Ethical Care and Use of Animals in Research
Animal use definition and examples
History of animal welfare regulations
Ethical and humane use of animals
Requirements before working with animals
“Any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes”
Why Use Animals in Medicine, Biology and Biomedical Research?

Animals as spare parts
Animals as factories
Animals as models for human disease
Animals as test subjects

Animals to study basic physiological principles and integration of systems
- Evolutionary and comparative physiology
- Novel solutions to complex problems
- Bioinformatics, comparative genomics, proteomics, metabolomics
- Systems biology
- Immunology
- Neurobiology

Animals for the study of animals and the environment
- Conservation biology
- Ecological interactions and community structure
- Veterinary medicine

Animals to study basic principles in biology
- Evolutionary biology
  - Experimental evolution
- Population genetics
- Population genomics
- Animal behavior

Animals for the study of disease
- Virology and viral evolution
- Cancer
Benefits of Animal Research

- Penicillin
  - Mice

- Blood Transfusions
  - Dogs

- Tuberculosis Medicine
  - Guinea pigs

- Meningitis Vaccine
  - Mice

- Kidney Transplants
  - Dogs and Pigs

- Breast Cancer Treatments
  - Mice, Rats and Dogs

- Asthma Inhalers
  - Guinea Pigs and Rabbits

- Polio Vaccine
  - Mice

- Insulin for Diabetics
  - Dogs

- Deep Brain Stimulation for Parkinson's Disease
  - Monkeys
Benefits Continued...

- Vaccine for Smallpox
- Vaccine for Anthrax
- Rabies Vaccine
- Typhoid Vaccine
- Cholera Vaccine
- Treatment for Beriberi
- Treatment for Rickets
- Corneal Transplants
- Local Anaesthetics
- Discovery of Vitamin C
- Canine Distemper Vaccine
- Coronary Bypass Operation
- German Measles Vaccine
- MMR Vaccine
- Antidepressants and Antipsychotic
- CT Scanning for Improved Diagnosis
- Chemotherapy for Leukaemia
- Medicines to Treat Ulcers
- Inhaled Asthma Medication
- Combined Therapy for HIV infection
- Medicines for Type 2 Diabetes
- Cervical Canker Antibodies
- Bird Flu Vaccine
- Malaria Vaccine

- Modern Anaesthetics
- Tetanus Vaccine
- Diphtheria Vaccine
- Anticoagulants
- Streptomycin
- Kidney Dialysis
- Whooping cough Vaccine
- Heart Lung Machine
- Hip replacements
- Cardiac Pacemakers
- High Blood Pressure Medicines
- Replacements of Heart Valves
- Chlorpromazine Psychiatric Medicine
- MRI Scanning for improved Diagnosis
- Prenatal Corticosteroids for Premature Babies
- Treatment for River Blindness
- Life Support for premature Babies
- Medicines to control Transplant Rejection
- Hepatitis B Vaccine
- Leprosy Treatment
- Oral and Inhaled Insulin for Type 1 Diabetes
- Angiogenesis Inhibitors for Cancer and Blindness
- Gene Therapy for Muscular Dystrophy
- Alzheimer's Vaccine
US Yearly Benefits of Animal Research

450,000  Prescriptions for anabolic (growth) hormones

520,000  Heart bypass operations

1,500,000 Prescribed for Erythropoietin (for Anemia)

34,000,000 Anticoagulants dispensed

95,000,000 Prescriptions for asthma

150,000,000 Prescriptions for antibiotics

2. Source: IMS Health, ClinicalPlus
5. Source: IMS Health, IMS National Prescription Audit
6. US Center for Disease Control and Prevention
Veterinary advances

Vaccines developed to protect pets, farm animals, working animals and animals in the wild

**Dogs**
- Leptospirosis
- Canine viral hepatitis
- Canine parvovirus
- Canine parainfluenza
- Kennel cough
- Rabies

**Cats**
- Feline enteritis
- Feline parvovirus
- Feline leukaemia
- Cat flu syndrome
- Chlamydid
- Rabies

**Foxes**
- Rabies

**Horses**
- Equine influenza
- Equine herpes
- Tetanus
- Rabies

**Pigs**
- Aujeszky's disease
- Swine erysipelas
- E coli infections

**Rabbits**
- Myxomatosis
- Viral haemorrhagic disease

**Sheep**
- Enzootic abortion
- Pasteurialia
- Clostridial toxoids

**Cattle**
- Louping ill
- Orf
- Lungworm
- Clostridial toxoids
- Foot and mouth disease
- Rinderpest
- Bovine respiratory syncitial virus
- Bovine influenza type 3
- *Pasteurella* infections

