

# Working with Animals



Walter Jeske, PhD

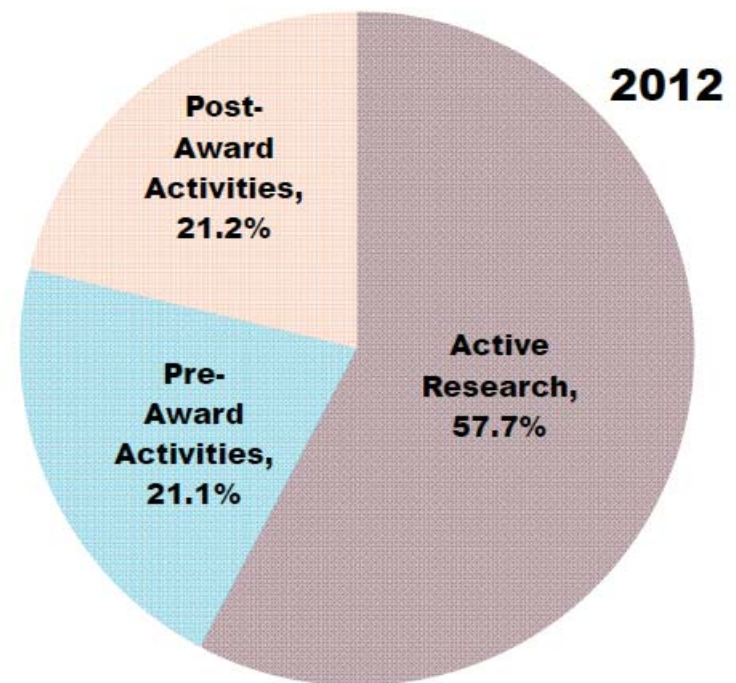
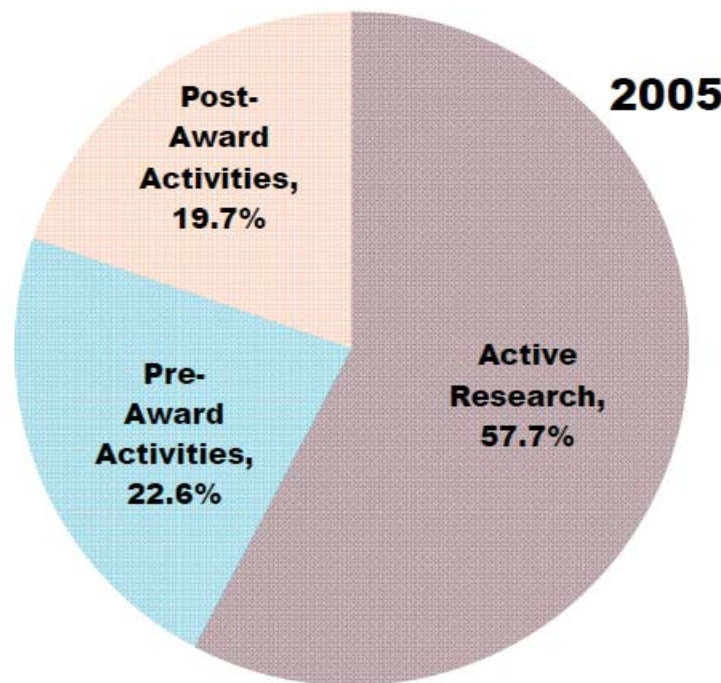
Professor, Thoracic & CV Surgery,

