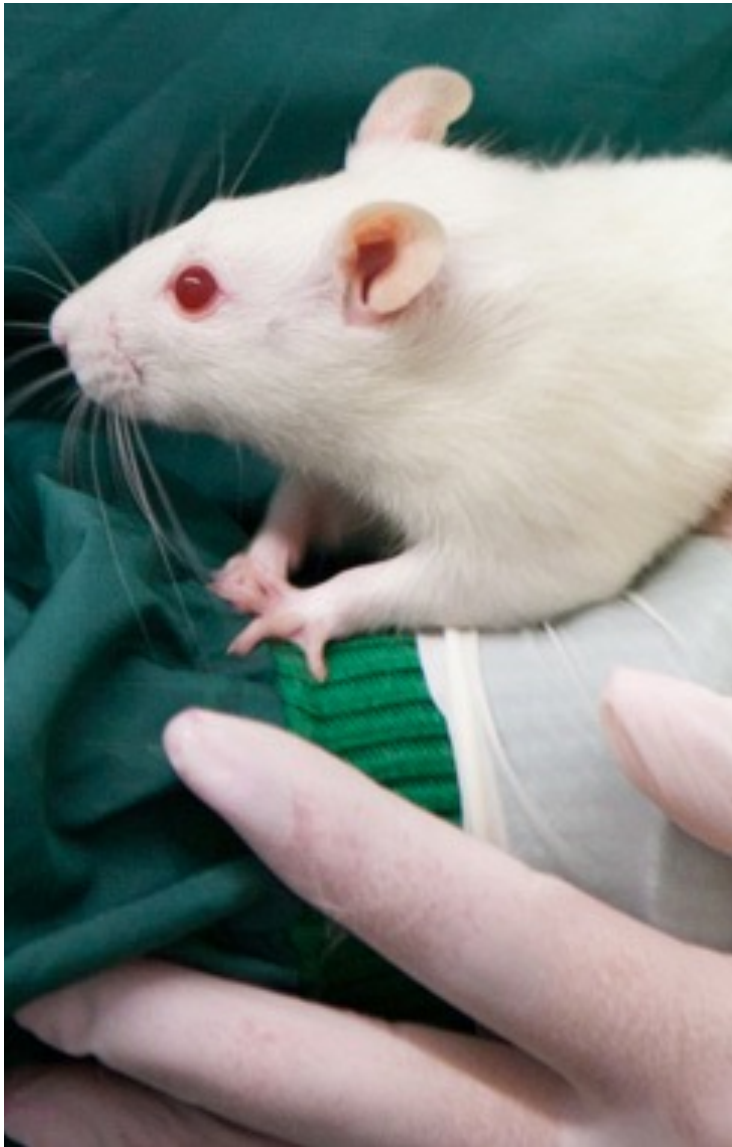




# INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE - IACUC

## Initial Animal User Training

Ramaswamy Chidambaram, DVM, PhD  
Attending Veterinarian



# Overview

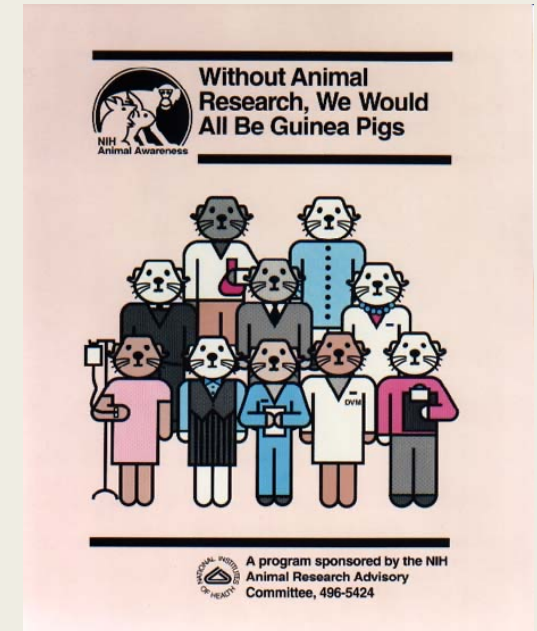
- Animal Use Research
  - *Historical Background/Progress*
- Animal Welfare Act (AWA)
- Public Health Service (PHS) Policy
- Institutional Animal Care & Use Committee (IACUC)
  - *Composition, Policies and Practices*
- Animal Care & Use
  - *Training, Surgery & Euthanasia*

