



The ACC Connection

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WELCOME to the third edition of the **ACC Connection**, a quarterly newsletter designed to help researchers with questions regarding animal research at the University of Connecticut Health Center. Our third issue is designed to help you become familiar with the USDA and PHS requirements of the 3R's and the Search for Alternatives to Painful Procedures. The Health Center is required to ensure that animal use conforms to a multitude of state and federal regulations which include compliance with the Animal Welfare Act in accordance with the Animal Welfare Regulations (9 CFR, 1985), the Public Health Service Policy on Humane Care and Use of Laboratory Animals (2002), and the recommendations promulgated by the *Guide for the Care and Use of Laboratory Animals*.

The 3R's: Replacement, Reduction, and Refinement- An Overview

The concept of Replacement, Reduction, and Refinement was first introduced in 1959 by two British researchers, W. Russell and R. Burch. In their landmark book "The Principles of Humane Experimental Technique", they were the first to argue that, far from being a hindrance to animal research, humane treatment and care of laboratory animals resulted in healthier animals and better research results. Their work eventually resulted in new animal research legislation in Great Britain in the 1970's and, by 1985, in the United States. Both Public Health Service (PHS) Policy and the USDA (via the Animal Welfare Act) require that the 3R's be addressed in every research protocol involving animal use.

Replacement: is the act of replacing the animals in a research project with non-animal techniques or lower organisms. This can include species that are phylogenetically lower than the proposed animal, bacteria or fungi, cell culture, or computer simulations. Replacement can also be absolute or relative; that is, completely replacing your animals with an alternative or replacing part of your animals. What is ultimately chosen as a replacement methodology depends upon the goals of the research project; there are no "standard replacements" available to the researcher. One way to determine if there are replacement options for your research is to perform a good literature search **prior** to writing your research protocol.

Reduction- is the act of minimizing the number of animals involved in a research project. Though the concept may be theoretically simple, it is sometimes hard to actually apply. Having a sound experimental design is vital in determining the appropriate number of research animals any protocol needs. It is also wise to perform a power analysis to ensure that your results will be statistically valid.

Refinement- is the most tricky concept of the 3R's. It is typically thought of as making sure what procedures being performed on the laboratory animals are designed to induce the least amount of pain and/or distress to those animals. Therefore, most researchers consider the appropriate uses of anesthetics and/or analgesics to total picture of replacement, but this is not accurate. Careful, and possibly updated, design of your experiment- taking into account all the possible causes of pain and/or distress- is a refinement technique. Using enrichment strategies that are appropriate for the species you are using is a refinement of the protocol. There are others as well. **Please note** that if you are using a USDA-regulated species, the law requires you to consult with a veterinarian during the **planning** stages of your experimental design if you are going to perform procedures that have the potential to cause pain and/or distress to the animal.

Search for Alternatives to Painful and/or Distressful Procedures

There are very few aspects of the animal care and use protocol that are as misunderstood as the "Search for Alternatives" requirement. Researchers should be aware that this search for alternatives is a USDA **and** institutional requirement and is a **search for alternatives to painful and/or distressful procedures which are contained in the protocol**. It is not a search for an alternative to animal use or a search for duplication of research (though those may comprise part of the

search for alternatives strategy). One protocol quite possibly can require more than one search as **each** potentially painful and/or distressful procedure performed on the laboratory animal **must** be addressed. Reviewing the Search for Alternatives information on the [ACC website](http://clacc.uhc.edu/ACC/AlternativeSearchHelp.htm) (<http://clacc.uhc.edu/ACC/AlternativeSearchHelp.htm>) is recommended to all researchers.

How to get started with the search- The best way to get started is the following: when planning your experimental design, perform a literature search to “see what’s out there”. This will help you satisfy the 3R requirements you must do as well as possibly providing you with new techniques that are being performed by other researchers in the field. The next step is to list all of the potentially painful and/or distressful procedures the experimental design employs (“D” and “E”). This may include surgical procedures, other non-surgical invasive procedures, and other obvious painful techniques. But the requirement also includes distressful procedures which can include food/fluid restriction, prolonged restraint, and multiple injections and/or blood collections from the animals. **A good rule of thumb is the following:** if the procedure has the potential to cause more than momentary pain or distress to humans, it has the potential to cause more than momentary pain or distress to the research animals. This also includes terminal procedures performed under general anesthesia.

Once you have a list of your painful procedures, then you are ready to perform the search for alternatives. This does **not** have to be a literature search (though the USDA maintains that a literature search remains the best way to fulfill the search for alternatives requirement).

Literature search: If you decide to perform a literature search to meet the Search for Alternatives requirement, you must first decide on your **search strategy**. Improper strategies are the most common reason this search requirement is not met. You must pick your key words carefully and link them appropriately. For more detailed information on how to do this, ask the ACC Office for a copy of “Meeting the Search for Alternatives Requirement”- a handout that is available to you. The search information that must be detailed in your protocol include: search strategy used, the date you performed the search, the years searched, and the databases searched (this must be at least two). Databases recommended include BIOSIS and AGRICOLA as well as the standard MEDLINE. If the search yields a *bona fide* alternative, and you decide not to use it, you must state the reason(s). Similarly, if there are no alternatives to your potentially painful and/or distressful procedures, you need to state that in your protocol as well.