Pathology, Physiology

Vice-chair, IACUC

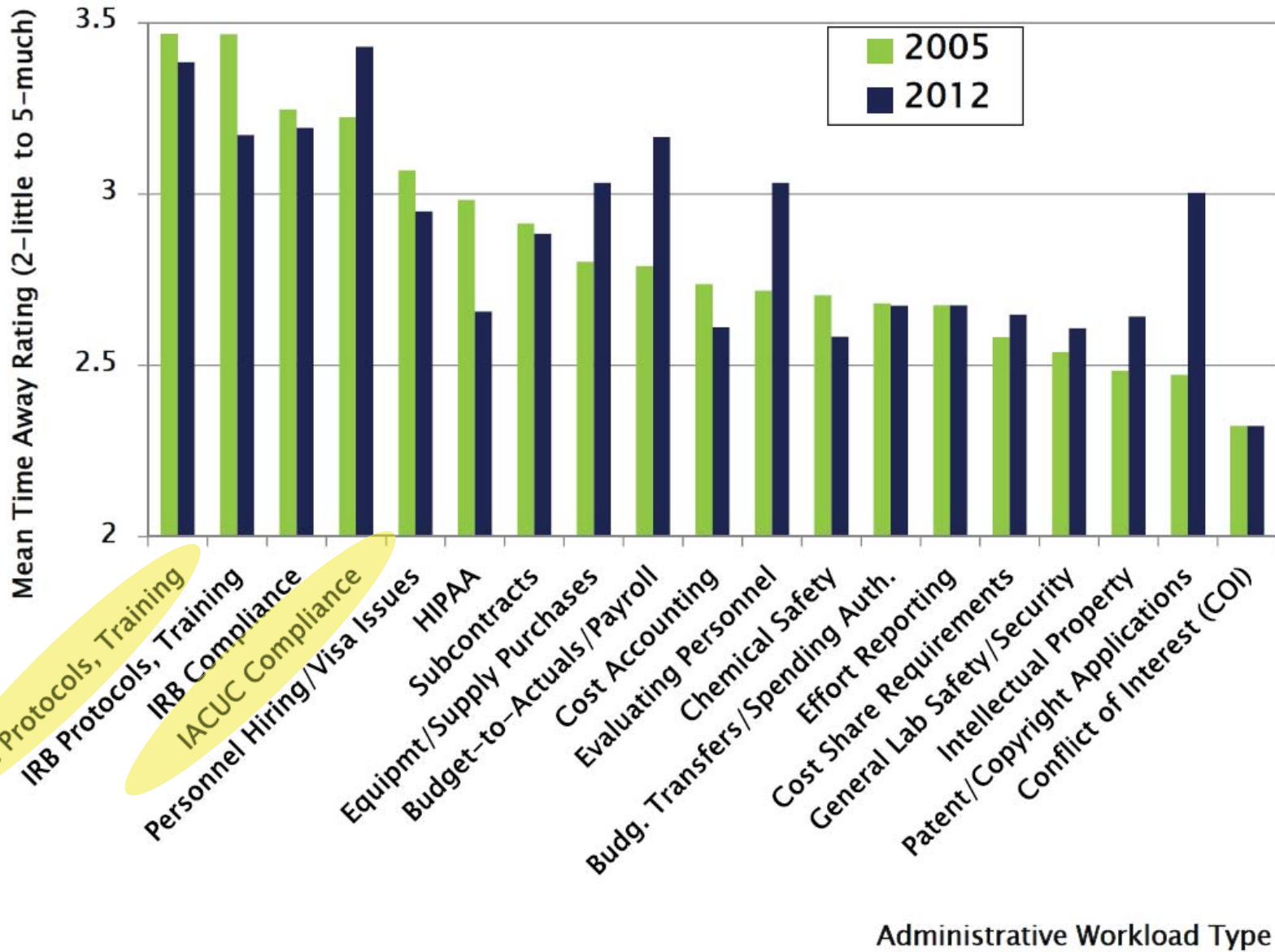
02/27/14

# Workload on Federally-funded Projects



Researchers still report spending less than 60% of their research time actually engaged in research. 42% of their federally-funded research time is spent completing pre- and post-award requirements.

## Burden Rating Comparisons Between 2005 and 2012



# Animal research is as carefully regulated as human research...

- ...but for different reasons
- For humans, we need to assure that the benefits that all gain from the research does not impose an unacceptable burden on research participants.
- Most animal research is conducted for the benefit of humans and unlike humans, animals can not consent to participate or comment on their treatment

# Obligations of the Animal Researcher

(US Govt Principles for the Utilization and Care of Animals Used in Testing, Research and Training)

- Transportation, care and use of animals should be in accordance with the AWA.
- Procedures should be designed with consideration of their relevance to human/animal health, advancement of knowledge or the good of society.
- Selected animals should be of an appropriate species and quality so that a minimum number can be used to obtain valid results.
- Minimization of discomfort, distress or pain. Unless there is proof to the contrary, procedures leading to pain/distress in humans should be considered to cause the same in animals.