# Acronyms

- AWA – Animal Welfare Act
- AWAr – Animal Welfare Regulations
- AAALACi - Association for Assessment and Accreditation of laboratory Animal Care International
- IO – Institutional Official
- IACUC - Institutional Animal Care and Use Committee
- NIH – National Institute of Health
- OLAW – Office of Laboratory Animal Welfare
- PPE – Personal Protective Equipment
- PHS – Public Health Service
- USDA – United States Department of Agriculture

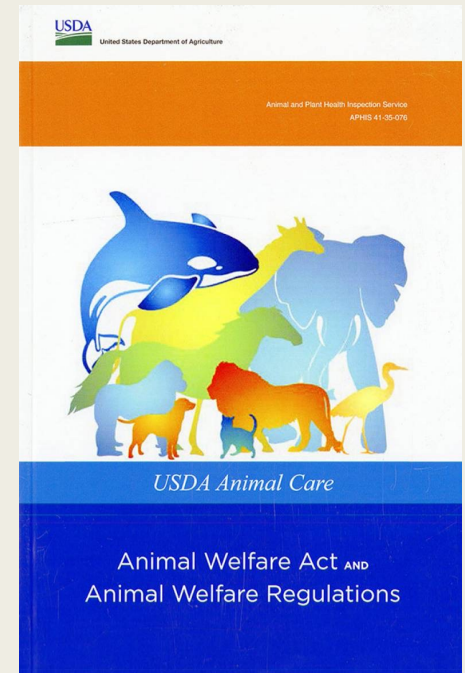
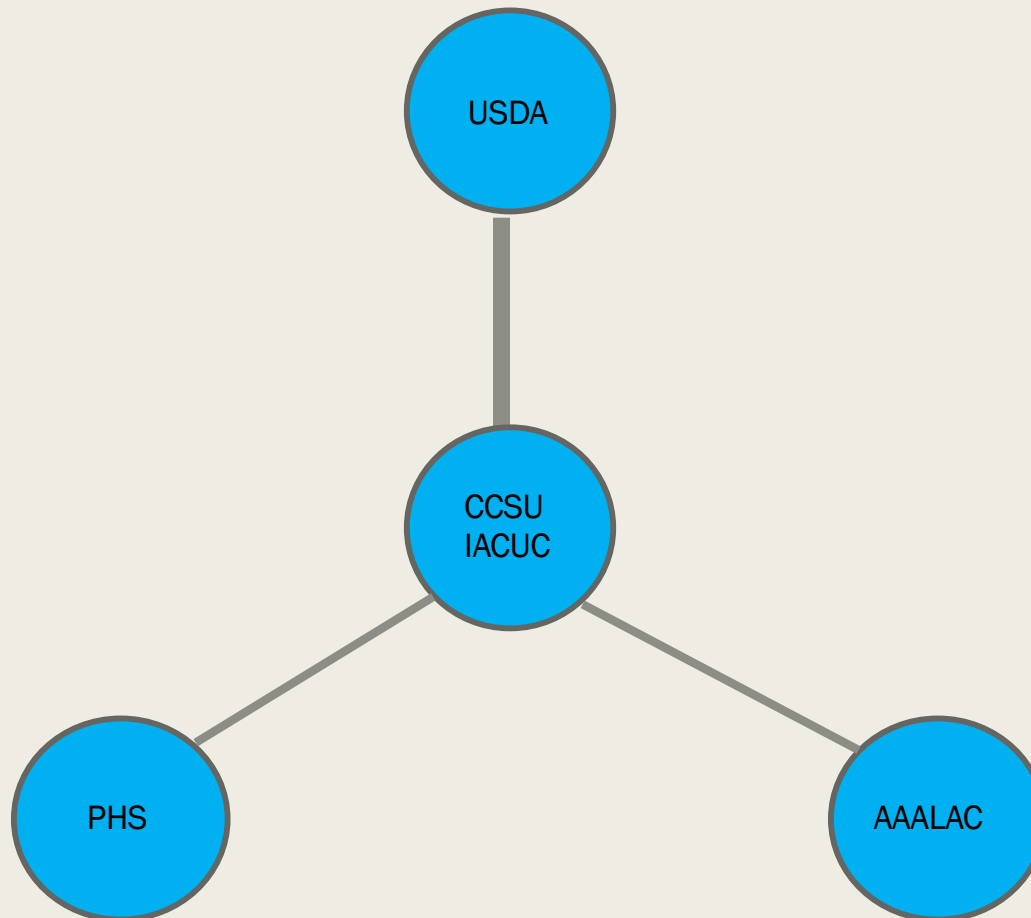
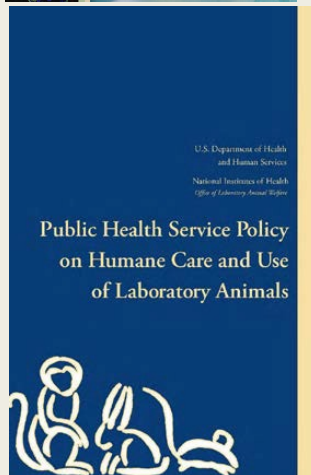
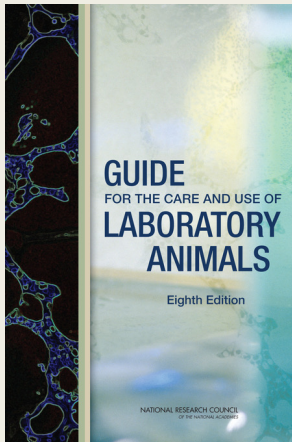
# Animal Use in Biomedical Research

