2019 Research Compliance Conference
Orlando, FL
June 10, 2019

From Paper to Electronic: Evolution of an IACUC Protocol Management System

Denise Ancharski-Stutler, MS, CPIA
Administrative Director of the Office of IACUC Administration at the Children's Hospital of Philadelphia

1

Objectives

- Provide an overview of Institutional Animal Care and Use Committee (IACUC) and protocols.
- Identify opportunities within the electronic protocol form to reduce burden.
- Discuss methods to transition from paper to an electronic system.

2

2

Why do we use animals as research subjects?

- Research animals serve as surrogates for humans and other animals. They are our substitutes!
- Point #3 of the Nuremberg Code makes it clear that experiments on humans "…should be … based on the results of animal experimentation…"

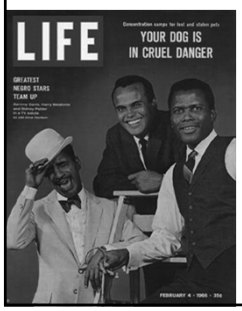
3

3

Animal Research Regulations and the Need for IACUCs - HOW IT ALL BEGAN

- **1960's and 1970's There was public outrage about pets stolen for research.** ***Life and Sports Illustrated***
- **Early 1980's Evidence provided by the press of inappropriate behavior of researchers involved in animal research.**
- **1985 Congress responded to public outrage.**

"The Lost Pets That Stray to The Labs"



"Concentration Camps for Dogs"
Vol. 60, No. 5
Feb. 4, 1966

4

4

The United States Department of Agriculture (USDA)

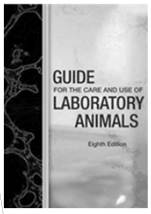
USDA: Law leads to Regulations
Animal Welfare Act
Implemented in 1966.
Animal Welfare ACT revisions 1985
Animal Welfare Regulations 1989

- **The Animal Welfare Act (AWA)**
  - It is the institution's responsibility to represent society's concerns regarding the welfare of animal subjects used at the facility.
  - It is the institution's responsibility to establish at least one committee to assess animal care, treatment, and practices in experimental research.

5

5

National Institute of Health (NIH) Office of Laboratory Animal Welfare (OLAW)



- Health Research Extension Act of 1985
  - Implemented on November 20, 1985.
  - Public Law 99-158. Law Leads to Policy
  - The Guide is to be used "as a basis for developing and implementing an institutional program for activities involving the care and use of animals in Public Health Service (PHS)-funded research.
  - Defined the establishment of Institutional Animal Care and Use Committees (IACUCs).
  - Outlined the responsibilities of the IACUC.
  - PHS Policy requires institution to follow USDA AWRs and the "Guide"

6

6

AAALAC, International

- **AAALAC International is a private, nonprofit organization that promotes the humane treatment of animals in science through voluntary accreditation and assessment programs.**
- **Voluntary accreditation process in which research programs demonstrate that they meet the minimum standards required by law, and are also going the extra step to achieve excellence in animal care and use**
- **<u>Site visits every three years for accreditation.</u>**

7

7

The Institutional Animal Care and Use Committee (IACUC)

- Chairperson
- Attending Veterinarian
- Non-affiliated person
- Other
  - Scientist (PHS Policy)
  - Non-scientist (PHS Policy)
- There may not be more than three members from the same administrative unit

8

8

THE IACUC

- Two functions:
  - Ensure compliance with laws, regulations and policies.
  - Ensure the welfare of animals used in research, testing or teaching.
- Responsibilities include:
  - Review and Approve research protocol and proposed changes to protocols
  - Semi-annual inspection of animal facilities; review of animal care and use program.
  - Investigate complaints about animal care and use.
  - Suspend animal use activities.
  - Provide written reports to and advise the Institutional Official.

9

9

Research Subjects

- USDA-Regulated Species: warm-blooded animals alive or dead (excludes common lab mice and rats, birds bred specifically for research, and farm animals that are used for food or fiber or food or fiber research).
- PHS: all live, vertebrate animals (fish, amphibians, reptiles, birds and mammals).
- Special considerations: multiple survival surgery, food/water restriction, prolonged restraint, novel/innovative experiments.

