

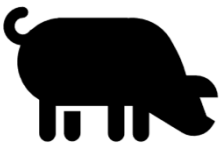





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Presentation Outline

- Laws of the Jungle: Overview of major laws & regulations governing animal research
- Kings of the Jungle: Discussion of the main regulatory agencies.
- Jungle Lore: Working with institutional committees and individuals involved in the regulation of animal research

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Map of the Acronyms

- ▶ AAALAC = formerly Association for Assessment and Accreditation of Laboratory Animal Care International
- ▶ APHIS = Animal and Plant Health Inspection Service
- ▶ AWA = Animal Welfare Act
- ▶ IACUC = Institutional Animal Care and Use Committee
- ▶ IO = Institutional Official
- ▶ OLAW = Office of Laboratory Animal Welfare (part of Nat'l Institutes of Health (NIH), Office of Extramural Research)
- ▶ PHS = Public Health Service
- ▶ USDA = US Dept. of Agriculture

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The Kings of the Jungle



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U.S. Department of Agriculture

- Oversees implementation and enforcement of Animal Welfare Act (AWA).
- Enforcement is carried out through USDA's Animal and Plant Health Inspection Service (APHIS).
- Conducts annual inspection of registered research facilities.



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Office of Laboratory Animal Welfare – OLAW

- **Office of Laboratory Animal Welfare**
 - Part of the U.S. Public Health Service (PHS), National Institutes of Health (NIH) Office of Extramural Research.
 - Oversees implementation and enforcement of Public Health Service Policy on Humane Care and Use of Laboratory Animals (Public Health Policy).
 - Public Health Policy applies to all animal research funded by PHS, e.g., NIH-funded studies.

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AAALAC



- Mini-King -- Private accrediting agency.
- Uses *Guide for Animal Care & Use* as main standard for accreditation.
- Initial and continuing site visits and annual reports.
- Officially recognized by government regulators.
 - IACUC may use AAALAC accreditation site visit as semi-annual inspection if IACUC members participate.

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The Laws of the Jungle

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The Three R's

- Basic principle underlying all laws regulating animal research.
- Refine – Methods minimize animal suffering & help welfare.
- Reduce – Methods minimize number of animals used in experiments.
- Replace – Methods avoid or replace the use of animals in experiments.
- *From: Recognition and Alleviation of Pain and Distress in Laboratory Animals, National Research Council, 2008*

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U.S. Government Principles

- ▶ *U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research and Training*
 - ▶ Applied whenever any U.S. government agencies develop requirements for testing, research or training procedures that use vertebrate animals.
 - ▶ Basic principles for designing and carrying out animal research.

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Summary of the Principles



Don't use animals needlessly! What is the relevance of the procedures to human/animal health & advancing knowledge?



Use the appropriate species of animal and minimum number necessary to obtain valid results.



Avoid or minimize discomfort, pain and distress in designing research. If it hurts a human, it hurts an animal unless otherwise established



Use sedation, analgesia or anesthesia for more than momentary pain or distress.

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Summary of the Principles



Use appropriate euthanasia for severe or chronic pain or distress that can't be relieved.



Provide appropriate living conditions and care directed by a vet.



Ensure investigators are qualified and have been trained in how to use animals.



Follow applicable federal regulations. Any exceptions must be approved by an IACUC.

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The Guide

- *Guide for the Care and Use of Laboratory Animals* ("The Guide")
 - PHS Policy requires compliance
- ▶ Covers institutional policies and responsibilities.
- ▶ Monitoring care and use of lab animals.
- ▶ Veterinary care.
- ▶ Personnel qualifications & training.
- ▶ Occupational health and safety for animal users and animal care personnel.
- ▶ Husbandry.
- ▶ Physical Plant – detailed facility requirements.

GUIDE FOR THE CARE AND USE OF LABORATORY ANIMALS

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Animal Welfare Act (AWA) & Regulations

- Federal Agency with Oversight: USDA
- APHIS – Animal & Plant Health Inspection Service
- Title 7 United States Code §§ 2131 - 2159.
 - Regulations: 9 CFR §§ 1.1 – 4.11
 - Sections re. Research Facilities: §§ 2.30 – 2.38



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When Does the AWA Apply?