- The knowledge gained with animal experimentation benefits and justifies the animal experimentation, but it must be done following the ethical principles/humanely
- **Animal welfare** “a human responsibility that encompasses all aspects of animal well-being, including proper housing, management, nutrition, disease prevention and treatment, responsible care, humane handling, and, when necessary, humane euthanasia” (AVMA)



# Animal Welfare Regulations

## How we got here



# Historical Background

## In 19<sup>th</sup> century

- *Port Royal Abbey in France pioneered vivisection*
  - Descartes depicted animals as organic machines lacking sentience
- British Society for Prevention of Cruelty to Animals (1876)
  - Cruelty to Animal Act
- Universities Federation for Animal Care (UFAW) in the UK (1954)
- Russell and Birch (1959) – Principles of Humane Experimentation technique

## Regulations in US (post-WW-II)

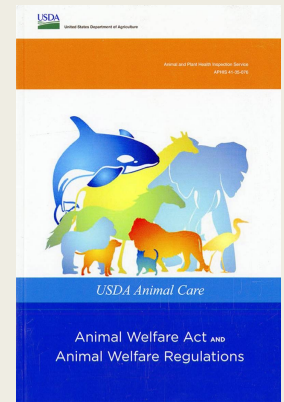
- Industrial Agriculture replacing husbandry-based agriculture & Public funding for research
- Societal concerns regarding animal abuse and neglect – ‘Pound Seizure’ - Resnik Bill (1965)
- Life Magazine exposed concentration camps for animals in a photo essay that struck at the heart of American’s love for dogs!!!



Pepper

# Animal Welfare Act – A Timeline

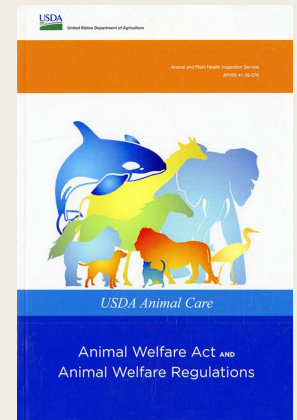
- 1966: Congress passes the Laboratory Animal Welfare Act to regulate the care and handling of dogs, cats, nonhuman primates, guinea pigs, hamsters, and rabbits at licensed research institutions and animal dealer facilities.
- Implementing regulations are published in the **Code of Federal Regulations (CFR)**, Title 9, Chapter 1, Subchapter A, Parts 1, 2, and 3, and are administered by the U.S. Department of Agriculture (USDA)
- 1970: The act was, with certain exceptions, expanded to cover all warm-blooded animals in research as well as to cover animals in circuses, zoos, roadside shows, and commercial breeding operations.
- 1976: Congress approved amendments to the act to cover animals in transportation as well as those forced to fight.
- 1985: Congress passed amendments requiring the use of pain killers and presurgical and postsurgical care; animal care training for personnel who work with animals; and euthanasia of an animal upon completion of an experiment. The amendments, also required exercise for dogs and a physical environment to promote the psychological well-being of nonhuman primates.





# Animal Welfare Act

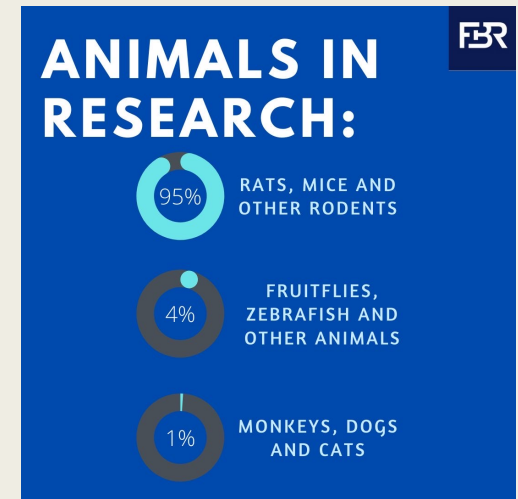
- Animals – all warm-blooded vertebrates **except** lab mice (*Mus*), lab rats (*Rattus*), birds bred-for-research, and farm animals and horses that are not used in biomedical research
  - *With >90% animals used in research are rodents, its not a comprehensive act aimed at animal welfare.*
- Animal Facility
  - *Any building, room or area used for confinement, transport or experiments including surgery*
  - *If animals are kept >24hrs in a lab, then it is considered as an animal facility or satellite animal facility*
- Each Institutions should have an
  - **IACUC**
  - *Compliance with AWA*
- Applies to all US institutions using animals in research, testing, and testing





