Navigating Animal Research Rules & Regulations

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Overview

- Introduction to animal research ethics
- Rules and regulations
- IACUC function
- Available resources
- Discussion

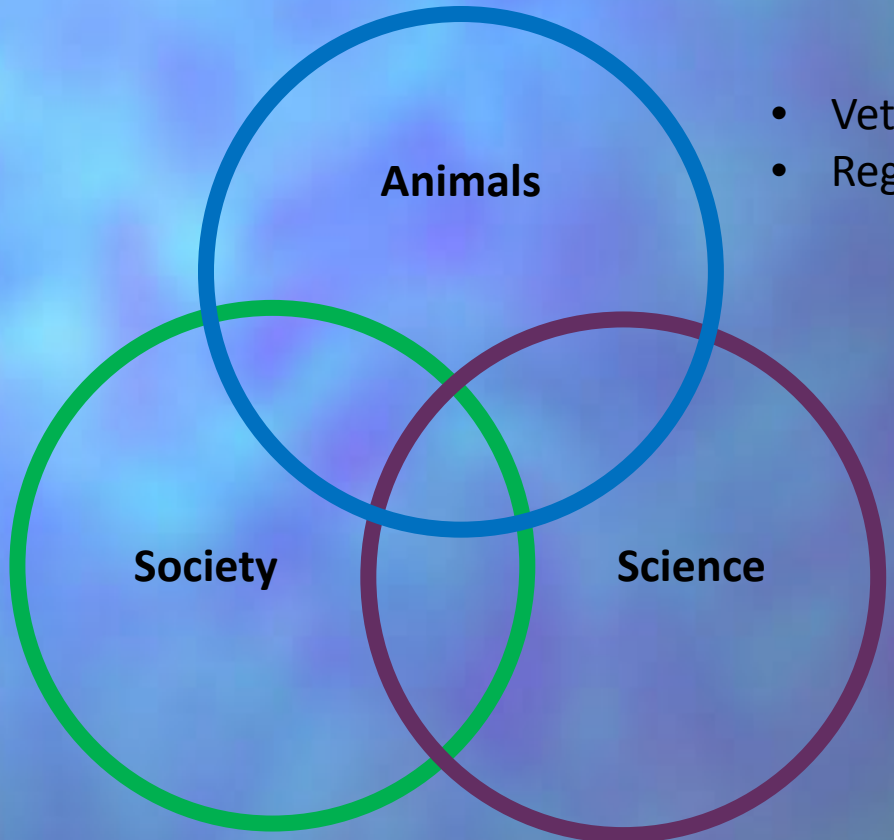
Ethics & Research Compliance…

- Ethical research is better research
- Compliance with regulations makes for better science

Ethics & Research Compliance…

- Ethical behavior and compliance with regulations is important
- Scientists hold a position of trust with the public
  - We use tax dollars for our research
  - We perform clinical trials on people
  - We conduct animal experiments
  - We use biohazards!
  - We teach and mentor students
  - We consult for companies that make drugs and devices that we use in our research

Animals in Research



- Veterinarians
- Regulations

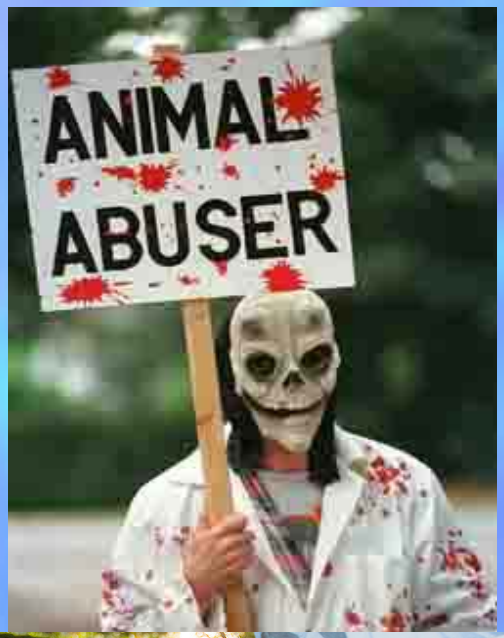
- Scientists
- Public

- Regulations
- Public Opinion/Trust

Ethics & Research Compliance…

- Maintaining the public trust has benefits
  - We keep getting tax dollars because we use them responsibly
  - Training students and early stage scientists with respect
  - Reduces additional regulatory oversight