Workshops / Meetings: There are occasions where a literature search is not the most appropriate way to determine if there are alternatives (e.g., highly innovative research). One way to satisfy the Search for Alternatives requirement is to reference information presented at scientific workshops or meetings. If you choose to do this, you must detail in your protocol the following information: meeting or workshop attended, who presented the information and his/her credentials, and the date the meeting or workshop was held.

Experts: Another way to meet the requirement is discussion with experts in the field. If information is provided from a reference book, for example, you must detail the name of the book, the author and his/her credentials, and publication date. If you converse with the expert, you must provide the name, his/her credentials, and the date of your conversation.

Frequently Asked Questions

My protocol is a surgical procedure which has no alternatives. What exactly am I supposed to do in this case?

This provides a difficult situation. In this case, the best thing to do is to ensure that anesthetics/analgesics are most appropriate via a literature search or, possibly, a reference book. Discussion with the veterinarian is also a good idea and **mandatory if you are using a regulated species**. You must ensure that post-operative care for pain management is accomplished and adequate. You need to state that there are no alternatives. For example, if you are performing a craniotomy in order to implant electrodes, you need to state that there is no other way to implant electrodes into the brain without performing a craniotomy. Supplemental information required would be that there is **no other way to get the data you need other than by implanting the electrodes**.

This appears to be awfully complicated. I never had to do this before, why do I have to do it now?

Admittedly, this may seem to be a new regulatory requirement, but it has been the law since December, 1985 for USDA regulated species when the Farm Bill was passed. Our PHS assurance statement makes it a requirement, at this institution, for all species. In the past, the requirement was presented as a search for alternatives to animal use or duplication of research efforts. Though these two topics must be addressed in research protocols, this is not the search requirement as written in the Animal Welfare Act. We can look at it as a misinterpretation of the regulations, and move on from there.

Where does this information go in the protocol?

The concept of replacement is covered in section 8, Rationale for Using Animals in the animal care and use protocol. The Search for Alternatives is covered in section 5a and possibly 5b, depending upon what painful and/or distressful

procedures are being performed. Though section 8 is simply check boxes on the protocol form, the researchers should be prepared to justify, in writing, their rationale for using animals and appropriateness of the species chosen if the ACC should require them to do so.

How will my search be evaluated?

The ACC will review the search to see if it is appropriate and that all potentially painful and/or distressful procedures being performed are addressed. In literature searches, some things will raise a “**red flag**”: only one database searched, terms included would provide information on duplication of research or non-animal use only, the term “alternative” used alone, keywords not relevant to the protocol’s painful procedures, keywords and concepts linked incorrectly, and inadequate time period searched (e.g., <5 years). In the other methods, the ACC will evaluate the credentials of the authors and/or experts, the applicability of the workshop/meeting information on the submitted protocol, and the references provided from a standard reference book.

If you have questions you’d like to see answered in future issues, please send them to pohl@uchc.edu and we will do our best to answer as many questions as possible.

Upcoming Training, April 2006 – June 2006

Animal Users Basic Core Training

Monday, April 17, 2006	9:00 am – 12:00 pm	Building 20 conference room
Monday, May 22, 2006	9:00 am – 12:00 pm	Building 20 conference room
Monday, June 29, 2006	9:00 am – 12:00 pm	Building 20 conference room

Animal Users CLAC Training- Limited to 20 people (sign-up sheet for additional sessions will be available)

Wednesday, April 19, 2006	11:00 am – 12:30 pm	Building 20 conference room
Topic: Sick/Dead reports and Extra Husbandry Services Charges		
Wednesday, May 17, 2006	11:00 am – 12:30 pm	Building 20 conference room
Topic: Understanding the monthly Animal Care Invoice and how to code for FRS		
Wednesday, June 21, 2006	11:00 am – 12:30 pm	Building 20 conference room
Topic: Requesting Imports and Exports with Granite		

New Institutional, State, or Federal Regulations

Federal- USDA

Animal Care Policy #10 Revision, effective date 3/7/06: In February 2005, the American Anti-Vivisection Society petitioned the Animal Care (AC) program of the USDA to examine its regulatory authorities under the AWA in regard to pet cloning companies, as well as facilities that conduct genetic engineering of animals. AC has determined that a facility conducting genetic engineering that results in a live (whole) animal species covered by the AWA should be regulated as a research facility under the AWA. Furthermore, the welfare of genetically engineered animals is protected by the AWA when the animals are used in other regulated activities (i.e., dealing or exhibition). The USDA also determined that the act of cloning an animal does not alone determine if a facility must be licensed or registered with the USDA. A facility producing cloned animals is considered to be breeding animals, and if they are being utilized for an AWA-regulated purpose (such as selling to pet stores or for exhibition), the facility must be licensed. This policy has also been updated to differentiate between certain activities of licensed exhibitors.

Animal Care Policy #15 Revision, effective date 3/7/06: All research facilities regulated by the AWA are expected to have IACUCs to oversee and approve their protocols to ensure that adequate consideration of alternatives has been made for any potential painful and/or distressful results; that the activities do not unnecessarily duplicate previous experiments; that the animals’ living conditions will contribute to their health and comfort; and that animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly euthanized at the end of the procedure or, if appropriate, during the procedure. The USDA has revised policy #15 to provide clarification on the qualifications required of members of the IACUC. The research facility is responsible for ensuring that IACUC members are qualified to assess the research facility’s animal program, facilities, and procedures. This responsibility includes the provision of training and instruction to ensure that IACUC members have an understanding in areas such as the AWA, protocol review, and facility inspections.



Next Issue: Laboratory Inspections

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