

# Research with Humans and Animals: IRB and IACUC Basics

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# Research is Regulated

- Use of human subjects and animals in research is a privilege
- Numerous regulatory bodies authorize, monitor, and have authority to halt human and animal research
- Effective oversight supports the research enterprise (no compliance= no money)

# Ethical Principles

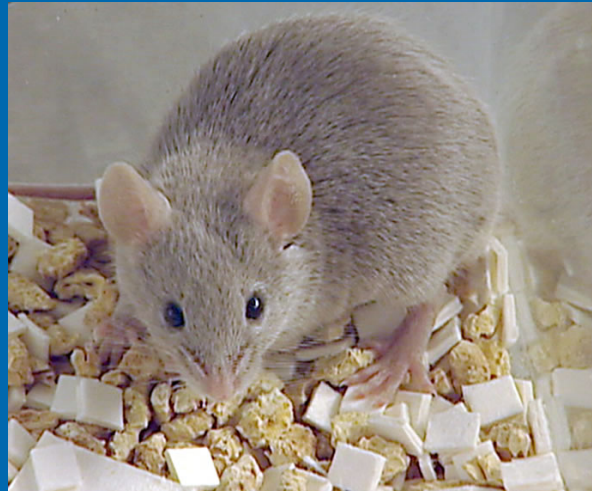
## BELMONT (Human)

- Respect for Persons
- Beneficence
- Justice

## SUNDOWNER (Animal)

- Respect for Life
- Non-Maleficence
- Societal Benefit

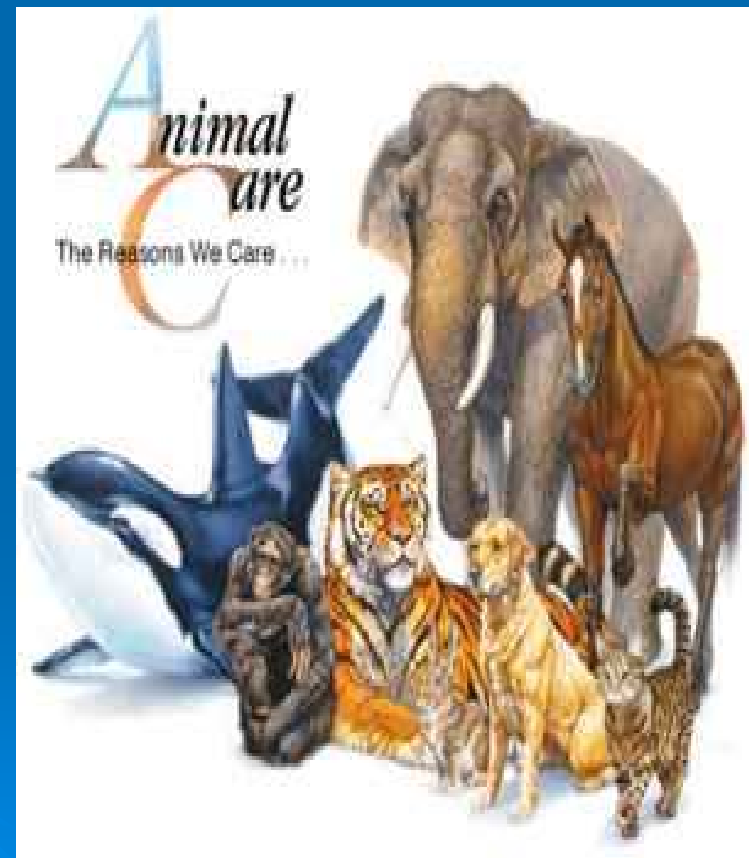
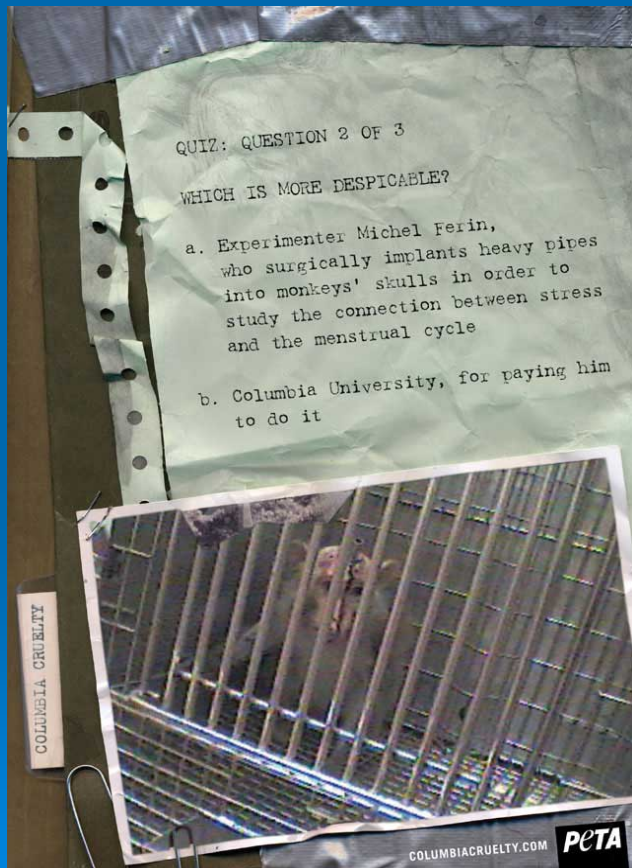
# Use of Animals



