

Best Practices for Animal Care Committees and Animal Use Oversight

W. Ron DeHaven

Abstract

Regulatory authorities around the world with oversight responsibility for the welfare of research animals have placed heavily reliance on local oversight committees. These animal care committees (ACCs) are part of an institutional animal welfare team that includes the institutional administration, principal investigators, attending veterinarian and animal care staff, as well as regulatory organizations and authorities. As a key component of this team, most ACCs function as an agent of the institution to ensure regulatory animal welfare compliance. Although regulatory testing involving animals presents some unique circumstances, the focus of all animal care committees is to minimize animal pain and distress. Federal requirements are often couched within a regulatory framework that is performance based and therefore very flexible. Thus, it is important for ACCs to establish very simple and specific institutional requirements and procedures and to work at promoting a broad understanding of them within their respective institutions. Experience suggests that ambiguity at the local level results in many unintended side effects and confusion. There are many “best practices” that can help the ACC promote institutional compliance and good animal welfare. These practices, although not universally appropriate for all institutions or activities, include ACC coordinator or administrator, designated protocol reviewer, alternate or dual ACC members, generic protocols and standard operating procedures, centralized controls and animal care facilities, conducting pilot studies, and ensuring the most humane endpoints.

Key Words: 3Rs; animal welfare; best practices; humane endpoints; performance standards

Most countries actively engaged in biomedical research using animals have a requirement for oversight committees with responsibility for the welfare of the animals. These committees are known by several names, which include animal care committees, animal ethics committees, animal care and use committees,

ethical review committees, and institutional animal care and use committees. For the purposes of this discussion, all are referred to as “animal care committees” (ACCs¹) and are discussed in the context of regulatory testing. Although they vary somewhat in structure and function, all ACCs play a critical role in ensuring the welfare of research animals and compliance with the applicable laws and regulations. Good animal welfare at research facilities depends on a team approach involving the institutional administration, principal investigators, the attending veterinarian and animal care staff, the ACC, and the regulatory organizations and authorities. Thus, as a key part of this team, most ACCs function as an agent of the institution to ensure regulatory compliance. In this capacity, they not only follow institutional policies and procedures, but they also are usually involved in establishing such procedures and policies as they relate to animal care and use. In addition, ACCs receive varying degrees of direction, guidance, and oversight from the applicable federal regulatory authorities.

Minimizing Animal Pain and Distress

Although regulatory testing that involves animals presents some unique requirements, the focus of animal care committees remains the same: Although they must satisfy the “letter of the law,” they must, more importantly, embrace the spirit of the law to minimize animal pain and distress. Minimizing pain and distress is accomplished by application of Russell and Birch’s (1959) 3Rs—reduction, refinement, and replacement.

Many professional organizations throughout the world have adopted and actively promote the 3Rs. For example, the Position Statement Regarding the Use of Animals in Toxicology (SOT 1999) from the Society of Toxicology (SOT¹) states, “The Society is committed to: the development and use of alternatives to the use of animals (replace); the use of research designs that employ less painful or stressful procedures and improve animals care (refine); a reduction in the number of animals used for research and testing when this is scientifically appropriate and valid (reduce).” The SOT Code of Ethics goes on to say that Society

W. Ron DeHaven, D.V.M., is Deputy Administrator of the Animal Care division of the US Department of Agriculture’s Animal Plant Health Inspection Service.

¹Abbreviations used in this presentation: ACC, animal care committee; SOP, standard operating procedure; SOT, Society of Toxicology.

members shall “observe the spirit as well as the letter of the laws, regulations, and ethical standards with regard to the welfare of humans and animals involved in their experimental procedures.” These statements are consistent with the overall concern within the biomedical research community at large to minimize animal pain and distress, including in the regulatory testing arena. Thus, the primary role of the ACC is to minimize pain and distress to the extent practical without compromising research data. This fundamental principle should guide committees through all of their respective activities and deliberations.

Performance Standards Versus Ambiguity

Many federal regulatory authorities have appropriately adopted a “performance-based” approach to regulations, including those pertaining to ACC responsibilities. This regulatory methodology is outcome oriented and focuses on expected results rather than the process used to achieve those results. Thus, performance-based regulations provide some degree of flexibility in committee operations, allowing the institution to establish procedures that complement its organization, specific activities, and even institutional preference.

Unfortunately, this regulatory flexibility has caused some institutions to create very convoluted and complex processes, usually with the intent of exceeding minimum requirements. However, the end result is often just the opposite, with the institution creating misunderstanding, actual or perceived disparate treatment, unnecessary regulatory burden, and eventually failure to comply with applicable regulations. For example, consider the institution that requires a statistical power analysis to justify the number of animals to be used for every protocol when, in fact, a simple common sense justification may be all that is necessary or even feasible in some circumstances with limited knowledge about expected outcome.