# Obligations of the Animal Researcher

(US Govt Principles for the Utilization and Care of Animals Used in Testing, Research and Training)

- Sedation, analgesia or anesthesia should be used for procedures that cause more than momentary pain/distress.
- Animals that would otherwise experience severe or chronic pain should be euthanized.
- Living conditions should be appropriate for the species and contribute to health and comfort.
- Investigators shall be appropriately qualified and experienced.

# Harm-Benefit Analysis



## Scientific Value

To humans  
To animals  
To science  
To society

## Ethical Cost

Pain  
Discomfort  
Distress  
Morbidity  
Mortality

# Relevant Legislation

- **Animal Welfare Act** as Amended (7 USC, 2131-2156).
  - Originally signed into law in 1966 in response to public outcry over reports of dogs and cats being stolen, kept under neglectful conditions and ultimately sold for research use.
  - Now broadly regulates minimum standards of care and treatment of animals in research, exhibition, transport and by dealers.
  - Covers live and dead cat, dog, hamster, rabbit, nonhuman primate guinea pig and other warm-blood animals.
  - Does not cover birds, laboratory rats and laboratory mice
  - Assigns authority for the responsible transportation, care and use of animals to the USDA (APHIS)

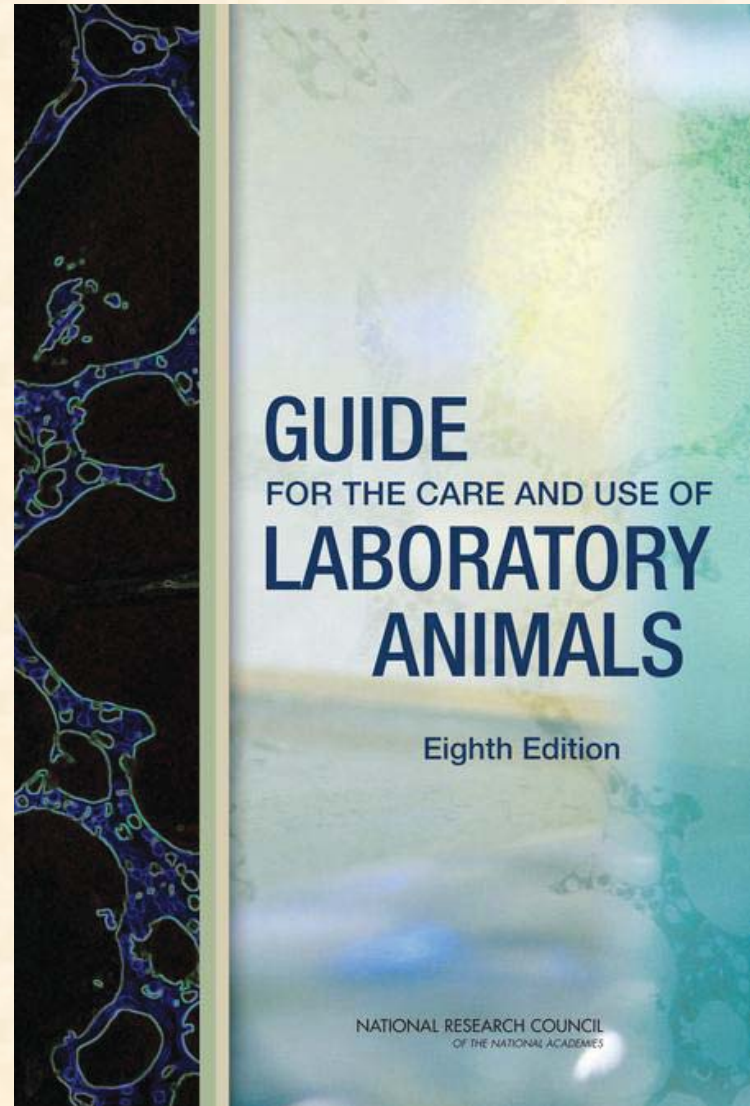


# Relevant Legislation

- **Health Research Extension Act, Sec. 495**
  - Made the [Public Health Service](#) (PHS) Policy on Humane Care and Use of Laboratory Animals statutory
  - Delegates authority for the responsible use of animals in biomedical and behavioral research to the Office of Laboratory Animal Welfare (OLAW) at the NIH.
  - Includes all vertebrate species including rats and mice.