**Birds**
- Marek's disease
- Paramyxovirus
- Herpes
- Infectious bursal disease
- Avian encephalomyelitis
- Newcastle disease
- Infectious bronchitis
The Numbers…

Number of Animals Used Annually for Research in the US (Species covered by the Animal Welfare Act)

- Cats
- Primates
- Dogs
- All Other Animals

Year

Number of Animals Used
Numbers in Perspective

Millions of animals killed

Research exc. Mice, rats and birds: 1
Research inc. Mice, rats and birds: 26
Hunting: 150
Killed by Automobiles: 365
Ducks for food: 27
Cattle, sheep, calves for food: 38
Pigs for food: 105
Chickens for food: 9,031
Pain - The Percentages

“Some Pain, No Anaesthesia”

This is only the case when anaesthesia (or other pain relief) would have affected results e.g., when testing another pain relief drug.
Examples of Animal Use at UCI

- development of new therapies for humans and animals
- development of novel imaging techniques for diagnostics
- pre-clinical drug/device trials
- classes to teach surgical and other medical techniques
- behavioral studies
- tissue harvest for in-vitro studies
- comparative and evolutionary studies
Why Worry about Animals?

- Required by Law
- It’s the right thing to do
  - Morally and Ethically
  - Scientific Validity
Ethical Arguments for Animal Use

• Nuremberg Code of Ethics in Medical Research
  – “... be designed and based on results of animal experimentation and a knowledge of the natural history of the disease…” 1947

• Declaration of Helsinki
  – “Medical research involving human subjects...generally accepted scientific principles...and, where appropriate, animal experimentation.”
    - World Medical Association, 1964
Animals in Research

• The use of animals is a privilege, not a right
  – Society grants permission to use animals with the expectation that knowledge will be advanced, and health benefits may be derived
  – The perceived value to society must balance the adverse effects imposed on individual animals.
• Animal Welfare Act (AWA): USDA Animal Welfare Regulations

• PHS Policy - Health Research Extension Act (HREA)

• The *Guide for the Care and Use of Laboratory Animals* (The Guide)
The dog's name is Lucky. He is a brown-colored English mastiff with a few brown spots on his ears. In the early 1960s, he was placed in a makeshift cage at a veterinary hospital in New York City. The hospital staff took care of him for several weeks, but eventually decided it was time to find him a new home. They contacted a local animal shelter, who agreed to take him in. Lucky was later adopted by a family who had been looking for a dog for some time. They named him Lucky because they felt he was lucky to have found a new home.
• Raid of a Baltimore, MD animal dealer by Humane Society of the United States (HSUS)
• 29 charges of animal cruelty brought against Lester Brown
• Congress put forth eight bills to outlaw inhumane treatment of animals
• 1966: Congress enacted the Pet Protection Act
  – Protected against theft of pets by research dealers
  – Gave authority to USDA to enforce and administer the Act
  – Provided protection to dogs, cats, rabbits, monkeys, guinea pigs and hamsters
Pet Protection Act (cont’d)

- Established humane standards for treatment of animals
- Set licensing requirements for animal dealers
- Required annual USDA inspections of dealers and research institutions
1985 Animal Welfare Act Amendment

• Establishment of an Institutional Animal Care and Use Committee (IACUC)

• Requirements for veterinary consult and oversight

• Requirements for canine exercise and non-human primate psychological enrichment

• Requirements for consideration of alternatives to animal use and painful procedures and avoidance of unnecessary duplication of already-conducted studies
• Enforces and administers the Animal Welfare Act (AWA)
• Enforces the AWA through Animal Welfare Regulations (AWRs)
  – 9 CFR Chapter 1, Parts 1-3
• Provides clarification of AWRs through Animal Care policies
• Set requirements for committee (IACUC) composition and function
• Provide performance standards for:
  – veterinary care
  – animal husbandry
  – animal transportation
• Covers all “warm-blooded” animals
  – excludes rats, mice and birds
• Health Research Extension Act is the legislative mandate for Public Health Service (PHS) policy
• Covers all vertebrate animals
• NIH funded institutions must adhere to the PHS Policy
• Office of Laboratory Animal Welfare is responsible for assuring compliance with PHS policy
Federal Oversight