10

10

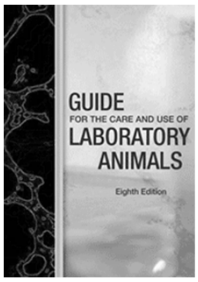
Pain Categories

B No Pain or Distress	C Slight or momentary pain or distress or no pain or distress	D Pain or distress appropriately relieved by analgesia, tranquilization or anesthesia.	E Unrelieved pain or distress
Animals being maintained without any research manipulation.	Holding, weighing or transporting animals (relatively short distances under non-stressful conditions)	Survival/terminal surgical procedures	Burns or trauma
Observation of animal behavior	Injections (nonirritating)	Any post procedural outcome resulting in evident pain, discomfort or distress	Application of noxious stimuli (i.e. electrical shock) that cannot be avoided or escaped
Physical restraint	Blood collection or catheterization of superficial vessels	Genetically engineered phenotype that causes pain or distress that will be alleviated.	Toxicological or microbiological testing, cancer research or infectious disease research that requires continuation until clinical symptoms are evident or death occurs.
Routine husbandry procedures	Collection of body fluids or tissues post mortem	Exposure of blood vessels for catheter implantation	Exposure to abnormal or extreme environmental conditions

11

11

"The Guide for the Care and Use of Laboratory Animals"
(The Guide)



- Guidelines to be followed by all PHS conducted or supported activities involving animals.
- Details
  - Institutional policies and responsibilities.
  - Animal husbandry requirements.
  - Veterinary medical care.
  - Physical plant (facility requirements).

12

12

Protocol review

- What is a protocol?
- A contract between an Institution's IACUC (acting on behalf of the institution) and the research team.
- A document that provides each IACUC member with enough information to allow them to approve animal use in important science that may expose animals to pain and distress and will involve animal death.

- Animal Use Protocols must be compliant with
  - The PHS Policy
  - The Guide
  - The AWA
  - AAALAC
  - AVMA Panel on Euthanasia
  - State and Institutional regulations

13

13

Elements of a Protocol

- Lay Summary.
- Justification for the research.
- Justification for animal numbers and species.
- Description of procedures.
- Search for alternatives.
- Describe pain/distress and methods to decrease or alleviate.
- Support personnel and training.
- Euthanasia

14

14

The Three R's

- **Replacement** – to replace the use of animals with non-animal models (such as virtual models)
- **Refinement** – to refine procedures to minimize pain and distress (including the use of analgesics and appropriate endpoints)
- **Reduction** – to reduce the number of animals used (such as avoiding unnecessary duplication and use of statistical methods)

15

15

Topics to Consider

- Rationale and purpose of the proposed use of animals.
- Availability or appropriateness of the use of less invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation.
- Justification of the species and number of animals proposed; whenever possible, the number of animals and experimental group sizes should be statistically justified.
- Unnecessary duplication of experiments.
- Nonstandard housing and husbandry requirements.
- Impact of the proposed procedures on the animals' well-being.
- Appropriate sedation, analgesia, and anesthesia.
- Conduct of surgical procedures, including multiple operative procedures.
- Description and rationale for anticipated or selected endpoints.
- Criteria and process for timely intervention, removal of animals from a study.
- Method of euthanasia or disposition of animals.
- Adequacy of training and experience of personnel in the procedures and their roles and responsibilities.

16

16

IACUC Review of Animal Use Protocols

- IACUC can approve, require modifications, or withhold approval of protocols.
- There are a few different processes for review of protocols:
  - Designated Member Review (DMR)
  - Full Committee Review (FCR)
  - Administrative Review
  - Veterinary Verification and Consultation (VVC) 2014

17

17

Special Considerations

- Experimental and humane endpoints.
- Unexpected outcomes.
- Physical restraint.
- Multiple survival surgery.
- Fluid or food restriction.
- Use of Non-Pharmaceutical-Grade Chemicals and Other Substance.
- Field studies.
- Agricultural animals.

18

18

Timeline for Regulatory Burden

- 1999: Initiative by the National Institutes of Health.
- 2005 and 2012: Federal Demonstration Partnership Faculty Workload Surveys.
- 2008: University of Michigan article on self-imposed burden.
- 2014: OLAW Notice for VVC.
- 2015: OLAW Notice for animal number justification.
- 2016: 21st Century Cures Act.
- 2017 and 2018: RFIs from USDA and OLAW.

- Reducing burden does not equal reduced animal welfare.