# The Guide

- *Guide for the Care and Use of Laboratory Animals*
- Prepared by the National Research Council of the National Academy of Sciences
- Regarded as the most authoritative source of information on animal care and use
  - Institutional policies and responsibilities
  - Animal husbandry
  - Veterinary medical care
  - Physical plant



# USDA

- Relies on an inspection-based system to ensure compliance.
- Carried out by USDA veterinary medical officers.
- Institution is subject to fines and penalties if violations are found.

The screenshot displays the A.C.I.S. SEARCH TOOL interface. The search results show an inspection report for Loyola University Chicago. The report details the inspection date (February 14, 2013), the inspector (Kenneth Kirstein, D.V.M.), and the institution's information. The report notes that no non-compliant items were noted and that the inspection was completed with the Institutional Official. Below the report, there is a table for the animal inventory.

Inspection Animal Count	Animal Common Name	Animal Group Name
11	CAT ADULT	CATS
108	JAPANESE MACAQUE	NONHUMAN PRIMATES
7	RHESUS MACAQUE	NONHUMAN PRIMATES
13	RHESUS MACAQUE *MALE	NONHUMAN PRIMATES
74	EUROPEAN RABBIT	OTHER FARM ANIMALS

Customer 683

Direct 0  
Indirect 0  
Repeat 0

# OLAW

- Relies on the 'assurance' mechanism to monitor institutional compliance with PHS policy.
- Assurance is a signed agreement stating that the institution will:
  - Provide a description of the institution's program for animal care and use
  - Comply with applicable rules and policies for animal care and use
  - Maintain an appropriate IACUC
  - Appoint a responsible IO for compliance
- Assurance is considered to be the terms and conditions for receiving PHS funds.

# AAALAC

- Association for the Assessment and Accreditation of Laboratory Animal Care
- Voluntary accreditation program
- Program evaluations are performed by council members (animal care and use professionals and researchers)
- Institutions use this to demonstrate their commitment to high standards for the care and use of animals.

# Guiding Principles

- The Three R's – Russell and Burch, 1959
- **Reduction**
  - Using methods aimed at reducing the numbers of animals such as minimization of variability caused by the environment, appropriate selection of animal model, careful experimental design, statistical analysis, use of newer techniques
- **Refinement**
  - Modification of husbandry or experimental procedures to eliminate or reduce unnecessary pain and distress through less invasive techniques, optimal anesthesia/euthanasia, environmental enrichment
- **Replacement**
  - Absolute: non-animal models such as microorganisms or cell culture techniques, computer simulations
  - Relative: use of species lower on the phylogenetic scale

# What is an IACUC?

- Institutional Animal Care and Use Committees are local institutional committees, comprised of individuals with experience and expertise in the use of animals in research, with federally mandated oversight responsibilities.
- At LUC-HSD:
  - Attending veterinarian
  - 16 faculty members
  - 3 community members (non-scientific, non-affiliated)
  - 2 CMF staff
  - IACUC coordinator
  - Compliance officer
  - Representative from Hines

# Why Were IACUC's Developed?

The requirement to establish animal care committees is intended to provide the most constructive assurance that NIH guidelines for the care and treatment of animals are met. **It is far preferable to place primary responsibility for assuring compliance with NIH guidelines on committees within institutions** rather than relying on intrusive Federal inspections.



# Duties of the IACUC

- Reviewing animal use protocols
- Reviewing significant changes to the protocol
- Evaluating institutional compliance with PHS policy, USDA animal welfare regulation and institutional policies
- Monitoring institutional animal care and use programs including inspecting animal facilities
- Reviewing concerns about animal care
- Reporting noncompliance and suspensions to OLAW

# PHS Policy IV.B

“As an agent of the institution, the IACUC shall...

- review and approve, require modifications in (to secure approval), or withhold approval of those components of PHS-conducted or supported activities related to the care and use of animals...
- review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing studies..”