# What is Animal Care and Use?

- For purposes of this session, the word “**animals**” means live, vertebrate animals used in research, testing, teaching, health surveillance, or for related purposes.
- For purposes of this session, the phrase “**care and use**” means procurement, housing, transport, husbandry, health maintenance, experimentation, treatment and humane euthanasia.

# Animal Rights v. Animal Welfare



# Current U.S. Regulations

- Animal Welfare Act, 1966 [USC Title 7, Sections 2131 to 2156] as amended in 1970, 1976, 1985 and 1990.
- Animal Welfare Regulations [Title 9 CFR, Subchapter A, Animal Welfare, Parts 1, 2 and 3]
- Health Research Extension Act, 1985 [Public Law 99-158, November 20, 1985, Section 495]
- US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training, 1985
- PHS Policy on Humane Care and Use of Laboratory Animals, 1986
- 2000 Report of the AVMA Panel on Euthanasia [JAVMA, Vol. 218, No. 5, March 1, 2001]
- Guide for the Care and Use of Laboratory Animals (*Guide*) [NRC, 5th Ed., 1996]
- NIH Grants Policy Statement (03/01), Part II: Terms and Conditions of NIH Grant Awards Subpart A: General -- Part 2 of 7

# Enforcement

- USDA (regulations)
- OLAW (regulations)
- AAALAC, Int. (voluntary accreditation standards)
- States (statutes)
- Local Municipalities (laws)
- Institutions (policies)
- Attending Veterinarian/Institutional Animal Care Personnel
- Local IACUCs (policies, procedures)



# IACUC (What is it?)

- The IACUC is the institutional body with responsibility for review and oversight of the institution's program for the humane care and use of animals.
- The IACUC supports, facilitates, and promotes ethical and humane use of animals by upholding the standards set forth in all applicable laws, policies & guidance.
- Per PHS Policy, must consist of no fewer than five members, including a Veterinarian, one practicing scientist experienced in research involving animals, one member whose primary vocation is in a non-scientific area, and one member unaffiliated with the institution.

# IACUC Authorities

- Review institution's animal care and use program 2x/yr.
- Inspect institution's animal facilities, laboratories, and other areas where animals are used 2x/yr.
- Provide IACUC program evaluations and facility inspections to the IO.
- Review and approve, require modifications in (to secure approval) or withhold approval of proposed and continuing animal activities.
- Review and approve, require modifications in (to secure approval) or withhold approval of all proposed changes (modifications) to approved protocols.

# IACUC Authorities, cont.

- Notify investigators in writing of its decision to approve, require modifications in (to secure approval) or withhold approval of proposed animal activities.
- Investigate concerns involving the care and use of animals.
- Suspend animal activities that are not being conducted in accordance with applicable requirements.
- Make written recommendations to the IO regarding any aspect of the institution's animal care and use program.