People care about the humane use of animals



Animal activists will tell you :

- Animal research is **unregulated**
- Animal research is **never humane**
- **Nothing of value** comes from animal research

Increased Regulatory Oversight…

- Does not happen in a vacuum
- Additional regulatory burden is (almost) always a result of loss of the public trust
  - Misuse of grant funding
  - Falsifying data
  - Performing clinical trials without informed consent
  - Accidental release of biohazards
- Regulations are a response to public concerns

Increased Regulatory Oversight…

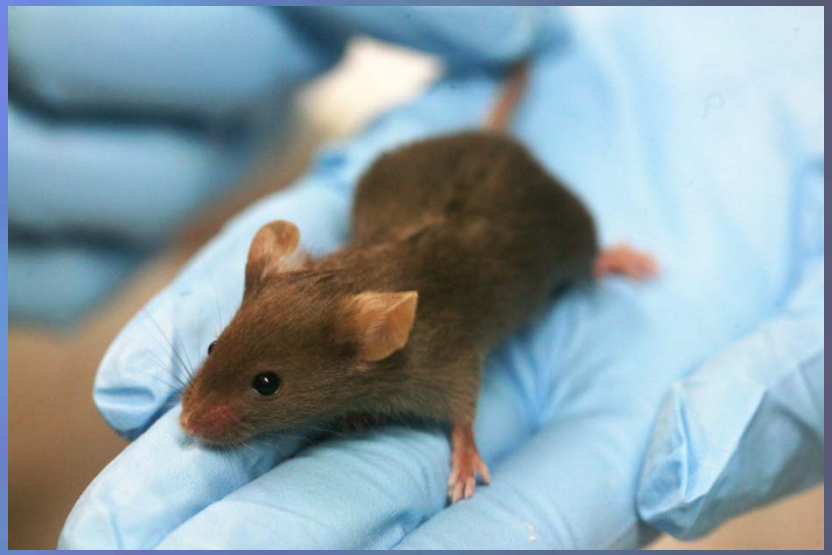
- New York Times article (January, 2015)
  - *"U.S. Research Lab Lets Livestock Suffer in Quest for Profit"*
    - The Meat Animal Research Center develops better methods/breeds to produce meat more efficiently
    - The article claimed that many animals were subjected to inhumane conditions
- In less than 3 weeks, federal lawmakers proposed a bill (the AWARE Act) to amend the Animal Welfare Act

How should we use animal research?

After careful consideration of the scientific value compared to the ethical cost of using animals

AND

With the utmost concern for their welfare



Laboratory Mouse

Education

Caltech, Oxford, Stanford, Harvard, MIT, Princeton, Cambridge, Imperial, Berkeley, Chicago, Yale, ETH Zurich, Columbia, UPenn, John Hopkins, UCL, Cornell, Northwestern, UMichigan, Toronto, Carnegie Mellon, Duke, UWashington, UTexas at Austin, GA Tech, Tokyo, Melbourne, Singapore, UBC, Wisconsin-Madison, Edinburgh, McGill, Hong Kong, Santa Barbara, Karolinska Institute, UMinnesota, Manchester ... and just about every other major university, medical school & research institution in the world.