LU# 205844  
Oral Availability of Heparin - Pilot Stu  
(PI)  
**Select LU Number**

- LU# 205844 (Approved)**
  - View Status
  - Routing Form
  - Deactivate Project
  - Place Order
  - DATA Documents
- Research Channel**
  - Instructions
  - New Routing Form
  - Conflict of Interest
  - Review Charges
  - General Research Info
    - Edit Your Keywords
    - Others Profiles
    - Secure Inbox
  - Health Sciences Library
  - Regulatory Compliance
  - Other Tasks
  - Office of Research Services
  - Pivot
  - Reports
  - Manage Rights

Select Existing Create New Discussion Amend Current Duplicate Current Instructions

Click to Select IACUC Form to View IACUC Version 2

Print

**Lu Number: 205844; Species: Rat**

**Primary Investigator: Jeske, Walter**

**Title: Oral Availability of Heparin - Pilot Study**

**Funding Agency: PLx Pharma Inc**

**Other:**

**LOYOLA UNIVERSITY - STRITCH SCHOOL OF MEDICINE**  
Loyola Version: 01 Nov 2010

**ANIMAL COMPONENT OF RESEARCH PROTOCOL(ACORP)**

**Note: Use a separate form for each species.**

The deadline for submission is the last Tuesday of the month. For a schedule of deadline dates and other help on submission, refer to the Office of Research Services website:  
[http://www.stitch.luc.edu/research\\_services\\_internal/node/14](http://www.stitch.luc.edu/research_services_internal/node/14)

For questions regarding the ACORP, or to submit supporting documents, contact the IACUC Administrator and/or secretary.

For USDA policies governing animal research, refer to <http://www.usda.gov/wps/portal/usda/usdahome>

Many policies followed by Loyola, the federal government and outside organizations are based on the Guide for the Care and Use of Laboratory Animals (hereafter called the Guide), available at: <http://www.nap.edu/readingroom/books/labrats/>

The Comparative Medicine Facility, a core facility with the Loyola Office of Research Services, has established standard operating procedures (SOPs) for many aspects of animal use. To view SOPs, refer to: [http://www.meddean.luc.edu/res\\_serv/ors/animal/compmed/facility.htm](http://www.meddean.luc.edu/res_serv/ors/animal/compmed/facility.htm)

# Animal Component Of Research Protocol (ACORP)

- Who will be performing the procedures?
  - Experience, training
- What happens to the animal?
- # of animals, strain and species needed
  - Justification
- Animal care
  - Housing, veterinary care
- Alleviation of pain/distress
  - Anesthesia, analgesia
- Consideration of alternatives
- Euthanasia
- Test substances
- Sample collection

# USDA Training Requirements

## **Animal Welfare Act and Regulations (AWARs):**

“Training of scientists, animal technicians, and other personnel involved with animal care and treatment at research facilities...

Each research facility shall provide for the training of scientists, animal technicians, and other personnel involved with animal care and treatment in such facility...” (Sec. 2143 (d))

# Why is training important?

- Laboratory animal science and medicine are rapidly changing and evolving disciplines
- Helps ensure high quality science is conducted and animal well-being is prioritized
  - Ensure that individuals are trained and qualified in species-specific housing methods, husbandry procedures and handling techniques.
  - Ensure that research staff members performing experimental manipulation are qualified through training or experience to accomplish procedures humanely in a scientifically acceptable fashion.
  - Ensure that staff whose work involves hazardous agents have training or experience to assess potential dangers and select and oversee the implementation of appropriate safeguards.

# Training Requirements at LUC-HSD

- AALAS learning library
- **All investigators:**
  - Basic Training - Working with the IACUC: non-VA version
  - Occupational Health Training
- **Those with direct animal contact:**
  - Species specific
  - Surgical, anesthesia, post-op care

# Experimental Design

- **Lay description**

- How might this research improve the health of people and/or other animals? (harm-benefit analysis)
- Describe the experimental design in a way that reveals what will actually happen to the animals.
- Use non-technical language, avoid jargon
- Mention animals!

- **Scientific plan**

- Brief statement of major specific aims, rationale, objective or didactic/training value of the project.
- The sequence of events to reveal what happens to the animal and their ultimate fate.
- All procedures and manipulations; explain why they must be performed.
- The numbers and types of animals to be used in each specific aim should be listed as accurately as possible.
- For complicated experimental designs, a flow chart, diagram, or table(s) is strongly recommended to help the IACUC understand what is proposed.