# IACUC Review

- Importance of research question justifies use of animals?
- Study personnel have training in species/techniques?
- **R**efine- consider alternatives to any procedure that causes more than momentary pain or distress
- **R**educe- the number of animals used should be the minimum that is consistent with the aims of the experiment
- **R**eplace- use non-animal models when possible (e.g., *in vitro* methods)

# Modifications

- Any change in an ongoing study must be approved prior to implementation\*
- Most common changes: personnel, procedures, animal numbers
- Significant changes reviewed by Full Committee

\*except to avoid an immediate apparent hazard


# Continuing Review

- OLAW covered species are reviewed *de novo* every three years
- USDA covered species are reviewed at least annually
- Most universities look at all protocols annually, with more in-depth (or “from scratch”) review every three years
- Investigator’s responsibility to request continuing review sufficiently prior to expiration of approval to avoid a lapse

# Animal Care

- Attending Veterinarian
- Animal Care Staff: vet techs, husbandry techs, procurement staff, transport staff, cagewash personnel, etc.
- Compliance/post-approval monitoring  
(may reside with IACUC)

# Animal Care Duties

- Housing
  - Daily Health Checks
  - Pathogen Control
  - Feed, Bedding
  - Transport
  - Monitoring of Surgery/Other Procedures
  - Necropsy
  - Physical Plant Upkeep
  - Equipment Maintenance
  - Scientific/Clinical Input on IACUC Review
  - IACUC's "eyes and ears" in the Field
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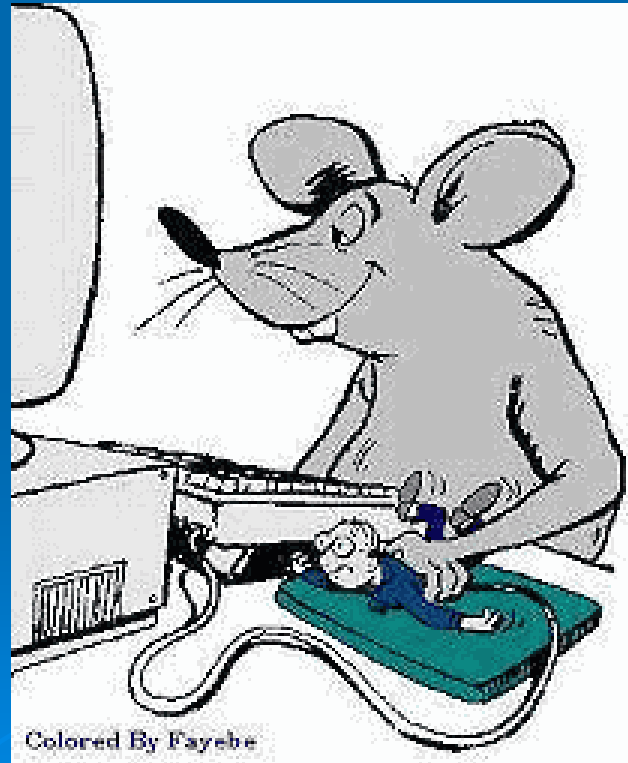
# Training Is Required

- Federal law mandates that all individuals who work with animals in biomedical research be appropriately qualified and trained.
- Training program should be available to all investigators, fellows, students, and technicians who work with research animals.
- Various media can be used: web-based, in-person, brochure, hands-on, classroom style, etc.

# Compliance Activities

- Lab Inspections at least twice annually
- Post-approval Monitoring (not for cause)
- Investigations (for cause)
- Semi-annual Program Evaluations
- Report to OLAW (and UDSA, if covered) serious/continuing problems in a timely fashion; summarize for AAALAC annual report

# Keep Good Records!!





# What is AAALAC?

- AAALAC, International is a private, nonprofit organization that promotes the humane treatment of animals in science through a voluntary accreditation program.
- Formal site visits are conducted at three-year intervals and are a method of ensuring that animal care and use programs maintain high standards.


# What Does AAALAC Do?

- AAALAC site visitors evaluate all aspects of an animal care and use program, including conformance with established procedures and overall performance in the area of animal care and use in research, education, testing or breeding.
- The basic components of a program that are evaluated include (but are not limited to) institutional/IACUC policies, animal husbandry, veterinary care, and the physical plant.