APPLIES TO: Live or dead warm-blooded animals used or intended for use in research, teaching, testing, experimentation, exhibition or as pets.

APPLIES TO: Cats, dogs, nonhuman primates (monkeys, etc.), guinea pigs, hamsters & rabbits, marine mammals.

DOES NOT APPLY TO:

- Birds; rats of the genus *Rattus*; or mice of the genus *Mus* that are used for research.
- Horses not used for research or farm animals used for food, fiber, breeding or husbandry purposes.

DOES NOT APPLY TO:

- Field studies of natural animals in the wild UNLESS there are invasive procedures, or procedures that harm or materially alter behavior of animal.

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Where Does the AWA Apply?

- Applies to Research Facilities
 - Research Facility = any school (except elementary or secondary school), institution or organization or person that uses or intends to use live animals in research, tests or experiments and that purchases or transports live animals in commerce OR that receives funding from a federal agency for carrying out the research, tests or experiments.
- Applies to dealers, transporters and exhibitors
 - If a Research Facility sells, exhibits or trades animals it may have to be licensed as a dealer or exhibitor too.

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Does the AWA apply to Tiger King?

Joseph Maldonado-Passage, also known as "Joe Exotic," with one of his tigers. Credit: Netflix published in NY Times @ <https://www.nytimes.com/article/tiger-king-updates.html>

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AWA Requirements

- Humane handling, care and transport of animals by dealers, research facilities and exhibitors.
- Species-specific standards for feeding, veterinary care, housing, sanitation and ventilation
- Minimization of pain and distress for animals used in research, i.e., use of analgesics, anesthetics, tranquilizers or euthanasia.
- PI's must consider alternatives to use of animals.
- Veterinarians must review experimental procedures that may cause more than momentary pain or distress in animals.
- Prohibits use of an animal in more than one major operative experiment from which it is allowed to recover unless there is specific showing of scientific necessity.

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AWA Requirements

- Establishment of an IACUC.
 - IACUC must inspect facilities semi-annually
 - IACUC must have method to receive complaints about non-compliance with AWA.
- USDA annual inspection of facilities
- Prohibits retaliation against persons who report non-compliance.

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AWA Required Documentation: Registration

- ▶ Registration as a research facility.
 - ▶ Must be filed initially and every 3 years thereafter.
 - ▶ Must be updated as necessary.
- ▶ Must be signed by Institutional Official.
 - ▶ Institutional Official – Person at the institution who has the legal authority to bind the institution and who has the authority to commit the resources necessary to ensure compliance.
- ▶ Requires certification of compliance with AWA and all regulations.

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USDA Non-Compliance Reporting Requirements

- Report any protocol suspension by the IACUC.
- Report any significant deficiency that is not corrected within the period prescribed by the IACUC.
- Significant deficiency = Is or may be a threat to the health or safety of the animals.
- Reporting is done through the Institutional Official.

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AWA Required Documentation: Annual Report

- ▶ **Annual Report**
 - ▶ Annual assurance of compliance with AWA.
- ▶ **Lists Facilities.**
- ▶ **Lists Pain & Distress Classes:** Type and Number of Animals held in each Pain and Distress Classes
 - ▶ **Class B:** Held but not used in research yet.
 - ▶ **Class C:** Used in research that involves no pain or distress and no use of analgesics, anesthetics or tranquilizers (AAT drugs).
 - ▶ **Class D:** Used in experiments causing pain and distress, but AAT drugs used.
 - ▶ **Class E:** Used in experiments causing pain and distress, but AAT drugs NOT used because of adverse effect on research.
 - ▶ Must describe procedures and reason AAT drugs were withheld.