19

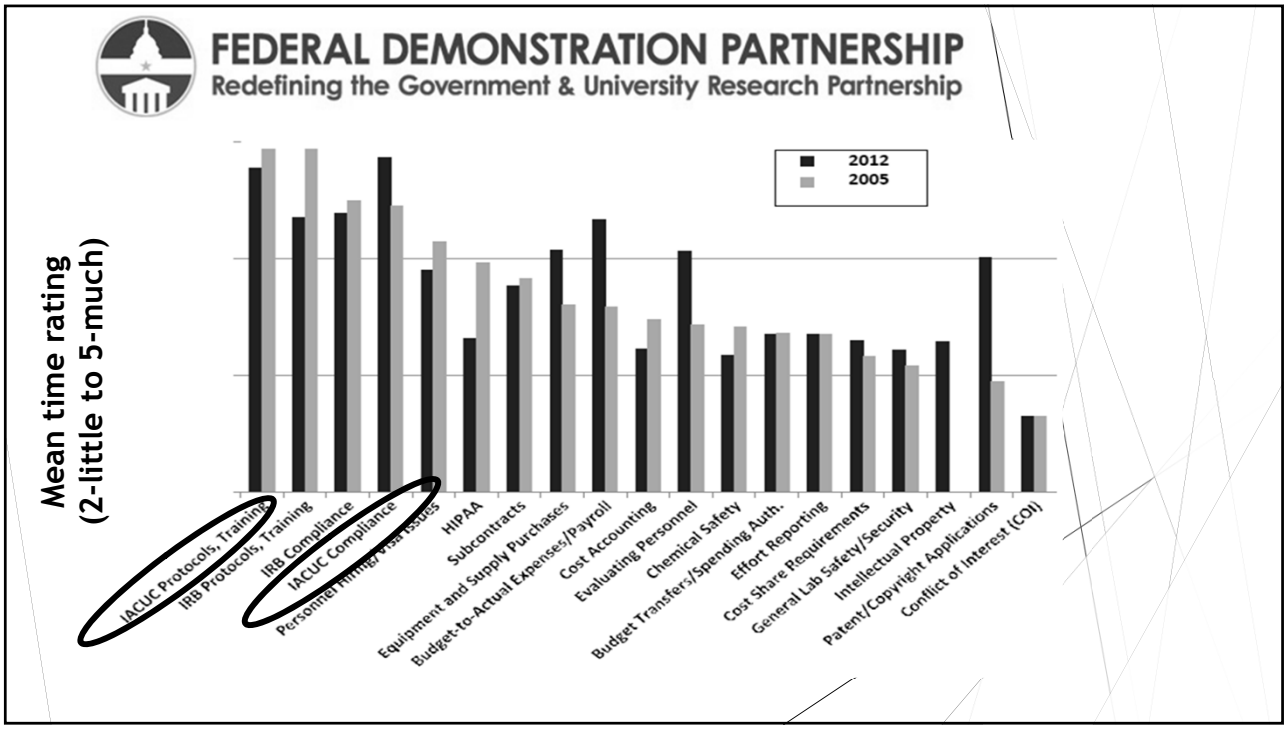
19

Regulatory Burden

- Investment of time and money.
- Source of frustration for scientists.
- Difficulty in recruiting new scientists who want to do animal research.
- Less money and time for animal care and welfare.

20

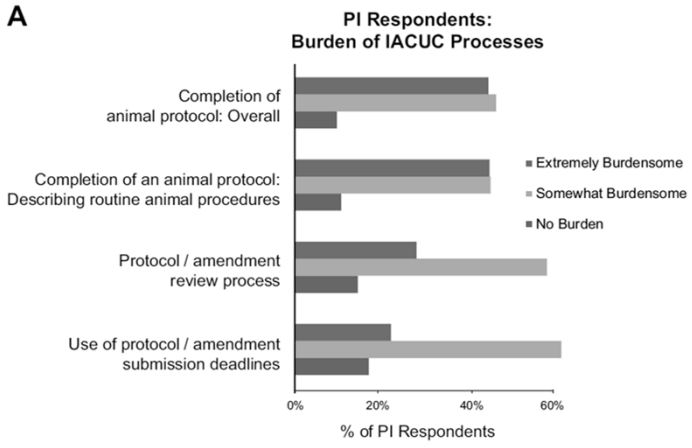
20



21

Sources of Burden

- Specific requirements in laws and regulations.
- Interpretive requirements or guidance by regulatory agencies.
- Institutional interpretations ((self-imposed regulatory burden).



22

22

Many institutions have self-imposed regulatory burden..