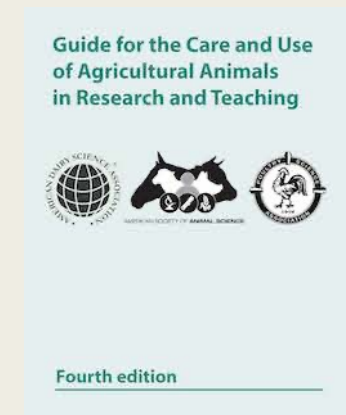
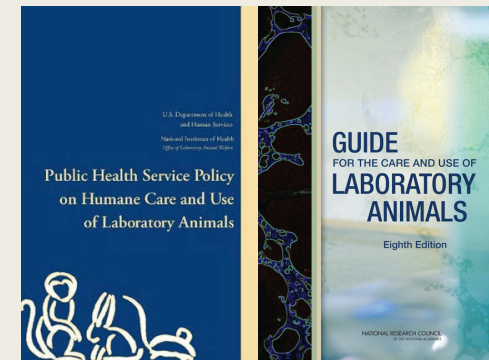
# AWAr - Enforcement

- Enforced by the Animal and Plant Health Service (APHIS) agency of the United States Department of Agriculture (USDA)
  - *Unannounced annual on-site inspections*
    - Inspects all facilities, relevant records and documentation
  - *Based on findings, may impose series of disciplinary actions from the noncompliance*
    - It may vary from citations, warnings, fine, court order and loss of registration



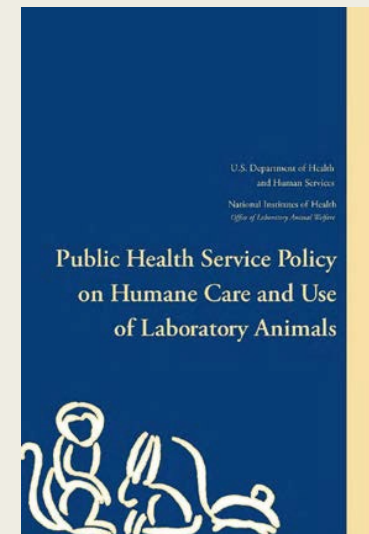
# Office of Animal Welfare - PHS

- **OLAW provides guidance and interpretation of PHS policy**
  - supports educational programs and monitors compliance
  - ensure the humane care and use of animals in PHS-supported research, testing, and training, thereby contributing to the quality of PHS-supported activities.
- **PHS policy on Humane Care and Use of Laboratory Animals**
  - Incorporates US government principles (IX) for the Utilization and Care of Vertebrate animals used in Testing, Research, and Training
  - **The Guide for the Care and Use of laboratory Animals**



# Public Health Service Policy

- Provides Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training promulgated in 1985 by the Interagency Research Animal Committee and adopted by U.S. Government agencies (NIH/OLAW)
- Applies to all PHS conducted or supported research activities
- PHS policy (2015 Edition)
  - Animals – Any live vertebrate
  - IACUC Composition – no more than 3 member from same dept
    - Must include
      - Veterinarian – certification, training, experience
      - Practicing Scientist – in animal research
      - Public member – community interests



# Animal Welfare Assurance

- CCSU– Assurance #D16-00566 (A4033-01)
- Assurance describes three major components of the animal program
  - Animal Care and Use program – lines of authority/Veterinary Coverage/IACUC memberships/Occupational Health Program and Animal facility square footage
  - IACUC - Membership roster and qualifications

Assurance valid up to 5 yrs.