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NIH National Institutes of Health
Office of Laboratory Animal Welfare

Office of Laboratory Animal Welfare

Policies and Laws Guidance Education

Home » Policies and Laws » PHS Policy on Humane Care and Use of Laboratory Animals

PHS Policy on Humane Care and Use of Laboratory Animals

PHS Policy

Agency with Oversight: OLAW

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When does the PHS Policy Apply?

- ▶ All PHS conducted or supported activities that involve animals.
- ▶ ANY live vertebrate animal used or intended for use in research, research training, experimentation or biological testing or for related purposes.
 - ▶ INCLUDES MICE & RATS
- ▶ Individuals receiving PHS support must be associated with institution that is responsible for complying with PHS Policy.
- ▶ Field Studies if study alters or influences the activity of the study animals of other species in the study area.

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Where Does the PHS Policy Apply?

- ▶ Covers activities that take place at in U.S., Puerto Rico, or U.S. territories at PHS agencies, PHS awardee institutions or other institutions (e.g., subcontractors).
- ▶ Applies to PHS funded activities in foreign countries, but adherence to other acceptable standards can be established with OLAW approval.

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PHS Policy Requirements

- Comply with the Policy and, if applicable, the AWA.
 - Act Species vs. Non-Act Species
- Establish an IACUC
 - Semi-Annual Inspections
 - Program Evaluations
- Process for reporting non-compliance to IACUC.
 - No explicit prohibition against retaliation for reporting violation.
- Include information in PHS grant applications about rationale for using animals, appropriateness of species and number, description of proposed use, and description of methods/drugs used to minimize discomfort and pain, as well as euthanasia methods.
- *Guide for the Care and Use of Laboratory Animals* must be followed.

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► PHS Policy Required Documents: Assurance

- File new assurance every 4 years; update as necessary
- Assurance requirements:
 - Lists all parts of institution covered by Assurance.
 - Describe who is responsible for program
 - Describe qualifications of vets in program.
 - Describe membership of and procedures for IACUC.
 - IACUC minutes and documentation must be maintained
 - Describe occupational health program for persons who work with animals.
 - Describe training for animal users and caretakers.
 - Describe facilities, species used, and animal inventory.
 - Describe specific approval lines of authority and responsibility.

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► PHS Policy Documentation: Annual Report

- Annual Report describes:
 - Program changes
 - Change in AAALAC accreditation status
 - Assurance that semiannual Program Evaluations and Inspections have been completed by IACUC with corrective action as appropriate.
 - Report of any minority views.
 - List of IACUC members.
 - Names of members other than chair & attending vet may be represented by a number or code

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PHS Non-Compliance Reporting Requirements

- Report to OLAW:
- Serious or continuing non-compliance with PHS Policy or the Guide.
- Serious deviation from the Guide.
- Suspension of the protocol by the IACUC.
- Reports are made through the Institutional Official

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Scenario A

- Professor X is conducting an IACUC-approved experiment in which he tests an anti-cancer drug on mice. He decides he wants to try the drug on hamsters as well because they have a different metabolism. He administers the drug to 5 hamsters he originally purchased for use in a behavioral experiment. The IACUC does its semi-annual inspection and sees that the hamsters are being administered the anti-cancer drug.

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POLL 1: Who has jurisdiction?

- 1. USDA
- 2. OLAW
- 3. Both
- 4. Neither

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Scenario B

- A complaint to the IACUC's hotline from a graduate student in Prof. A's lab states that Prof. A is not giving the mice in his NIH-funded study the appropriate analgesics after surgery. The IACUC contacts Prof. A who says that he is not giving the analgesics because it interferes with the results from a blood test that needs to be performed. Prof. A asks the IACUC who make the complaint, so that he can let them know why he is not giving the analgesic.

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POLL 2: The IACUC should:

- 1. Give Prof. A the student's name and let him take it from there
- 2. Refuse to give Prof. A the name and explain to the student why Prof. A is not using the drug.
- 3. Refuse to give Prof. A the name and ask Prof. A to halt the study until an amendment is filed.

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POLL 3: Does anything need to be reported to regulators?