2017 IACUC-admin listserv survey of 58 institutions

- 69% annually review all protocols
- 67% require annual reports from PIs
- 31% don't use VVC
- 69% have ≥2 IACUC members for all semiannual inspections
- 83% require a literature search for category D & E procedures in all species

23

23

Identification of opportunities to reduce burden within the electronic protocol form

- COGR Administrative Burden Checklist

- Simplify the IACUC protocol form.
- Standardized and template language .
- Procedure libraries.
- Standardized pre-approved perioperative plan templates for rodents.
- A built-in commonly used drug formulary that will provide the pre-approved dosage, route and frequency of administration.
- Convert formatted text boxes to simple drop down lists for fast data selection/entry and enhanced reporting capabilities.
- Drop down list of euthanasia methods/dosages that are pre-approved for a given species

24

24

Electronic Protocol Enhancements

- Original system was paper based with protocols existing in PDFS and Word documents.
- Reports were mainly generated manually within Excel.
- eIACUC Huron Research Suite® customized through Bad Rabbit Consulting.
- Began in 2010 and rolled out in 2012.
- Two phase rollout: Back Office and then Researcher Implementation.
- Continued refinement and enhancements over the past seven years.

25

25

Standardized Procedure Library

- Architecture has been developed within the protocol form.
- Currently in the process of generating entries for standard procedures that are done at our institution.
- Goal is to have institution standard procedures and research team specific standard procedures.
- Research teams can utilize these standard descriptions or have the option to modify to meet their needs. These changes would be flagged so the IACUC can focus on the edits.

26

26

In System Collaborative Review

- Collaborative review tool utilizing Microsoft Word-like functionality.
- Inline comment functionality—highlight a section and leave a comment right where you want it
- On-the-page collaboration—respond to comments, direct reviewers to specific sections, all within the document itself.
- Research teams reply to comments in line and the identity of reviewers is unknown to the research team.
- Want to explore tagging functionality that will let commenters tag each other in comments, and send notifications to catch their attention.

27

27

Identification of opportunities to reduce burden within the electronic protocol form

- Allow for approximate or range of numbers of animals needed.
- Allow for flexibility within the protocols.
- Replace required documentation on how a proposed protocol was not unnecessarily duplicative with a simple attestation.
- Discontinue the USDA pain and distress classifications for non-Animal Welfare Act regulated species.
- Reduce IACUC requirements for experimental details that are unrelated to the health and safety of animals.

28

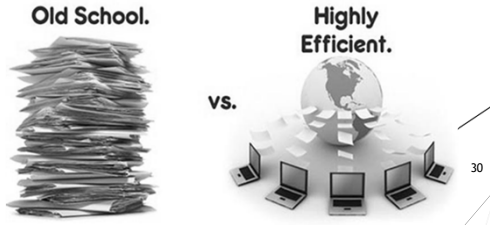
28

Compliance Unit Standard Procedure (CUSP)

29

Transition from paper to electronic..

- Many different electronic protocol management systems available.
- There are some institutions that have a "home-grown" system.
- The shift from paper to electronic system will be substantial. Items to consider:
  - Cost for development and continued maintenance.
  - Impact to all stakeholders.
  - Other systems used within other areas of research compliance.
  - Communication is key to all stakeholders, especially the researchers.
  - Ability to generate reports from the system.
  - Contingency plans.
  - Time investment by all parties.



30

30

Methods of Transition

- There is no right or wrong way.
- Need to retain the current data that is in the protocol.
- May need to consider running dual systems until all protocols are transitioned over.
- The shift from paper to electronic system will be substantial. Items to consider:
  - Cost for development and continued maintenance.
  - Impact to all stakeholders.
  - Other systems used within other areas of research compliance.
  - Communication is key to all stakeholders, especially the researchers.
  - Ability to generate reports from the system.
  - Contingency plans.
  - Time investment by all parties.

31

31

Methods of Transition

- Upload PDFs of all protocol documents into the electronic system.
- Create a bulk import process for sections or the entire protocols.
  - Take information that is on paper form and match it to the electronic form.
  - Create excel sheets that have this correlation data.
  - Develop code and process to run this electronically.
- Have research team convert their protocols from paper to the electronic system.
  - Offer this as an option at the time of transition.
  - At next annual or three year renewal.
  - At time of next amendment submission.
- Have IACUC staff enter all paper protocols into new electronic system.
  - Consider hiring additional staff to complete this.
  - Once entered, research teams are responsible for ensuring accuracy of information.

32

32

THANK YOU!

33