U.S. Department of Health  
and Human Services  
National Institutes of Health  
*Office of Laboratory Animal Welfare*

Public Health Service Policy  
on Humane Care and Use  
of Laboratory Animals



# AAALAC International

- Founded in 1995 as a private, non-profit organization
- Voluntary – It demonstrates institution's commitment to the highest standard
- Promotes the humane treatment of animals in science
- Science based standards, regulations, guidelines, and the peer review process
- 3-year accreditation
- Use the Guide for the care and use of laboratory animals (The Guide)

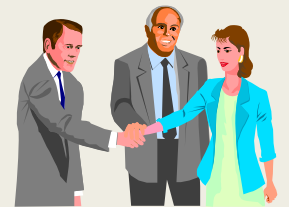


# CCSU - Institutional Animal Care and Use Committee

- IACUC committee appointed by the Institutional Official, currently has 9 members
- Dr. Betsy Dobbs-McAuliffe – IACUC Chair
  - [dobbsmcaulibel@ccsu.edu](mailto:dobbsmcaulibel@ccsu.edu)
- Dr. Ramaswamy Chidambaram – Attending Veterinarian
  - [Ramaswamy@uchc.edu](mailto:Ramaswamy@uchc.edu)
  - 860-805-1139

# CCSU-IACUC – Role and Responsibilities

- Reviews all aspects of the animal care and use program at least once every six months
- Inspect housing and study areas every 6 months; and submit reports of IACUC evaluations and submit to Institutional official (IO), with major and minor deficiencies and plan for correction
- Reviews concern involving care and use of animals at the institution
- Make recommendations to IO regarding the any aspect of animal care program
- Ensures training of animal care staff and researchers
- Be authorized to suspend any activity of animals





# Field Studies

‘Field Study means any study done on free-living wild animals in their natural habitat, that doesn’t involve any invasive procedures, and which doesn’t harm or materially alter the behavior of the animals under study’



# Using Wildlife in Research

- CCSU-IACUC requires that a Animal Use Protocol be submitted for any study conducted on free-living wild animals in their natural habitat that involves procedures that don't harm (observational) or harm or materially alter the behavior of the animals under study (i.e., trapping/capture, physical/chemical restraint, and/or invasive procedures causing stress, including removal from nest and habitat for short durations).
  - Depending on the field research site, specific local, state, national, or international wildlife collection or trapping permits would be required
  - ***Fish and Wildlife Services***
  - ***Endangered species act, Lacey Act, Marine Mammal Protection Act, Migratory Bird Treaty Act, Wild Bird Conservation Act, etc..***



Courtesy: US National Park Service

# Animal Care and Use protocol

- All research and teaching activities involving vertebrate animals MUST be under an active and approved IACUC protocol
- Animal Use protocol must address the following
  - Rationale and Purpose of the species used
  - Justification of species and numbers of animals
  - Adequate and appropriate training and experience of the personnel
  - Housing and care of animals
  - Procedures to minimize pain and distress
  - Method of disposition of animals at the end of study

*Should follow US Government Principle IV – Unless the contrary is established, investigators should consider the procedures that cause pain or distress in human beings may cause pain and distress in other animals (Page 117)*

# Alternatives to Painful Procedures

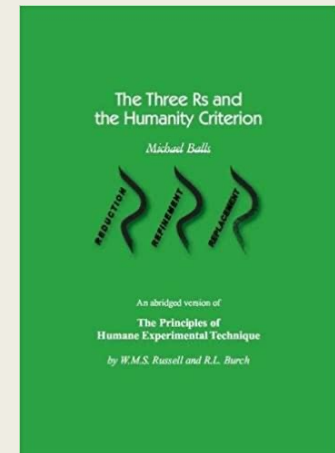
- WMS Russell and RL Burch's - *Principles of Humane Experimental Technique*, 1959
  - *Replacement, Refinement and Reduction*

## Reduction

- *Using fewer animals to obtain the same amount or more scientific information*
- *Improved statistical design*
- *Sharing results*

## Refinement

- *Altering experimental procedures to minimize pain and discomfort*
  - Training/proper handling/Use of restraint device
  - Pain management
  - Imaging
  - Improved husbandry



# Principle of 3R's

## ■ Replacement

- Cell cultures in labs? Collaborate
  - Substituting conscious living “higher” animals with less sentient materials
  - Transgenic rodents than using dogs, mice with zebrafish or drosophila or with invertebrates
  - Computer models?
- 
- Overall, it reduces the number of animal being used, ethically used and alternates are considered and assures results from research are performed on highest ethical standards.
    - *USDA Animal Care Policies*
      - #11 Painful and Distressful Procedures (examples)
      - #12 Consideration of Alternatives to Painful/Distressful Procedures