Nobel Prizes

1905 - Transmission and treatment of TB
1906 - Structure of Nervous System
1907 - Role of protozoa in disease
1908 - Immunity to infectious diseases
1928 - Investigations on typhus
1929 - Importance of dietary vitamins
1939 - Discovery of antibacterial agent, Prontosil
1945 - Discovery of penicillin
1951 - Yellow fever vaccine
1952 - Discovery of streptomycin
1954 - Culture of the polio virus
1960 - Understanding of immunity
1970 - Understanding of neurotransmitters
1974 - Structural & functional organisation of cells
1975 - Tumour-viruses and genetics of cells
1977 - Hypothalamic hormones
1984 - Techniques of monoclonal antibody formation
1986 - Nerve growth factor and epidermal growth factor
1990 - Organ transplantation techniques
1992 - Regulatory mechanisms in cells
1996 - Immune-system detection of virus-infected cells
1997 - Discovery and characterisations of prions
1999 - Discovery of signal peptides
2000 - Signal transduction in the nervous system
2004 - Odour receptors and organisation of olfactory systems
2008 - Role of HPV and HIV in causing disease
2010 - Development of in vitro fertilization
2011 - Discoveries around innate and adaptive immunity
2012 - Reprogramming mature cells to pluripotent ones

CV of a Lifesaver

Overview

- Involved in around 75% of research
- Short life-span and fast reproductive rate means mice are suitable for studying disease across whole life cycle
- 98% of genes have comparable genes in humans
- Similar reproductive and nervous systems and suffer many of the same diseases as humans including cancer diabetes and anxiety
- Can be genetically modified to include human genes in enhance biological relevance
- Can act as an avatar for a human cancer to allow drug therapies to be trialled safely

Research Areas

Alzheimer's disease, anaesthetics, AIDS & HIV, anticoagulants, antidepressants, asthma, blindness, bone and joint disease, brain injury, breast cancer, cardiac arrest, cystic fibrosis, deafness/hearing loss, Down's syndrome, drugs for high blood pressure, transplant rejection, Hepatitis B, C & E, Huntington's disease, influenza, leukaemia, malaria, motor neurone disease, multiple sclerosis, muscular dystrophy, Parkinson's disease, prostate cancer, schistomiasis, spinal cord injury, stroke, testicular cancer, tuberculosis,

Contact

www.understandinganimalresearch.org.uk
www.animalresearch.info
www.amprogress.org
www.speakingofresearch.com


It's the animals you don't see
that really helped her recover.
Foundation for Biomedical Research

Animal Welfare Act and Regs

- Prevent theft of dogs and cats in 1966
- Established 8 areas of minimum standards
  - Housing, feeding, watering, sanitation, shelter, separation of species, ventilation, adequate veterinary care
- 1985 Amendment
  - Established the 3 member IACUC
  - Environmental enrichment for non-human primates
  - Exercise requirements for dogs
- Animal Care Policies (20)

“Animal” Definition

Applies to any live or dead warm-blooded animal which is being used, or is intended for used for **research, teaching, testing, experimentation,** or exhibition purposes, or as a pet.

The AWA Exclusions

- The AWA covers all warm-blooded, vertebrate animals, except:
  - Farm animals used for agriculture
    - Cattle, pigs, sheep, goats, llamas, horses
    - Used for food or fiber, for production efficiency or as work animals
    - Fall under other USDA regulations
  - Cold-blooded vertebrates (reptiles, fish)
  - Birds
  - **Mice and rats bred for use in research**
    - Push back by NIH (1985)
    - Led to the development of the PHS Policy on the Humane Care and Use of Lab Animals

The AWA Regulates…

- Transport
- A comfortable living environment
- Basic veterinary care
- **Research procedures**

