory animal husbandry and welfare provides particularly valuable information.

Inasmuch as advances in the technical and scientific aspect of laboratory animal care and use may be anticipated, the Committee advised that any scientifically valid information which may be published in the future that appears to negate or disprove any performance standard for animal care and use described in the *Guide* should be brought to the attention of ILAR and the NIH.

## **Recommendations**

To meet NIH's current needs, the Committee recommends that:

- the *Guide*, as a living document, should become a web-based document to enable periodic updating of its Appendices.
- Appendix A should be periodically revised as necessary to contain a) an up-to-date bibliography of references to best practices or validated hypothesis-driven research, and b) new topics including, but not limited to, alternative methods, genetically engineered animals, and non-traditional animals.
- inclusion of new references should occur only after critical review for scientific validity and consistency with the PHS Policy through a peer review process such as an ILAR Committee.

- published cyclic reviews, such as the AVMA Panel on Euthanasia and revisions of guidelines produced by scientific and professional societies, such as the American Society of Mammalogists and the Ornithological Council, should be incorporated into Appendix A of the *Guide*.
- enhanced communications is desirable between ILAR and the AVMA and other scientific and professional societies to expedite the flow of information between these groups and help ensure consistency between the guidelines they produce.
- as the volume of new information for a component of science increases, it would be advantageous to have continued development of new reports along the lines of the ILAR *Guidelines for the Care and Use of Mammals in Neuroscience and Behavior Research*; the references found in these documents may in some cases fill complete voids found in Appendix A of the *Guide* or may update important bibliographies.