# Classification of Pain categories

- **USDA Category B – CCSU Category A**
  - *Animals being bred, held or conditioned for use in teaching, research or surgery*
  - *E.g., breeding colonies*
- **USDA Category C – CCSU Category B**
  - *Procedures that produces no or momentary pain and distress*
  - *E.g., needle stick for blood draw, euthanasia, manual restraint, radiography, etc.*
- **USDA Category D – CCSU Category C**
  - *Procedures upon experiments/surgery/test involves pain and distress and for which appropriate anesthetic, analgesic or tranquilizing drugs are used*
  - *E.g., Biopsy, Surgeries, periorbital blood collection, drugs which cause pain and distress when given (adjuvants) etc.*
- **USDA Category E – CCSU Category D**
  - *procedures producing pain or distress in these animals and the justification for not using anesthetic, analgesic or tranquilizing drugs must*
  - *Death as end point, certain stroke models, toxicity studies etc.*

# Use of Drugs for Animal Research



- USDA Animal Care Policy #3 — Veterinary Care
  - Prohibits use of expired medical materials
  - Prohibits use of non-pharmaceutical-grade chemical compounds
    - Exceptions – Scientific justifications should be provided in the animal protocol
  - Requires good record keeping
- Ensure that drugs are provided to animals as described in the protocol
- If other drugs are to be given for animal care, it should be given under the direction of veterinarian
- Controlled substances
  - *Each secure storage site requires CT registration*
  - *Should ensure safe and effective mechanism for identifying and disposing controlled substance in place*
    - <https://www.deaiversion.usdoj.gov/schedules/>
    - <https://portal.ct.gov/DCP/Drug-Control-Division/Drug-Control/Laboratory-With-Controlled-Substances>



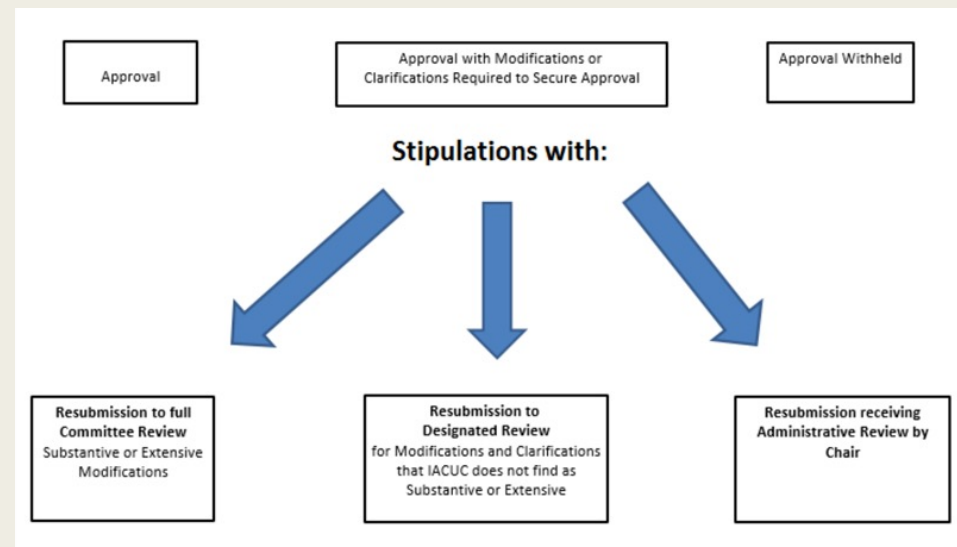


# IACUC Protocol Applications

- IACUC meets as needed
- Veterinarian pre-reviews all applicants
- IACUC must review all applications and must approve prior to start of research
- New protocols are discussed by full committee review (FCR)
- Designated Member Review (DMR)
  - *Renewal Protocols (3-yr renewal)*
  - *Protocols that study animals in natural settings*
  - *Breeding colony protocols*
  - *Animal tissue only protocols*
  - *Protocols involving pain category*

# IACUC review type/Outcome

- Approved
- Modifications required
- Deferred
  - *Resubmission after substantial review*



Reference: <https://www.uvm.edu/rpo/iacuc-policies-and-procedures>

# IACUC Modification Reviews

## ■ Amendments

- Change in personnel, funding, anesthesia/analgesia
- Reviewed as DMR
- Addition of a strain of the same species
- Change in species requires new application and full review

## ■ Procedural change

- Minor procedural change only, addition of animals and change of PI
- Change in funding

# Reporting Misconduct

- The IACUC is mandated to evaluate any concerns regarding animal care and use at the Institution
- Any concerns can be reported by any staff/employees of the institution, individuals in the community or members of IACUC to the committee
- Reports can be made to IACUC chairperson/or any members of IACUC including the veterinarian or the IO
- Concerns may be reported **anonymously** (locked drop box in animal facilities)

