Navigating through the Regulatory Milieu in an Animal Care & Use Program

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Oversight and Regulations

- National Institutes of Health
- AAALAC International
- U.S. Food and Drug Administration
- USDA
A community that cannot govern itself... the government will govern it
History

- 4th century BC Greeks - Earliest references to animal testing
- Aristotle - Among 1st to perform experiments on living animals
- 1655 Edmund O’Meara – *The miserable torture of vivisection places the body in an unnatural state*
- O’Meara - Argued that animal physiology could be affected by pain during vivisection, rendering results unreliable
History

• 1822 - First animal protection law enacted in British parliament
• 1866 - American Society for the Prevention of Cruelty to Animals (ASPCA)
• 1959 - 3 R’s published
• 1963 - Publication of The Guide for the Care and Use of Laboratory Animals
• 1965 - Formation of Association for the Assessment and Accreditation of Laboratory Animal Care (AAALAC)
History

- 1966 - U.S. Congress passes Animal Welfare Act (AWA)
- 1979 - Research institutions that receive federal money required to have an IACUC to oversee the use of vertebrates
- 1985 - U.S. Congress amends AWA to require that researchers minimize animal pain and distress through use of anesthesia, analgesics, and humane euthanasia
Most Relevant Laws, Regulations & Guidelines

- U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training
- Animal Welfare Act and USDA Animal Welfare Regs
- PHS Policy on Humane Care and Use of Lab Animals
- Guide for the Care and Use of Laboratory Animals (National Academy of Sciences)
- Good Laboratory Practice Standards (FDA)
AAALAC

Association for the Assessment and Accreditation of Laboratory Animal Care, International

- UTD’s next step
- Voluntary accreditation (has no regulatory authority)
- Provides an independent evaluation of procedures and policies related to animal care & use
Institutional Official (IO)

- Highest ranking official in institution or person appointed by highest ranking official
- Responsible for the overall conduct of the Animal Care & Use Program
- Appoints IACUC members
- Reviews semiannual reports of IACUC animal facility and programmatic reviews
- Can disapprove a protocol approved by IACUC
  Cannot approve a protocol disapproved by IACUC
“Bibles” of IACUC

- USDA’s ‘Animal Welfare Act and Animal Welfare Regulations’
- OLAW’s “PHS Policy on Humane Care & Use of Laboratory Animals”
- ‘Guide’
- AVMA Guidelines for the Euthanasia of Animals - 2013 Ed
UTD’s Assurance Statement

- Required ‘contract’ with NIH of all institutions receiving NIH money
- Commits UTD to adhere to all regulations (whether AAALAC accredited or not)
- Describes animal care & use program details
Attending Veterinarian (AV)

- Authority & responsibility for activities involving animals at the institution
- Oversees veterinary care
- Provides consultations on animal care & use to include the planning stages of proposed animal activities that involve more than momentary pain or distress
IACUC’s Authority

- Oversees all aspects of animal care and use
- Semiannual program review & facility inspection
- Investigates reported animal welfare concerns
- Reviews protocols
- Develops policies
- Can suspend previously approved animal work
Investigator Responsibilities

And the Protocol Application

Important Features
3 R’s

Protocol review must evaluate how adequate PI addressed the 3 R’s:

– Reduction of animals #’s
– Refinement to minimize pain or distress
– Replacement animals for lower animals, tissue culture or non-living models
Literature Search

- Addresses 3 R’s
- Avoid unnecessary duplication
- Emphasis on minimization of animal suffering
Training & Experience

- Good training results in reduced stress
- Ethics
- Unskilled researchers produce bad science
- Results in improved data
Animal Numbers

- Statistics should drive most numbers
- Too many animals = waste
- Too few animals = waste
Pain Management

• Strong reason for existence of IACUCs and regulations
• AV input
• Often dismissed ‘in the name of science’
• What’s worse?
  – Effects of anesthetics & analgesics on research data or
  – Effects of pain on research data? See next 2 slides
Effects of Pain

- Activation the sympathetic nervous system
- Increases cardiac output
- Increases systemic vascular resistance
- Increases blood pressure
- Increases oxygen demand
- Vasoconstriction of coronary arteries
- Spleen ischemia
- Adverse renal effects
- Increases aldosterone output
- Increases sodium and water retention
- Release of endogenous glucocorticoids, which are immunosuppressive = delayed healing
Effects of Pain

- Higher rate of metastasis
- Self mutilation
- Stop grooming
- Anorexia
- Weight loss
- Catabolic state
- Increased clotting
- Increased blood viscosity
- Increased platelet aggregation
- Altered mental status (anxiety)
- Interference with normal activity
Euthanasia

• AVMA Guidelines for the Euthanasia of Animals – 2013 Edition
• Requires specific training/proficiency verification
User Protection

- Occupational health program offered to all at risk personnel
- Address and mediate all hazards in protocol
Description of Procedures

- All injections, blood collections & manipulations must be detailed
- Only then can IACUC evaluate true animal welfare
- Alternatives must be stated to painful & distressful procedures
Surgery

• Details very important
• Aseptic technique
• Surgical procedure, closure, sutures
• Training/experience
• Drugs used
• Pain management
• Post op care
Humane Endpoints

• Should describe
  – Precise definition of expected endpoints
    • Stating “when animals appear ill, they will be euthanized” is not good enough
  – Frequency of observations appropriate for the expected clinical signs
  – Training of personnel to identify when the pertinent endpoints are reached
  – Response/action when endpoints are reached
Physiological Stabilization of Newly Arrived Animals

- Acclimation to new environment before any experiments
- Gives time to get over the stress of shipping & new environment
- Acclimated animals = physiologically stable = diminished research variables
Consequences of Noncompliance

- Protocol suspension
- Loss of funding
- Fines to university
- Loss of reputation