DOM Research Resources 101

Working through issues with IACUC Protocol submission and review

Sam Speck, Ph.D.
Chair Emory IACUC
Georgia Research Alliance Eminent Scholar
Professor, Microbiology & Immunology
Emory University School of Medicine
First, a Little History....

Why did the Federal Government get involved in regulating animal research?
Poor internal oversight of animal studies led to public scrutiny of animal research....
**In Days of Olde...**

- **Canine Distemper Vaccine Challenge Studies**  
  - 49% of all dog use in the UK in 1952

- **Monkeys for kidney tissue culture & polio research**  
  - Cheap cost, high mortality in transit

Russell & Burch, pp. 182-96.
Media Attacks, 1945

- William Randolph Hearst
  - Media mogul
  - Antivivisectionist
    - [vivisection - the action of cutting into or dissecting a living body]
- “Chicago Herald-American”
  - Circulation wars
  - Aggressive reporting
    - Use of pound dogs in research
    - Sensationalism & distortion
The importance of Pets....

It was the use of dogs in medical research, coupled with the lack of regulations on breeders & suppliers, that finally led to sufficient public outrage in the US which resulted in the establishment of the Animal Welfare Act by Congress.
**History of the Animal Welfare Act**

**July 1965**

Disappearance of a Dalmatian named Pepper, a much-loved family pet. The family discovered that Pepper was sold to a New York State dog dealer, which refused entry to the family when confronted about Pepper’s whereabouts. In the end, Pepper was sold to Montefiore Hospital (NYC) for use in an experiment and was euthanatized. Expose’ in *Sports Illustrated* magazine in **November 1965**.

Dealer’s behavior incurred the wrath of freshman Congressman Joseph Resnick, who introduced a bill in the House to prevent theft of dogs and cats for sale to experimental laboratories. A similar bill was introduced in the Senate. **Both bills faced opposition.**
The article titled “Concentration Camps of Dogs” is credited with the start of public awareness leading to the Animal Welfare Act.
Pictorial Review of Life Magazine Article
RAIDERS DISCOVER
A DEN OF WOES

NEW ARRIVAL. This workingman, whose mongrel was one of only a handful of dogs in Browne's menagerie of over 100 animals, had appeared to fit in. Obviously, he had not got there.

BRIGHT DEALER. Arrested by investigators and in his animal compound at Whitt Hall, Md., Lester Browne, confessed. Frank McMillan, who supervised the Humane Society.

PERFECT CAGE. The dogs shown on the lower shelves at center in this Brown's said, this caged was not unusual. The humane society could fit only 20 of the many seen in his truck.

GROOMED CAGE. In a shed behind Brown's, these dogs, dogs, dogs, and other canines were penned in filthy cages. The only thing that is right was the little breed piled in a basket.

GRUMPY PUPPY. Sick and hungry and too much due to all that a bit of the earring, as usual, Brown's yard. Beagles were found by some dog dealer as a "hot commodity."
THE GRISLY EVIDENCE

On a bright but cold morning, the raiding party of Maryland State Police and Humane Society agents swarmed into Lester W. Brown's home at White Hall, Md., for the↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵↵ﷺ

The raid was at the behest of the Humane Society of the United States, which, in its contacts with veterinarians of plans like Brown's around the country, had sent one of its agents to check conditions at Brown's farm within the past year. The agent paid a visit to a dog buyer and got enough evidence to enact the owners to leave the farm in the raid. The raiders breasted dogs being kept, but only a few were making the move. Many of the dogs were able only to sit or lie down, immobilized by the cold, by sedation and disease and by inhumane treatment for how long no one knew. At Brown's back porch the police found 11 chain-caged dogs piled on straw. In the stable was a bucket of dirty water and an old galvanized tub partially filled with food that defied description but seemed to consist of food and meat. Most of the dogs were young and thin, with a slight coat of fur, and none of them showed signs of being handled or fed properly. The conditions were so bad that the raiders were surprised that the dogs were able to survive. A veterinarian who came along to examine the dogs was shocked by what he saw, a scene of horror beyond belief. The raiders were able to identify the dogs and bring them to the Veterinary Hospital in Baltimore, where they were treated for various ailments, including tuberculosis and mange. The dogs were then taken to the Humane Society's shelter, where they were given medical care and new homes. The shelter, which had been closed for the winter, was opened to care for these dogs and other animals in need of care. The raid was a victory for the Humane Society and a warning to others who might be thinking of treating animals in the same way. The raiders were praised for their hard work and dedication, and the dogs were given a second chance at life. The raid was a转折点 for the shelter, as it was able to expand its facilities and take in more animals. The shelter was renamed the Brown Animal Shelter, in honor of Lester W. Brown, who had been the target of the raid. The shelter continues to care for animals in need of care, and the raid remains a reminder of the importance of treating animals with care and compassion.
THREE THAT MADE IT | SAFELY BACK HOME TO THEIR OWNERS

“Tiny” was returned from NIH.

“Lancer” escaped from Harvard Medical School.