Thus, within this flexible regulatory framework, it is important for ACCs to establish very simple and specific requirements and procedures and to promote a broad understanding of them within their respective institutions. Experience suggests that ambiguity at the local level results in many unintended side effects and confusion and is ultimately counterproductive to both efficient operations and animal welfare.

Animal Care Committee Best Practices

Personal experience and discussions with many individuals within the biomedical research community, regulatory officials, and US Department of Agriculture inspectors have yielded several recurring suggestions of “best practices” for ACCs with oversight responsibility for regulatory testing. Some of these practices are explained below; however, it is important to note that not all are applicable, recommended,

appropriate, or even legal in all circumstances. Additionally, the ACC should periodically review institutional animal care procedures and practices to ensure that they promote simplicity, add value to the process, are consistent with the applicable regulations, and are appropriate to the institution or study under review.

Animal Care Committee Coordinator/ Administrator

Many institutions have established an ACC coordinator or administrator position to perform the following important functions: screening protocols to ensure that all necessary components are included; distributing protocols scheduled for committee review; scheduling meetings; keeping and distributing meeting minutes; and generally ensuring that the ACC is fulfilling all of its regulatory requirements in a complete and timely manner. Although the ACC coordinator is an additional institutional expense, this person’s increased efficiency and improved compliance may be well worth the cost and even result in net savings, particularly at large institutions.

Designated Reviewer

Many regulatory authorities allow protocols to be reviewed by a designated reviewer as long as each ACC member has an opportunity to request review by the full committee. Judicious use of the designated reviewer for protocols that are routine, repetitive, and/or involve little or no animal pain or distress can conserve valuable ACC time and resources for protocols that are unique, more complex, or may involve moderate or severe pain or distress.

Alternate or Dual ACC Members

Most regulatory authorities have specific positions that must be filled for an ACC to be duly constituted and legally able to conduct business. The appointment of two or more persons for each of the required positions ensures that the possible resignation of one still leaves the committee duly constituted and able to conduct business uninterrupted. Similarly, the appointment of alternate members to the ACC ensures that the inability of one or more members to be present at a particular meeting will not affect the required quorum if each respective member has a designated alternate available to attend, and vote, on their behalf.

Additional ACC Resources

Some ACCs have either appointed or made available to the committee individuals with specific areas of expertise. Most commonly, ACC membership includes a biostatistician to

evaluate the number of animals to be used in a study or a librarian to assist in literature searches to ensure adequate consideration of alternative methods and to preclude unnecessary duplication of experimentation. Additionally, some ACCs will consult outside experts when a protocol involves areas outside the expertise of committee members.

Adequate Expertise/Training

It is important for the ACC overseeing regulatory testing to be familiar with all of the relevant regulatory requirements and guidelines rather than to assume that the principal investigator is familiar with them and is already applying the 3Rs to the extent possible. For example, some principal investigators may use particular tests or endpoints simply because they have always used them, when, in fact, there may be more humane tests or endpoints that are acceptable to the regulatory agency. In addition, administrators who are familiar with the requirements in multiple countries might need to modify protocols only slightly to satisfy the requirements of all possible authorities and to preclude the need to use more animals in additional testing. At the same time, the ACC must have a mechanism in place to evaluate the training and experience of individuals who will be involved in the care and use of the animals to ensure that they are qualified.

Generic Protocols and Institutional Standard Operating Procedures (SOPs)¹

By creating a generic protocol for frequently used tests or procedures, ACCs can reduce investigators' redundant paperwork and better ensure fulfillment of all relevant requirements. For example, by conducting a search for alternatives and unnecessary duplication at the institutional level, the ACC can better ensure that the search was done well and that it will be reviewed and updated as needed. However, many tests or procedures are similar but not identical (e.g., similar studies used to evaluate novel compounds). In these cases, the ACC may provide a basic protocol framework that is individualized by the investigator as needed to address all of the relevant animal welfare and regulatory concerns.

Similarly, protocols often incorporate frequently used procedures. By including such procedures into institutional standard operating procedures (SOPs¹), investigators can simply reference the procedure as described in the SOP rather than describe the procedure in detail for each protocol in which the procedure is used. Activities that might be included in SOPs include routine blood sampling procedures, species-specific pain relief regimens for commonly used drugs, and frequency and method of documenting animal observations. In light of recent (September 11, 2001) tragic events, ACCs should also consider developing an SOP or contingency plan for emergencies such as loss of

power, natural disasters, and flooding. In addition, the ACC should ensure that there is an institutional animal disease prevention and surveillance program in place to preclude, or quickly identify, diseases in the animal colony.