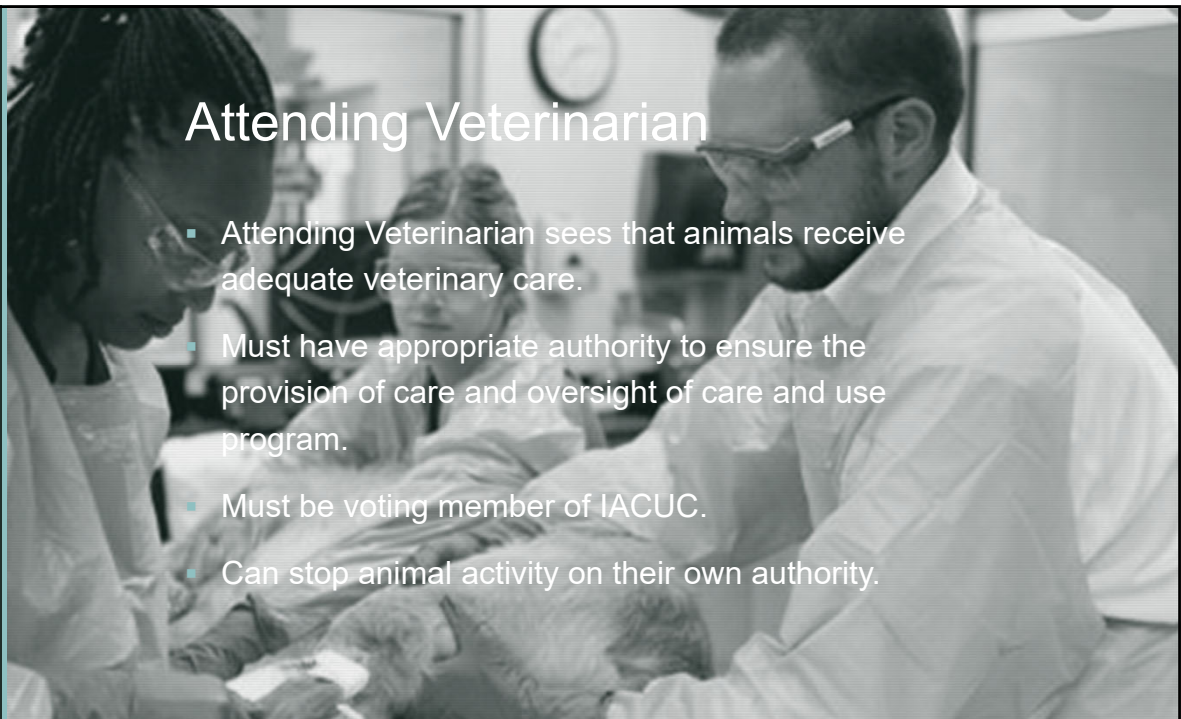
- 1. Report to USDA
- 2. Report to OLAW
- 3. Report to both
- 4. Report to neither

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Jungle Lore

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Attending Veterinarian

- Attending Veterinarian sees that animals receive adequate veterinary care.
- Must have appropriate authority to ensure the provision of care and oversight of care and use program.
- Must be voting member of IACUC.
- Can stop animal activity on their own authority.

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Institutional Official

- Person at the institution who has the legal authority to bind the institution and who has the authority to commit the resources necessary to ensure that the animal care and use program is in compliance.

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IACUC

- Institutional committee with oversight for animal research.
- Slightly different requirements under PHS Policy and USDA regulations.
- Basic duties:
 - Protocol review
 - Inspections
 - Program review

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IACUC Composition: USDA Requirements

- ▶ At least 3 members appointed by CEO (or delegate) – 1 chair and 2 others.
- ▶ Veterinarian with training or experience in lab animal science/medicine who has program responsibility.
- ▶ 1 member who is not affiliated with research facility; represents community interests.
- ▶ If IACUC has more than 3 members, then no more than three members may be from same administrative unit in research facility.
- ▶ Quorum = number; does not require specific persons.
- ▶ Reviewers may not be conflicted.
- ▶ Consultants may assist in review.