## *Guide, p26*

- ‘While the responsibility for **scientific merit** review normally lies outside of the IACUC, the committee members should evaluate scientific elements of the protocol as they relate to the welfare and use of the animals.’
- Primarily with funding body, scientific value relative to ethical cost remains with the IACUC.

# ACORP Review Cycle

- Pre-review
  - Modifications made, as necessary
- Full committee review at monthly meeting
  - Response to concerns, as necessary
- Annual review
- Triennial renewal
- Amendments

# Pre-review

- Administrative pre-review is carried out by the IACUC coordinator to assess completeness of the protocol
- The veterinarian provides the PI with guidance on:
  - animal welfare,
  - animal care,
  - along with design and implementation of study
- Exchanges between the investigator and the veterinarian before the submission of a proposal to the IACUC may address many of the Committee's concerns and could help expedite the review process.

# Methods of Protocol Review

- There are only two recognized methods of review of animal activities by and IACUC:
  - Full Committee Review (FCR)
    - Convened meeting of a quorum of members is required.
  - Designated Member Review (DMR)
    - Conducted by one or more members designated by the Chair
    - All voting members have been provided an opportunity to call for full-committee review

# *Guide* topics for protocol review

- Rationale and purpose of the proposed use of animals.
- Justification of the species and number of animals requested. Whenever possible, animal numbers requested should be justified statistically.
- Availability and appropriateness of the use of less invasive procedures, other species, isolated organ preparations, cell or tissue culture or computer simulation.

## *Guide* topics for protocol review

- Adequacy of training and experience of personnel in the procedures used.
- Unusual housing and husbandry requirements.
- Appropriate sedation, analgesia and anesthesia.
- Unnecessary duplication of experiments.
- Conduct of multiple major operative procedures.

## *Guide* topics for protocol review

- Criteria and process for timely intervention, removal of animals from a study or euthanasia if painful or stressful outcomes are anticipated.
- Post-procedural care
- Method of euthanasia or disposition of animal.
- Safety of working environment for personnel.

# Outcomes of Protocol Review

- There are three possible outcomes of FCR described in PHS policy:
  - Approval
  - Modifications required (to secure approval)
  - Withhold approval
- There are three possible outcomes of DMR described in PHS policy:
  - Approval
  - Modifications required (to secure approval)
  - Request FCR



# Pain Categories

## **USDA Category B - No experimental procedures:**

- Animals bred or purchased for breeding (parents and offspring),

## **USDA Category C – No or only very brief pain or distress, with no need for or use of pain relieving drugs:**

- Observational studies.
- Brief restraint (<15 minutes), behavioral studies of an adapted animal, intravenous and parenteral injections of non-irritating agents, blood collections from peripheral vein, euthanasia using AVMA recommended methods

## **USDA Category D - Potential pain or distress is relieved by appropriate anesthetics, sedatives, or analgesics**

- Major and minor surgery performed under anesthesia (survival or non-survival)
- Painful procedures performed under anesthesia (such as retro-orbital blood collection in rodents).
- Prolonged (>15 minutes) restraint accompanied by tranquilizers or sedatives.
- Invasive blood collection, such as intracardiac or periorbital collection from species without a true orbital sinus such as rats and guinea pigs.

## **USDA Category E - Pain or stress NOT relieved with the use of anesthetics, analgesics, tranquilizers, or by euthanasia.**




- Studies in which animals are allowed to die without intervention (i.e. LD50; mortality as an end-point).
- Studies with endpoints that are painful or stressful.
- Addictive drug withdrawals without treatment.
- Animal undergoing painful/distressful procedures where use of anesthetics, analgesics, or tranquilizers will adversely affect the procedures, results, or interpretation.
- Research on stress, shock or pain, toxicity studies, microbial virulence testing, and radiation sickness.