# Animal Care & Use



# Husbandry

- Factors that affect good science or animal care include
  - *Environment* -  
*Humidity/temp/airflow*
  - *Chemical - Biohazards*
  - *Microbial - Health status*
- Static vs microisolator or Individually ventilated cages
- Food & water
  - *Autoclaved, irradiated diets*
- Bedding
- Personal Protective Equipment (PPE)



**Good Animal Care  
and Good Science  
Go Hand in Hand**





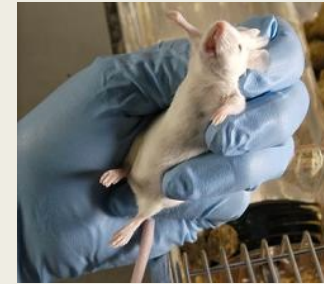
# Training

- PHS policy, USDA-AWA and the Guide require the Institution to address several topics (some specific) as part of training program for anyone who works with animals
- All animal related activities/methods should be described in the IACUC protocol
- Each lab personnel or students working in a project should know the protocol
- The Principal investigator is responsible for assuring animal training for all lab personnel

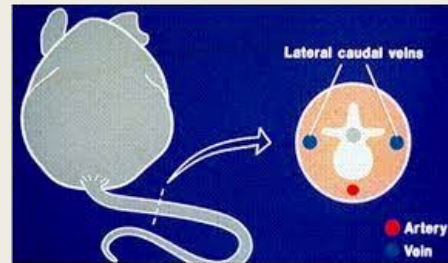
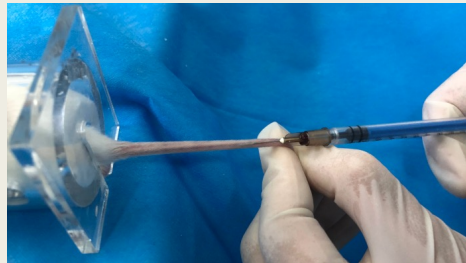


# Rodent – Bio-methodology

## Handling & Restraint



## Bleeding



# Rodent Surgery

- Laws and regulations dictate appropriate techniques and animal care
  - *Anesthesia/Surgery*
- Surgical variables affect research and animal welfare
- You have an obligation – approved animal use protocol with IACUC



**PHS Policy Governmental principle VIII** states investigators and other personnel should be properly qualified and experienced in conducting procedures on living animals

The **Guide** (page 116) – states the IACUC together with AV, is responsible for determining that personnel performing surgical procedures are appropriately qualified, and trained in the procedures

# Rodent Surgery

- Challenging
  - Smaller subjects
  - Repetitive
  - Single personnel
    - Surgeon, Anesthetist, Nurse
- Major and Minor Surgery
  - Entering animal cavity or not!
- Surgical Area
  - Dedicated Vs Non-dedicated
    - Easily sanitizable
    - Less traffic



# Rodent Surgery

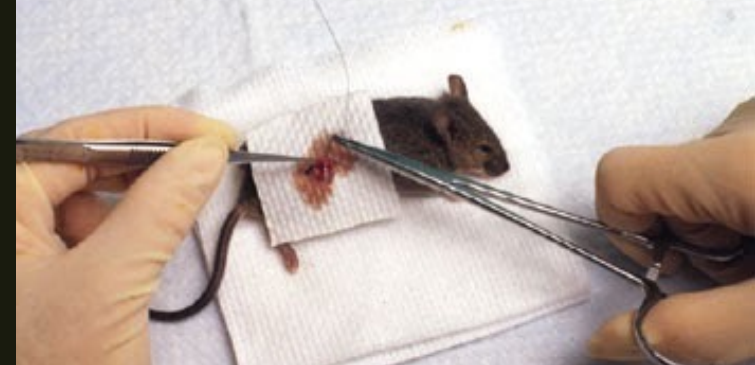
- Pre-operative preparation
  - General Health, Acclimation period
  - Proper handling
  - Avoid antimicrobial agents
- Instruments
  - Sterilization of equipment's
    - Steam/Chemical/Gas
    - For batch Surgeries – Start with sterile pack, and sterilizes between batches (4-5 animals per pack)



<https://www.ivis.org/library/laboratory-animal-medicine-and-management/principles-of-aseptic-rodent-survival-surgery>

# Rodent Surgery

- Aseptic Preparation of Surgical Site
  - Positioning of animal
  - Surgical site aseptic preparation
    - Alternate wipes with chlorhexidine and alcohol (2X)
    - Final wipe after surgeon donning sterile or clean gloves using iodine
- Surgeon Preparation
  - Hand scrub
  - Mask/ sterile gloves
  - Clean coat/dedicated/disposable
- Surgery
  - Depth of anesthesia – lack of Pedal Reflex
  - Incision & Closure - pattern
  - Suture materials – Absorbable and non-absorbable