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IACUC Composition: PHS Policy Requirements

- ▶ At least 5 members appointed by CEO or delegate.
- ▶ Veterinarian with training or experience in lab animal science/medicine who has program responsibility.
- ▶ 1 practicing scientist with experience in animal research.
- ▶ 1 non-scientist.
- ▶ 1 person not affiliated with the institution.
- ▶ A single person may meet more than one of the foregoing requirement, but there must be 5 members.
- ▶ Quorum = number; does not require specific persons.
- ▶ Reviewers may not be conflicted
- ▶ Consultants may assist in review.

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Scenario C:

- The IACUC at Big University is holding its monthly meeting. There is only one protocol to review. The protocol is NIH funded and uses dogs. 5 of the 7 members are present at the meeting, but Pete, the community member who is not affiliated with Big University and who is also the non-scientist member is not at the meeting. Pete is a plumber, but he is working on getting his bachelor's degree in biology and his class schedule has prevented him from attending 4 of the last 6 monthly IACUC meetings.

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POLL 4: Can the IACUC review the protocol?

- 1. Yes
- 2. No

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POLL 5: Can Pete be the non-affiliated member and the non-scientist member?

- 1. Yes
- 2. No

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IACUC Review Responsibilities

- ▶ Initial and Continuing Review
 - ▶ USDA Requirement – Continuing review annually
 - ▶ PHS Requirement – Continuing review not less than once every 3 years.
- ▶ Post-approval monitoring programs may occur between continuing review periods.
- ▶ Designated member review possible, but entire IACUC committee must be given description of protocol and offered chance to call for full committee review.
- ▶ Only the IACUC may suspend a protocol, but an Attending Veterinarian or Institutional Official can put a halt to animal use activities.

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IACUC Program Evaluations and Inspections

- ▶ Semiannual Program Inspections
 - ▶ Review of facility's program for humane care and use of animals under AWA and most institutional policies.
- ▶ Semiannual inspection of the animal facilities
 - ▶ Housing areas, study areas, surgical areas
- ▶ When does a facility require inspection?
 - ▶ USDA – Inspect if animals are kept there more than 12 hours
 - ▶ OLAW – Inspect if animals are kept there more than 24 hours
- ▶ Report findings from reviews and inspections to Institutional Official.
 - ▶ Distinguish between Significant and Minor Deficiencies
 - ▶ Include timeline for correction

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Other IACUC Responsibilities

- Investigate concerns and complaints about non-compliance.
- Make recommendations to the Institutional Official.
- Draft the PHS Annual Report
 - Provided to OLAW via the Institutional Official (IO).
- Report to OLAW (via IO)
 - serious or continuing non-compliance with PHS Policy or the Guide;
 - serious deviation from the Guide;
 - suspension of a protocol.
- Report to the USDA (via IO)
 - any protocol suspension;
 - any significant deficiency that is not corrected within the IACUC prescribed period

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Scenario D

- Apex University has an affiliated hospital with an imaging center. Professor Y is doing self-funded functional MRI studies on rhesus monkeys. The MRI in the veterinary center is broken and Prof. Y makes a deal with the imaging center to use its MRI to scan his 12 monkeys twice a week for 2 months. The Hospital tells Prof. Y that the scanning must be done between 6 p.m. in the evening and 7 a.m. the next day. Prof. Y brings the monkeys to the MRI at 6 p.m. & finishes up by 7 or 7:30 a.m. the next morning. A nurse at the hospital call the IACUC and asks why there are monkeys in the MRI suite.

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POLL 6: What does the IACUC need to do?

- 1. Notify NIH through the IO
- 2. Amend the protocol for Prof. Y
- 3. Inspect the hospital facility
- 4. Report the non-compliance to the USDA

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Scenario E

- The IACUC receives a protocol for an NIH-funded research project for a field study of gophers in Colorado. The study involves capture and retention of the animals for 10 minutes in a small burrow underground while the student snaps pictures with a camera placed underground. The study will last one month.

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POLL 7: Does this study require IACUC review?

- 1. Yes
- 2. No

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Questions?

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