# Protocol Amendments

- Proposed significant changes in ongoing animal activities must be reviewed and approved by the IACUC prior to implementation.
  - Objectives of the study
  - Non-survival to survival
  - Increase in discomfort
  - Greater degree of invasiveness
  - Species
  - # of animals used
  - Principal investigator
  - Anesthetic agent used or withhold anesthetic
  - Method of euthanasia
  - Duration, frequency or number of procedures performed

# Protocol Amendments

## IACUC Amendments

<b>* Denotes required field</b>	
<b>Lu Number</b>	204877
<b>Species</b>	Rat
<b>Sub Id</b>	1.03
<b>*Amendment Type</b>	<div style="border: 1px solid gray; padding: 2px;">Addition Corporate/Commercial Resubmission Revision</div>
<b>Requested By</b>	Jeske, Walter (WJESKE)
<b>*Justification</b>	<div style="border: 1px solid gray; height: 100px;"></div>
<b>*Identify Sections Modified</b>	<div style="border: 1px solid gray; height: 100px;"></div>
<b>Most Recent Literature Search Date</b>	<input type="text"/> 
<b>From</b>	<input type="text"/> 
<b>To</b>	<input type="text"/> 
<b>Search Terms Used</b>	<div style="border: 1px solid gray; height: 40px;"></div>
<input type="button" value="Save Information"/>	

# Top NCI for FY2012 – IACUC (36%)

- **Consideration of alternatives:** Search described is not associated with the procedures that cause more than momentary pain or distress.
- **Inspection of facilities:** not conducted on a semi-annual basis
- **Complete description of the proposed use of animals**
  - Number of animals used is not accurate with the protocol
  - Additional procedures performed that were not described in the protocol.
- **Semi-Annual reviews:** reports not timely and/or unsigned, minor and significant deficiencies not distinguished, no plan to correcting deficiencies

# Your protocol is approved, and then....

PHS Policy States:

“...the IACUC shall conduct continuing review of each previously approved, ongoing activity covered by this policy at appropriate intervals as determined by the IACUC, including complete review...at least once every three years.”

# Post-approval monitoring

- Does your IACUC?
  - Conduct annual protocol reviews
  - Track unexpected animal death or disease
  - Keep an eye on problem labs
  - Receive veterinary reports
  - Report noncompliance to OLAW
- If yes to any of these examples, you are conducting post-approval monitoring

# Annual Reviews

All continuing protocols are reviewed by the IACUC annually in order to inform the IACUC of the current status of the project; to ensure continued compliance with PHS, USDA and institutional requirements; and to provide for re-evaluation of the animal activities at appropriate intervals.

LU# 20                      Sub ID# 1.01                      Species: Mouse

**PI Submission for Annual Project Review# 1**

CERTIFICATIONS	Status	Section changed
Anesthesia	No Changes	na
Analgesia	No Changes	na
Euthanasia Method	No Changes	na
Experimental Design	No Changes	na
Experimental Drugs/Compounds	No Changes	na
Numbers of Animals Approved	No Changes	na
Lab/Procedure Location	No Changes	na
Personnel Listed on Protocol	No Changes	na
Post-Operative Plan	No Changes	na
Radioactive Elements	N/A	na
Species strain/age/sex/etc.	No Changes	na

Literature Search	
Most Recent	02/19/2014
Search Terms used	
Search Period	02/18/1984 - 02/18/2014

Personnel

[Print](#)

# Inspections

- Federal regulations requires that all animal housing areas, support areas and Principal Investigator laboratories, where animal work is done, be inspected semi-annually.
- CMF facilities:
  - Walls, ceilings, floors clean and well-maintained
  - Equipment and supplies labeled and properly stored.
- Investigator labs:
  - Copy of latest protocol
  - Review procedures being performed
  - Laboratory conditions
  - Controlled substances secured, drugs within date?



# Adverse Events

From time to time, there may be:

- an animal welfare complaint,
- any unusual or unexpected observation while performing experimental procedures,
- An inadvertent protocol deviation,
- an incident noted during post-approval monitoring,
- and/or a possible protocol violation

## INCIDENT REPORT FORM

LOYOLA UNIVERSITY CHICAGO – HEALTH SCIENCES DIVISION  
INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC)  
Bldg 101, Room #0745A  
Phone: (708) 216-4288  
Fax: (708) 216-9399  
[AVALERO@LUMC.EDU](mailto:AVALERO@LUMC.EDU)

This form should be used to notify the IACUC of an animal welfare complaint, any unusual or unexpected observation while performing experimental procedures which may require an amendment to the protocol, an inadvertent protocol deviation, an incident noted during post-approval monitoring, and/or a possible protocol violation. The form should be completed and submitted to the IACUC Office.