USDA Inspections

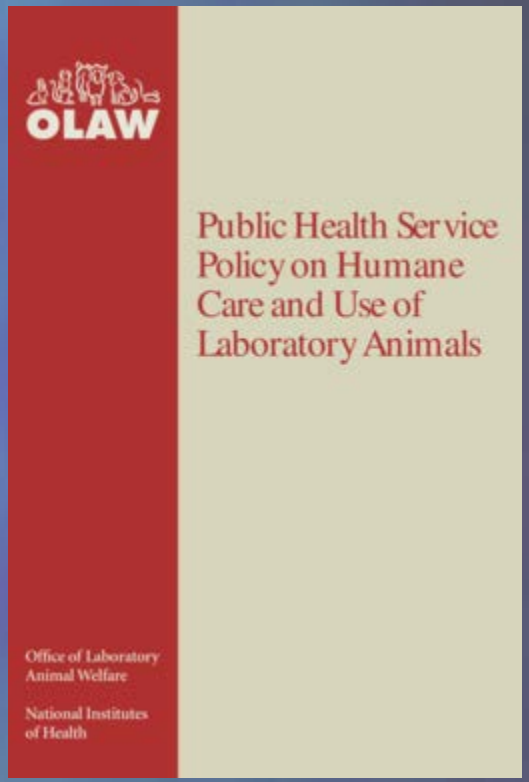
- Annual, unannounced inspections
- Conducted by USDA veterinarians
- Inspection of:
  - Housing areas
  - Labs were animals are used
  - Records (purchase; medical; disposition)
- Non-compliance with the AWA is published on the **USDA website**
- **Fines** are levied for serious violations

Who regulates the rest?

- Animals used in PHS-funded research are covered by the Office for Laboratory Animal Welfare (OLAW)
  - CDC, FDA
  - NCI, NIH
- Other government agencies also use these guidelines

Public Health Policy

- Health Research Extension Act
- All institutions receiving funds from NIH
- Requires compliance with the AWA/AWRs and more
- Self-governance
  - Prompt reporting of non-compliance
  - 5 member IACUC
  - Annual Assurance Statement

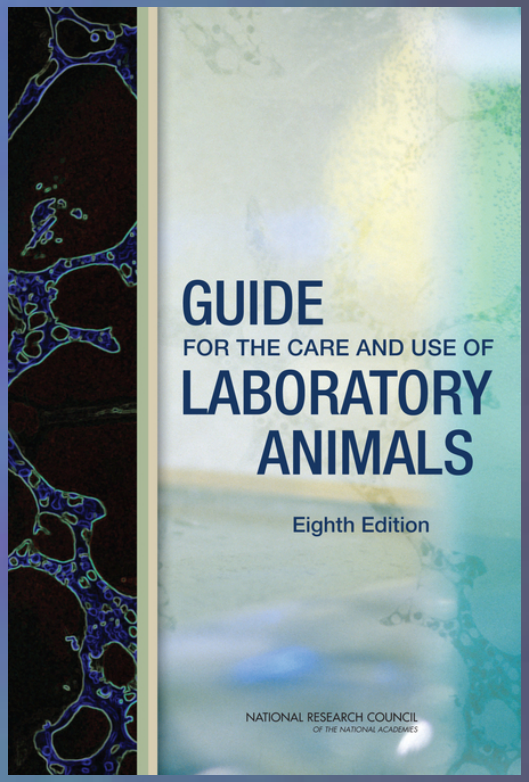


PHS Policy

Under the PHS Policy farm animals, birds, **laboratory rodents**, fish, amphibians, and reptiles, as well as all other vertebrates, are covered, as long as the study is funded by PHS.

OLAW Oversight

- OLAW uses a mechanism of self-policing and self-reporting
  - The institution identifies non-compliance and reports to OLAW with corrective actions
- Serious and uncorrected violations could result in the **loss of PHS funding** to individuals, or to the institution as a whole!



What Else?

- Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC)
  - AAALAC is a voluntary organization that makes recommendations based on results of site visits
  - Standards are continually updated to reflect current knowledge in laboratory animal science
  - Unlike the AWA or PHS Policy, AAALAC reviews the quality of animal care for all animals used in research

Animal Research Oversight

- The Institutional Animal Care and Use Committee (IACUC)
- The mechanism by which animal welfare regulations are administered
- Required and defined by the AWA and PHS Policy
- Committee composition
  - Veterinarian
  - Scientist
  - Non-scientist
  - Non-affiliated (community) member

Role of the IACUC

- Assure humane animal care
- Emphasize the 3R's (more to come…)
- Facilitate research
- Assure **public** of quality of animal care
- Justify the use of animals in research

IACUC Responsibilities

- Review and approve animal research and teaching
  - IACUC protocols and amendments
- Inspect animal housing and labs where research is performed
  - Every six months
- Oversee the Animal Care and Use Program
  - Make recommendations for improvements

IACUC Review of Research

- ~10 times as many regulations to conduct animal research compared to human research
  - People can get their own food and water…
  - As animals can't consent, the IACUC acts as the voice of the animal

IACUC Protocol Review

- Adherence is maintained to The Guide, AWRs
- Procedures are scientifically relevant, not duplicative.
- Appropriate species and numbers
- Minimize pain, discomfort, distress.
- Must alleviate more than momentary pain, discomfort, distress
  - Proper anesthesia, analgesia, sedatives
  - Consultation with veterinarian(s)
  - No paralytics without anesthesia
  - Unless scientifically justified
- Animals must be euthanized if unable to control pain, discomfort, or distress at the end of the procedure (or possibly before)
- Appropriate housing, food, husbandry for species
  - Directed by the Attending Veterinarian
- Veterinary care required
- Lab personnel trained
- Complete description of procedures
- Complete description of any medication or experimental agents

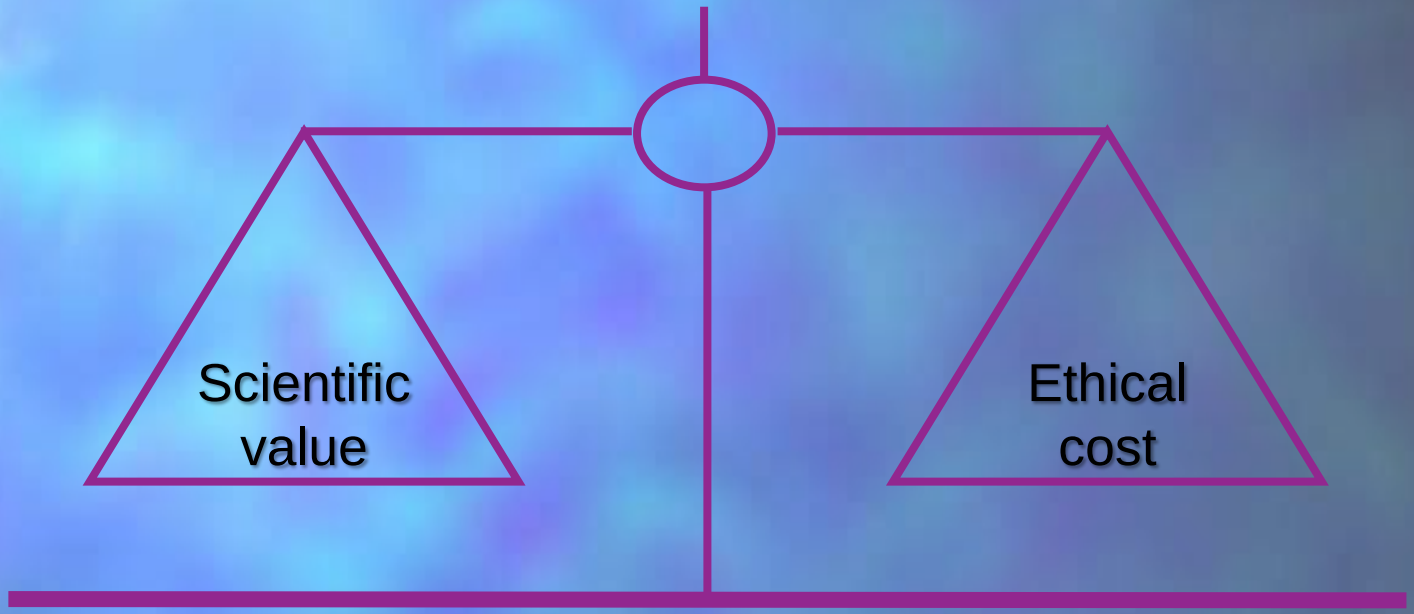
Scientific Merit

- The most important question the IACUC asks:
  - Does the value of the scientific data obtained justify the pain and distress of the animals?