Universities, Research Institutes and Private Companies
IACUCs

Local oversight
Key Elements of the Federal Regulations

• Justify why animals are necessary
• Minimize pain and distress
• Personnel must be qualified to perform their duties
• Provide appropriate husbandry and care
• Use of appropriate euthanasia methods
• 1996 NASA Principles for Ethical Care & Use of Animals: “Sundowner Report”

• Principles of Humane Experimental Technique by W. M. Russell and R. L. Burch, 1959
NASA Principles - “Sundowner Report”

• Respect for Life
  – All living creatures deserve respect

• Societal Benefit
  – Some valuable return in exchange for the sacrifice of the animal’s life

• Non-maleficience
  – “Do no harm”
  – Pain, distress and discomfort to the animals must be minimized
The “Guide”

Performance Standards
- Institutional policies and responsibilities
- Animal environment, housing, and management
- Veterinary medical care
- Physical plant (facilities)
Institutional Animal Care and Use Committee (IACUC)

• Required by the AWRs, PHS Policy and *The Guide*
• Provides local (institutional) oversight of animal use in research, teaching and testing
• Members appointed by the Institutional Official (Associate Vice Chancellor for Research Engagement at UCI)
Institutional Animal Care and Use Committee

- Campus committee charged with oversight of UCI’s animal program
- Member Composition:
  - Faculty with animal expertise
  - Attending Veterinarian
  - Non-scientific member
  - Unaffiliated member
  - Biosafety officer
The IACUC’s Role

• Review and approve activities involving animals (protocol review)
• Review the animal program and inspect all facilities every 6 months
• Review concerns involving animal use
• Investigate issues of non-compliance
• Report to regulatory agencies
What Activities Require Review?

Definition:

“Any live, vertebrate animal used or intended for use in research, research training, experimentation, or biological testing or for related purposes.”

- PHS Policy
IACUC Protocol Review

- Rationale for the use of animals
- Justification of the species and number of animals
- Conduct of experiments
- Unnecessary duplication of experiments
- Appropriate sedation, analgesia, anesthesia
- Adequate training of personnel
- Protocols must address the “3-Rs”
Principles of Humane Experimental Technique

The 3 Rs

- **Replacement**
  - Use of live animals as the research model should be replaced if possible

- **Refinement**
  - Procedures should be refined to minimize pain, distress and discomfort

- **Reduction**
  - Number of animals should be reduced to the minimum necessary to achieve scientific significance without increasing pain and distress
• Modifications to Existing Protocols
• Annual and three-year renewals
• Program Evaluation
• Facility Inspections
University Laboratory Animal Resources (ULAR)

- **Functions:**
  - Veterinary care & health surveillance
  - Daily husbandry/care
  - Animal procurement
  - Facility maintenance
    - Including vivarium access
  - Transgenic Mouse Facility
Veterinary Services

• Veterinary care of all research animals on campus
• Report to the IACUC regarding issues related to the animal care program
• Training for research personnel in animal handling, basic procedures, etc.
• Complete listing of services at ULAR website: http://www.rgs.uci.edu/ular/index.htm
Animal Models
Purpose bred rodents

dogs, cats, pigs etc

other vertebrates

http://www.statisticbrain.com/animal-testing-statistics/
The Guide

GUIDE FOR THE CARE AND USE OF LABORATORY ANIMALS

Eighth Edition

NATIONAL RESEARCH COUNCIL OF THE NATIONAL ACADEMIES
The design of animal facilities combined with appropriate animal housing and management are essential contributors to animal well-being, the quality of animal research and production, teaching or testing programs involving animals, and the health and safety of personnel. An appropriate Program (see Chapter 2) provides environments, housing, and management that are well suited for the species or strains of animals maintained and takes into account their physical, physiologic, and behavioral needs, allowing them to grow, mature, and reproduce normally while providing for their health and well-being.