# Worker Protection & Occ. Health



# Risks for Animal Users

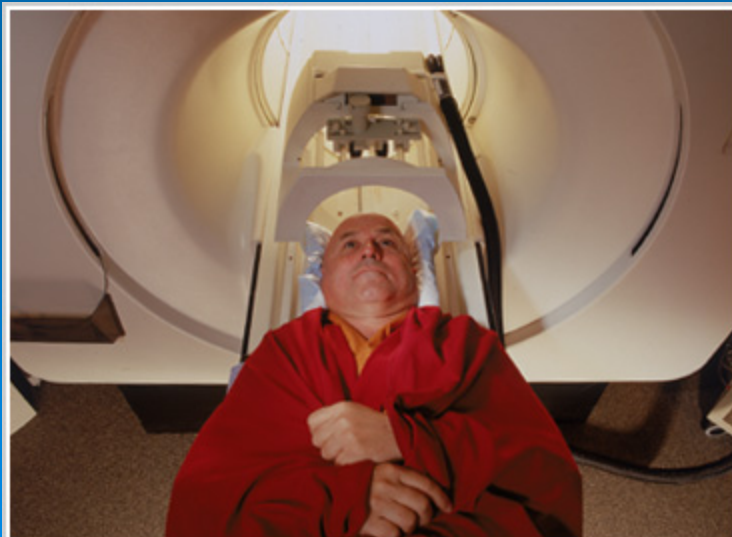
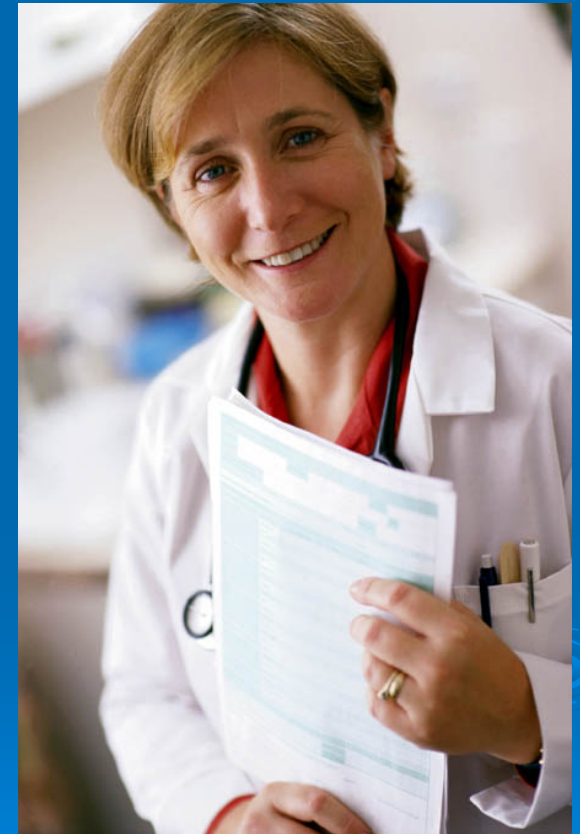
- Allergies
  - Asthma
  - Skin Rashes
  - Burns, cuts, needle sticks
  - Chemical exposures
  - Infectious agents
  - Repetitive stress, overexertion
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# Worker Protection Program

- Employee Health Clinic
- Brochure
- Health History Questionnaire
- Tutorial on risks for animal users and bystanders
- Access to hazards limited pending assessment/tutorial
- Consultation and referral to specialist
- Case management for Worker's Compensation claims



# Use of Human Subjects




# What is Human Research?

*“any systematic investigation that is designed to develop or contribute to generalizable knowledge, and which uses living humans or identifiable information about living humans”*

- 45CFR Part 46 (“The Common Rule”)



# Examples

- analyses of existing biological specimens
  - chart reviews
  - clinical trials
  - cognitive and perceptual experiments
  - evaluations of social or educational programs
  - interviews and focus groups
  - surveys and questionnaires
  - treatment outcome studies
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# Current Requirements

- 45 CFR Part 46 (PHS)
- 21 CFR Part 56 (FDA)
- 45 CFR Parts 160 & 164 (HIPAA)
- State statutes
- Local ordinances
- Institution/Campus policies and procedures
- Community standards

# 45 CFR Part 46

- “The Common Rule”: Federal Policy for the Protection of Human Subjects
- DHHS subparts
  - Subpart B: Pregnant women, Fetuses and Neonates
  - Subpart C: Prisoners
  - Subpart D: Minors