“Procedures involving animals should be designed and performed with due consideration given to their relevance to human or animal health, the advancement of knowledge, or the good of society.”

US Government Principles # II

The Ethical Balance



- To humans
- To animals
- To science
- To society

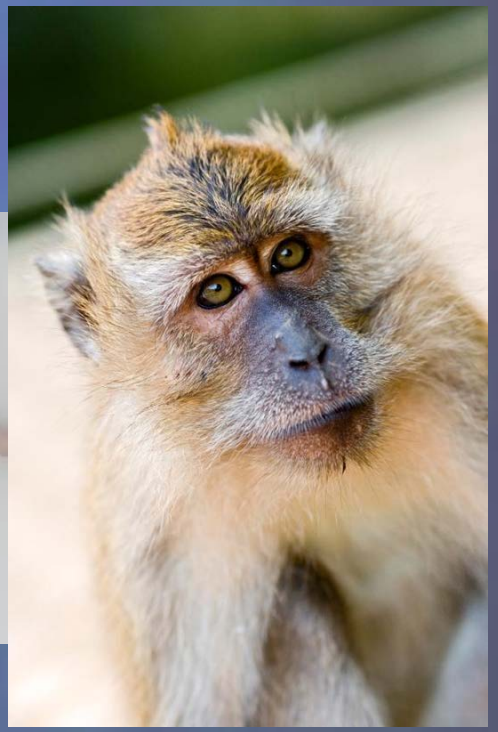
- Pain
- Distress
- Morbidity
- Mortality

The 3 R's (Russell and Birch, 1959)

- The 3 R's is one way that IACUCs evaluate ethical balance
  - Replace – can we replace the use of animals with a lower species or a non-animal model?
    - Society considers dog > mouse > fish > worm
    - Manikins used for medical training
    - Testing toxicity in a cell line
  - Reduce – can we reduce the number of animals, or procedures per animal, and still achieve statistically significant data?
  - Refine – can we refine the procedures to minimize or eliminate pain and distress?

Application of the Principles of Replacement, Reduction and Refinement (3 R's)

- How much animal pain, discomfort, distress, morbidity, and mortality is associated with the research (ethical cost)?
- How can ethical cost be minimized?



The Most Important "R" – Refine?

- Review current scientific literature to identify modified techniques that reduce pain or distress
- Use appropriate sedation, analgesia and/or anesthesia for painful or distressful procedures
- Limit the number of procedures experienced by any individual animal
- Ensure adequate post-procedural care
- Identify appropriate scientific and humane endpoints
- Remove animals from the study based on humane endpoints to minimize pain and suffering

Pain and Distress

Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in animals.

USGP IV; USDA Policy 11, 4/17/97

Back to ethics and research compliance…

- Research compliance is the contract between scientists and society
- Ethical standards evolve
  - From the Tuskeegee syphilis experiment (1932-1972) to personhood for primates (2014-2015)
- The fourth “R” - RESPONSIBILITY

NASA Principles for the Ethical Care and Use of Animals

- The use of animals in research involves responsibility - not only for the stewardship of the animals but to the scientific community and society as well.

1. Respect for life
2. Societal benefit
3. Non-maleficence

Use Your Resources

- IACUC office
  - Policies, procedures, guidelines
- Lab animal veterinarians
  - Experts in comparative biomedicine
  - Experienced IACUC members
- Other scientists

Web Resources

- http://grants.nih.gov/grants/olaw/olaw.htm
- https://awic.nal.usda.gov/government-and-professional-resources/federal-laws/animal-welfare-act
- http://www.primr.org/

Questions?