Centralized Controls and Animal Care

As a result of technological advances, it is now common to preclude ordering animals until after a protocol has been approved, and even then, to impose appropriate controls on the species and number of animals that can be ordered consistently with the protocol. Experience suggests that centralized animal facilities are likely to have better oversight and, therefore, better controls to ensure proper care and use of animals. Although there are many possible organizational configurations for animal facilities, those that have a centralized animal facility operated by an experienced institutional animal care staff appear to be in the best position to ensure good animal care. The most difficult organizational configuration to ensure adequate animal care occurs when there are geographically dispersed animal facilities wherein animal care is being provided by individual investigators and their respective staffs. In these cases, the quality of care is usually dependent on the quality of oversight by a number of individuals, many of whom may not have animal welfare as their primary concern. Although it is not possible for all animal housing facilities to be located in geographic proximity, institutions with geographically dispersed animal facilities might consider having an animal care staff with centralized oversight provide all of the animal care.

Pilot Studies

When there is insufficient information to proceed with a full-fledged study, a pilot study or a limited study that utilizes a small number of animals can reveal important information and, ultimately, reduce animal pain and distress dramatically. Pilot studies can be used for many purposes such as improving study design, determining the earliest and most humane endpoints, minimizing the number of animals and ensuring appropriateness of the species, adjusting dose ranges, assessing the need for analgesics or anesthetics, and identifying otherwise unanticipated events.

Additional Protocol Approval Considerations

The ACC should consider certain specific questions in reviewing regulatory testing protocols. For example, has the beginning of the study been timed to coordinate the anticipated onset of acute signs and the availability of appropriate staff? Has consideration been given to the use of supportive therapy and, if so, have "endpoints" been clarified for the onset of such therapy? Are procedures in place for dealing with unexpected or severe signs? If applicable,

will pain relief and supportive therapy be available after hours and on weekends? Are animals housed socially with appropriate environmental enrichments where possible and to the extent practical without compromising the study design or the data?

ACC Inspections and Reviews

Many ACCs are responsible for periodically reviewing institutional procedures and inspecting the animal facilities. Some committees report that they obtain the most accurate picture of the condition and activities in a facility on a day-to-day basis by conducting unannounced inspections. Others maintain that this practice is counterproductive because the people with whom they need to communicate are not always present and the unannounced inspection does not always promote positive, constructive communication and relationships with investigators and their staffs. Some committees report that by alternating unannounced with scheduled or announced inspections, they can reap the benefits of both systems.

The most frequent concern expressed by US Department of Agriculture inspectors about ACC activities at US facilities is inadequate postapproval monitoring of protocols (i.e., studies that are not being conducted in a manner consistent with the ACC-approved protocol). By establishing some system for postapproval monitoring, ACCs can ensure that animals are being monitored at prescribed frequencies, that analgesics are being administered as prescribed, and that documentation of observations and administration of medications are consistent with approved protocols or institutional SOPs. Such postapproval monitoring might be performed independent of, or as part of, required ACC facility inspections and program reviews.

Humane Endpoints

Nothing is more critical to the ACC protocol review process than to ensure the use of the most humane endpoint, with proper criteria to determine when that endpoint has been reached. Endpoint criteria must be identified, clearly defined, and consistent with the regulatory requirements and the responsible agency's guidelines. Frequency of animal observations should be clearly established, as should the criteria for initiating supportive therapy when appropriate. Procedures should be in place to terminate protocols when the study objectives have been realized, if it becomes clear that they cannot be realized, or whenever the degree of suffering is not required or justified by the protocol.

Death should rarely be an endpoint, and most regulatory

authorities discourage or prohibit death as an endpoint except when it is scientifically justified. The ACC must ensure that there are clear and predetermined lines of authority to euthanize animals and that they cover all possible scenarios. Unnecessary animal suffering should not occur solely because a person authorized to perform euthanasia is unavailable.

Information Sources for ACCs

Several excellent sources of information are available for ACCs involved in regulatory testing. A few particularly noteworthy examples include the following:

- **Guidance on the Conduct of Regulatory Toxicology and Safety Evaluation Studies**
This document (Home Office 2001) provides a comprehensive regulatory overview of the issues and expectations related to regulatory testing.
- **Guidelines on Choosing an Appropriate Endpoint in Experiments Using Animals for Research, Teaching and Testing**
This excellent document (CCAC 1998) defines humane endpoints and includes a list of questions ACCs should ask with regard to endpoint selection.
- **Guidance Document on the Recognition, Assessment, and Use of Clinical Signs as Humane Endpoints for Experimental Animals Used in Safety Evaluation**
This publication (OECD 2000) has an extensive list of clinical signs that can be used to assess the condition of animals in safety tests.

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