# 21 CFR Parts 50 and 56 (FDA)

- IDEs- New Devices
  - INDs- New Drugs/ Biologics
  - Emergency Use of Test Article
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# 45 CFR Parts 160 & 164 (HIPAA)

- Privacy Board
  - Authorization
  - Waiver of Authorization
  - De-identified Data Set
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# Enforcement

- DHHS- OHRP
- DHHS- FDA
- AHRPP (voluntary accreditation)
- State and Local Governments
- Institutions (e.g., universities, hospitals)
- Local IRBs



# IRB (What is it?)

- An IRB is an institutional body with responsibility for review and oversight of the human subject protection program.
- The IRB supports, facilitates, and promotes ethical use of human subjects by upholding the standards set forth in all applicable laws, policies & guidance.
- Per federal Policy, must consist of no fewer than five members, including one practicing scientist, one member whose primary vocation is in a non-scientific area, and one member unaffiliated with the institution.

# IRB Authorities

- Review and approve, require modifications in (to secure approval), or disapprove all research activities covered by the regulations;
- Require that information given to subjects as part of informed consent is in accordance with the regulations;
- Require documentation of informed consent or may waive documentation in accordance with the regulations;
- Notify investigators and the institution in writing of its decision to approve or disapprove proposed research or of modifications required to secure IRB approval of the research activity;

# IRB Authorities, cont.

- Conduct continuing review of research covered by the regulations at intervals appropriate to the degree of risk, but not less than once per year;
- May observe or have a third party observe the consent process and the research; and
- May suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.

# IRB Review

- Risks justified and reduced to fullest extent?
- Benefits maximized to fullest extent?
- Importance of research question justifies risks in light of anticipated benefits?
- Selection of subjects is equitable?

# IRB Review, cont.

- Proposed subject population not unduly harmed?
- Method, content, and documentation of consent appropriate?
- Provision for monitoring the data collected to ensure the safety of subjects?
- Provisions to protect subjects' privacy and maintain confidentiality of data?

# Informed Consent Must Be:

- consistent with regulations re: required elements;
- obtained from subject or legally-authorized representative;
- presented in language understandable to the subject/ rep.;
- in writing (unless IRB approved verbal or waiver); and
- obtained in circumstances that offer the subject/rep. sufficient opportunity to consider whether to participate.

# Modifications

- Any change in an ongoing study must be approved prior to implementation\*
- Most common changes: personnel, procedures, subject populations, recruitment methods
- Mods that affect risk/benefit ratio or increase subject safety reviewed by Full Board

\*except to avoid an immediate apparent hazard

# Adverse Events/Safety Data

- All AEs must be reported to the IRB within 10 days. All deaths and hospitalizations also must be reported by phone, fax or e-mail within 48 hours
- IRB Chairs review serious local AEs between meetings
- IRB AE data reports provided to members at time of CR
- PIs asked to submit copies of DSMB reports at time of CR



# Continuing Review

- Expedited and Full Committee studies are reviewed at least annually
- Opportunity to reevaluate importance of research question, appropriateness of risks
- Opportunity to review AEs and request modifications to protocol and/or consent
- Investigator's responsibility to request continuing review sufficiently prior to expiration of approval to avoid a lapse

# Compliance

- Policy for Regulatory Noncompliance
- Staff conduct Administrative Audits
- IRBs (or subcommittees) perform reviews
- Efforts made to resolve informally whenever possible
- IRBs empowered to impose corrective actions
- Report to OHRP (and FDA, if covered) serious/continuing problems in a timely fashion

# What is AAHRPP?



- AAHRPP is a private, nonprofit organization that promotes the protection of human subjects through a voluntary accreditation program.
- Formal site visits are conducted at three-year intervals and are a method of ensuring that human subjects protection programs maintain high standards.

# What Does AAHRPP Do?

- AAHRPP site visitors evaluate all aspects of a human subjects protection program, including conformance with established procedures and overall performance.
- The five domains that are evaluated include:
  - **Organization**
  - **Research Review Unit (including IRBs)**
  - **Investigator**
  - **Sponsored Research**
  - **Participant Outreach**

# Effective Compliance

- Have a policy and procedures for monitoring and enforcement (avoid S.L.A.G.I.A.T. method)
- Honor due process, document actions
- Keep the Institutional Official informed
- Emphasize training over punishment (an ounce of prevention...)

# Questions?