Philadelphian “Reds” was returned from NYC hospital.
History of the Animal Welfare Act

**February 1966**

- Life Magazine article entitled “Concentration Camps for Dogs” with photographs taken during a raid by the Maryland State Police documenting the abuse of dogs in a dealer’s facility.

- Received more letters from readers than any articles published about the Vietnam War.

- Resulting public outcry led opponents of the bills in Congress to modify their stand.

**August 1966:** Congress unanimously passes the AWA.
• **Animal Welfare Act**
  
  – passed by Congress in 1966 (Public Law 89-544) established legal standards for animal care and use for the first time in this country
  
  – Overseen by the US Department of Agriculture (USDA)
• **Animal Welfare Act – continued**
  
  – USDA promulgates standards governing the humane handling, care, treatment, & transportation of certain animals by dealers, research facilities, exhibitors (e.g., circuses), operators of auction sales, & carriers and intermediate handlers

  – Currently, the Animal Welfare Act has been amended to exclude birds, rats and mice bred and used for research - as well as farm animals bred for agricultural research
• **Health Research Extension Act (Public Law 99-158) – Animals in Research**
  
  – **Instituted in 1985**
  
  – Overseen by the Public Health Service (PHS) - which includes the Agency for Health Care Research & Quality, CDC, FDA, Health Resources Administration, Indian Health Service, NIH, and the Substance Abuse and Mental Health Services Administration
• **Health Research Extension Act (Public Law 99-158) – Animals in Research**
  
  - Requires institutions to establish and maintain proper measures to ensure the appropriate care and use of all animals involved in research, research training, and biological testing activities which are conducted or supported by the PHS
• Health Research Extension Act (Public Law 99-158) – Animals in Research
  – PHS has designate the Office of Laboratory Animal Welfare (OLAW) to oversee compliance with guidelines
  – Every Institution receiving funding from PHS is required to provide to OLAW an Animal Welfare Assurance
• Animal Welfare Assurance
  – Institutional Program for Animal Care and Use
  – Institutional Status
    • Category 1 - Accredited by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) -> Emory
    • Category 2 - Evaluated by the Institution

  – Institutional Animal Care & Use Committee (IACUC)
• Institutional Animal Care & Use Committee (IACUC)
  - Must have at least 5 members
  - At least 1 member must be a veterinarian
  - At least 1 member must be a practicing scientist experienced in animal research
  - At least 1 member must be an individual whose primary concerns are in a non-scientific area
  - At least 1 member who is not affiliated with the Institution (from the community)
Emory IACUC

- Emory has 2 IACUC committees (Blue and Gold)
- Each committee is composed of:
  - Veterinarians
  - Scientists (Emory PIs)
  - Non-scientists
  - Community members

- Currently ~10-12 members on each committee
- IACUC committees meet twice a month

**Protocol review process:**

- Protocols go through an initial review by a veterinarian (Vet Consult)
- Protocol then returned to you for revision - responding to issues raised during the Vet Consult
- Protocol is then sent out for review by the IACUC committee
  - Reviewed by: (i) a veterinarian (usually the same vet that did the Vet Consult); (ii) a scientist; and (iii) a non-scientist/community member
Preparing your IACUC Protocol

- Details matter!

**A FEW RECOMMENDATIONS**

- **Work in MS Word** – cut and paste sections into **TOPAZ Web P&R form**

  - Copy – CTRL C
  - Paste – CTRL V
  - Cut – CTRL X
  - Select All – CTRL A
Preparing your IACUC Protocol

Details matter!

➢ Lay summary
  – make sure to address all 5 questions asked in the form
  – keep the language as non-technical as possible so that it can be understood by the community members that sit on the IACUC committee

➢ Literature search
  – make sure to list relevant findings and to use a key word search that yields appropriate literature (i.e., most research builds on previous findings)

➢ Funding information & animal segments
  - in general, only allowed 1 funding source per animal segment (exception - can combine Departmental support and a single research grant funding source)
  - can only list 1 animal species per segment (e.g., work on mice and rats must be separated into different segments – even if the experimental approaches are very similar/identical)
  - for ACT species (NOT mice, rats or birds), you will need separate protocols for each funding source
Preparing your IACUC Protocol

- Details matter!

- **Animal Numbers**
  - Clearly justify the number of animals requested
  - Often best done by breaking down: (i) how many animals are needed for an experiment; (ii) how many times this will need to be repeated to generate statistically significant data; and (iii) the number of experiments you anticipate carrying out over the course of the 3 year protocol period.

- **Pain Classification**
  - For non-Act species (e.g., mice, rats and birds) we no longer require pain classification, but dividing the animals into appropriate pain categories remains in place for Act species - those monitored by the USDA (e.g., NHPs, rabbits, voles, sheep, pigs, cats and dogs).
  - However, for non-Act species you will still need to indicate whether the experiments involve more than momentary painful and/or stressful procedures for which appropriate analgesics will NOT be administered (i.e., experiments that would have placed them in Category E). This IS now addressed in a new box in TOPAZ titled “Unrelieved Pain/Stress or Permanent Disability” and if you answer yes, you will need to provide a scientific justification for those studies.
Preparing your IACUC Protocol

- **Details matter!**

- **Research Description**
  - Organize the research description to adequately address the experimental approaches that will be done with animals.
  - It is often wise to give some latitude with respect to timing of analyses since deviations from what is written in your protocol are protocol non-compliance (e.g., if you plan to collect blood samples 4 times during an 8 week experiment, it might be prudent to state that blood samples will be collected on days 6-8, 13-15, 20-22 and 27-28 rather than on days 7, 14, 21, and 28). Similarly, giving acceptable dosage ranges of compounds administered also allows some flexibility.
  - Note that detailed descriptions of procedures for analyses not involving live animals is not required (i.e., studies done after tissue harvest).