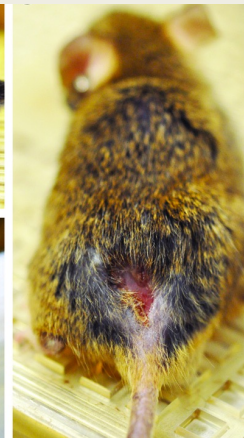
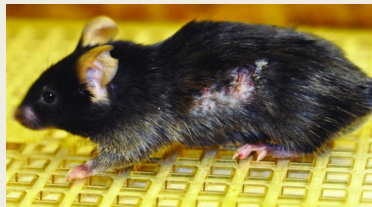
# Rodent Surgery

- Recovery
  - *Provision of warmth/extra bedding*
    - Normothermia
  - *Fluid therapy – Hydration is the key!*
  - *Analgesia – Post-operative monitoring*
  - *Placement of food inside the cage*
    - Supplementation of high calorie food








# Common Conditions in mice

- Sick Mice
  - Eye shut
  - Hunched
  - Piloerection
  - Lethargic
- Body Condition
- Dermatitis
- Alopecia
- Malocclusion
- Fight wounds
- Prolapse



## Body Condition Score

	<b>BC 1</b> Mouse is emaciated. - Skeletal structure extremely prominent; - little or no flesh cover. - Vertebrae distinctly segmented.
	<b>BC 2</b> Mouse is underconditioned. - Segmentation of vertebral column evident. - Dorsal pelvic bones are readily palpable.
	<b>BC 3</b> Mouse is well-conditioned. - Vertebrae and dorsal pelvis not prominent; - palpable with slight pressure.
	<b>BC 4</b> Mouse is overconditioned. - Spine is a continuous column. - Vertebrae palpable only with firm pressure.
	<b>BC 5</b> Mouse is obese. - Mouse is smooth and bulky. - Bone structure disappears under flesh and subcutaneous fat.

A "+" or a "-" can be added to the body condition score if additional increments are necessary (i.e. ...2+, 2, 2-...)

# Euthanasia

- Euth + Thanatos – good death
- Euthanasia is the act of humanely killing animals by methods that induce rapid unconsciousness and death without pain and distress
- Unless a deviation is justified for scientifically or medically reasons, they should be performed with the AVMA Guidelines for the Euthanasia of Animals (2020)



# Euthanasia

- All the methods are followed as described in AVM Guidelines for the Euthanasia of Animals: 2020 Edition  
<https://www.avma.org/sites/default/files/2020-01/2020-Euthanasia-Final-1-17-20.pdf>
- Should follow the methods as approved in the IACUC protocol
- Anesthetic Overdose
  - *Injectable Vs Inhalant Anesthetic agents*
- CO<sub>2</sub> narcosis
  - *Source: Compressed Cylinder*
- Confirmation of death – visual and physical method

# Occupational Health & Safety (OHS)

- Institutional Responsibility
- What makes an ideal OHS program?
  - Personal training
  - Risk assessment
    - Hazard related
  - Facilities, equipment and monitoring
  - Health assessment
  - Personal Protection
  - On-site health program

# Occupational Health & Safety (OHS)

- Protocol Related
  - *Infectious disease*
- Allergies
  - 46%
- Zoonoses
- Trauma
  - *Bites, needle stick*



# Occupational Health & Safety (OHS)

- All University Assistants, principal investigators, and students that work with animals are required to consult with the CCSU physician or other medically trained personnel in Health Services or a personal physician to determine if tetanus boosters are indicated and must provide proof of immunity to Health Services (a health release form will be completed to release tetanus booster status)
- Students and university employees with **health-related risks** will consult with the CCSU physician or other medically trained personnel in Health Services or a personal physician. Clearance to work with animals will be relayed to the principal investigator or supervisor. This information is then relayed to the IACUC Chair.
- In the event of bites, scratches, illness, or injury, the affected individual is directed to CCSU Health Services to seek immediate treatment or to call 911 in the case of an emergency. The event is reported by the individual to the principal investigator or supervisor, which is then relayed to the IACUC Chair.

# Training Resources

NIH Training Resources: [oacu.oir.nih.gov/training-resources](https://oacu.oir.nih.gov/training-resources)

- Aquatics Training Resources
- Rodent Breeding
- Rodent Restraint Procedures
- Rodent Blood Collection Procedures
- Rodent Compound Administration Procedures
- Rodent Genotyping & Identification Procedures
- Rodent Survival Surgery
- Rodent Euthanasia Procedures



**QUESTIONS**