- Complaint – Perceived deficiencies in husbandry standards, inhumane treatment of animals, research misconduct, facilities operations, administration/IACUC management and/or the safety/security of animals or other related deficiencies that reflect on our federal assurance or the quality of care and use of these animals.
- Unusual/Unexpected Observation – Any unexpected experimental outcome that may require a modification to an approved animal care and use protocol.
- Incident Review – Inadvertent protocol deviation by one of the individuals listed on the ACORP, which may be perceived as requiring IACUC review.
- Oversight Report – Observations made during routine post-approval monitoring of an animal protocol.
- Protocol Violation – May include animal use without IACUC approval or an activity being conducted that is not in accordance with the description of that activity provided by the Principal Investigator in the ACORP and approved by the IACUC.

DESCRIPTION OF THE INCIDENT:	
DATE AND TIME OF REPORT:	LOCATION:
PRINCIPAL INVESTIGATOR/LAB SUPERVISOR RESPONSIBLE:	
EMAIL:	BLDG./ROOM:
IU#: IACUC#	SPECIES INVOLVED:
REPORTED BY:	

# Just-in-Time

- To increase flexibility and reduce the burden on applicants and IACUCs,
- Allows verification of IACUC approval to be submitted upon request from the PHS when it determines that a grant proposal is likely to be funded.
- Institutions are not required to use JIT: they may still choose to follow the

## Prepare Your Just-in-Time Information

To see how we ask you for your just-in-time information, go to:

- [NIH's Request for Just-in-Time Information](#)
- [Sample Just-in-Time Email From NIAID](#)
- [How and when will I find out if I need to send information just-in-time?](#) in the Just-in-Time questions and answers

Prepare just-in-time information early, but don't send it until we request it.

**End-of-year warning.** We may skip over your application if it comes up for funding at the very end of the fiscal year and your just-in-time submission is not ready. While waiting for you, we are likely funding other applications—and you could lose your chance of funding if we run out of money or time.

**When it's due.** NIH's email doesn't set a due date. Within two weeks of receiving NIAID's just-in-time notification, your institution's business official should submit your other support and human subjects training information. Your grants management specialist may set a different due date.

You don't need to sign because you have a signature assurance on file with your institution.

Since IRB and IACUC approvals may take you more than two weeks to get, your business official may submit these approvals later.

**How to submit.** Your business official should submit PDFs through the just-in-time feature of the eRA Commons Status module.

As you must ensure that just-in-time information is accurate and current, notify us promptly of any substantive changes to information you submit before the award, including changes of PI, key personnel, and the use or approval of vertebrate animals or human subjects.

CS  
OW

# Tips for Protocol Preparation

- Lay abstract
  - Simple language
  - Mention what happens to the animals
- Experimental design
  - Step-by-step what happens to animals
  - Tables, figures (pdf)
  - Check (and re-check) animal numbers
- Training
  - Up-to-date
  - Reflects each procedure to be performed
- 3-year renewals
  - Appendix 8 is required – what was done, # of animals used
  - Update dates
- Breeding protocols
  - All animals count (desired experimental animals, breeders, non-desired animals (sex, genotype))
- Amendments
  - Highlight the changes made

# FAQs

## **Are approved ACORPs from other institutions acceptable in the event that exactly the same procedure is to be used?**

PI needs to submit a new ACORP if live laboratory animal studies will be conducted at LUC-Health Sciences Campus.

## **Can the funding source of an approved protocol be changed? If so what is the mechanism?**

PI e-mail new account# to IACUC office and CMF

PI submits a new and updated ACORP with the Status Info marked as 'This is an unchanged, approved ACORP intended for a new funding source'.

## **What is the mechanism to transfer animals from an existing protocol at another institution to Loyola for an incoming faculty?**

PI needs to contact CMF to request transfer of animals.

CMF request animals health record from source and reviewed by CMF Veterinarian.

If approved, animals transferred to Dr. Cera's holding ACORP or PI's approved ACORP

Quarantine

*It is our obligation when we use any animal in research, be it a rodent or a non-human primate, to do so with compassion, humility, sound ethics and humaneness.*

**Ernest D. Prentice, Ph.D.** University of Nebraska Medical Center  
OLAW Online Seminar June 10, 2010

# Important Contact Information

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