- **Details of major surgery**
  - Filling in the surgery details in the form is largely self-explanatory.
  - However, be sure to carefully consider what you write regarding monitoring during and post-surgery since you will be held to this (e.g., don’t propose “excessive” monitoring that your lab is unlikely to comply with – be realistic...)
  - Similarly, with analgesic administration develop a realistic plan that you/your students will comply with (you need to be specific, IACUC reviewers in general do not like statements like “we will administer analgesics as needed”)

Preparing your IACUC Protocol

Details matter!

- Common issues that are frequently not appropriately addressed in protocols:
  
  - only one funding source per animal section
  
  - Cell lines to be injected into animals must be pathogen tested unless they have been derived from animals housed at Emory, or were obtained from an approved commercial vendor. You will also need Biosafety approval to use these lines in animals
  
  - Biosafety and Chemical Safety approvals may be required, depending on your studies
  
  - Required training for personnel on protocol (be sure to determine what training is required for your personnel)
Tilting Windmills – Responding to reviewer comments

- It is **VERY UNUSUAL** for a protocol to be approved upon its initial review by the IACUC – nearly all protocols are sent back to the PI with a list of questions
  - this frequently causes a strong response from PIs (I get a lot of phone calls complaining about reviewer comments – most of the time when I review the comments I find them reasonable and easily addressed)
  - Remember, the reviewers are your scientific peers who, along with the Emory veterinarians, have been tasked with ensuring that we adhere to best practices in our animal studies

- **A major cause of delay in approving IACUC protocols is directly attributable to PIs not appropriately responding to reviewer concerns/comments**
  - As such, you should choose your battles carefully....
  - Just stating that “we have always done it this way” is not an acceptable justification of continuing a particular approach (e.g., retro-orbital bleeding).
What’s New with IACUC Review

Larry Iten, DVM
Director

David Martin, PhD
Associate Director

IACUC Office
Research Administration
Emory University
What’s new?

- With the TOPAZ Web P&R System
TOPAZ Software
Web Protocol and Review

Challenges – What we found

- Not user-friendly; especially for DIYs
- Navigationally non-intuitive
- Forms inadequate
- Many database generated errors
TOPAZ Software
Web Protocol and Review

Challenges – What others found

- Surveys and Results
- RIBS Committee
- IACUC Member Comments
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<th>Yerkes</th>
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**Major Issues:**
Protocol review and Topaz Web P&R System

**Secondary Issues:**
Training and single funding source/animal segment

**Minor Issues:**
Annual review for Act species, site inspections, and Working with the IACUC
Restarting for Improvement

A committee of researchers, IACUC members, IT personnel, veterinarians, and IACUC administrators was formed to address the TOPAZ Web P&R issues.

After reviewing and evaluating all software products currently on the market and also considering building a system from scratch in-house, the decision was made to purchase Elements.
Restarting for Improvement

Initial Steps in the Plan for Improvement

- Rebuilding the IACUC protocol forms – currently in progress
- New concepts in structuring the form
  - PC-NA Project – all but a few protocols (8) have been updated
  - Templates – for standard procedures
  - Suggested cut and paste verbiage for some text fields;
  - Many text boxes replaced by pick lists
- Grant Accountability: Possible solution – experimental groups
- Form Flow: First section to be the project overview; subsequent supporting sections to provide the topical details; last sections reserved for administrative data.
Restarting for Improvement

Initial Steps in the Plan for Improvement

- New concepts in structuring the form (continued).
  - Supporting detail sections grouped topically and logically.
  - No duplication of information.
- More complete instructions strategically placed throughout to encourage intuitive input to decrease and/or eliminate training [Training will still be available]
Restarting for Improvement

Initial Steps in the Plan for Improvement

- Forms Editing, Piloting, Implementing
  - When the initial draft is nearing completion (end of February), a series of demonstrations to various groups with opportunities to comment will be forthcoming.
    - Town Hall type forums
    - Online Webinars
    - Group Demonstrations
  - The form will be piloted to a small group then expanded
  - The IACUC module is to be fully implemented in 2015.
**Restarting for Improvement**

**Future Steps in the Plan for Improvement**

- Additional Element modules for animal ordering, census, billing, etc., will follow when ready.
- In 2016, Elements has a planned upgrade.
  - Conversion to HTML programming
    - No more Silverlight
    - No more issues with MACs
  - Text fields will be able to include pictures, graphs, and spreadsheets
  - Training tracking information to be integrated with Elements.
- More...