Essential Attending Veterinarian / IACUC Interactions in a Successful Animal Care and Use Program (ACUP)

(Communication and Networking Track)

April 1, 2016
4:15 pm - 5:30 pm

PRIM&R's 2016 Institutional Animal Care and Use Committee Conference • Bellevue, WA March 30-April 2

Disclosure:
Robert Barbee, John Bradfield, and John Norton

We have no relevant personal/professional/ financial relationship(s) with respect to this educational activity

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Panelists

- **R. Wayne Barbee**, Ph.D.
  Professor, Departments of Emergency Medicine and Physiology
  Chair, IACUC
  Virginia Commonwealth University

- **John Bradfield**, DVM, PhD, DACLAM
  Senior Director
  AAALAC International

- **John Norton**, DVM, PhD, DABT, DACLAM
  Professor, Department of Pathology
  Director, Laboratory Animal Resources
  Duke University

Essential AV / IACUC Interactions

- Day-to-day oversight of ACUP is shared between the AV and IACUC
- 8th edition of the *Guide* provided additional collaborative emphasis among ACUP participants while reinforcing the responsibilities of both the AV and the IACUC
- The AV may designate other individuals to perform tasks but retains the responsibility for those activities including responsibilities related to their role on the IACUC

Contemporary ACUPs are Complex

Many challenges:

- Varied animal models
- Animal Rights activists concerns
- Decentralized programs with aging facilities
- Regulatory expectations seem to always be increasing
  - Correspondingly, oversight by the IACUC and compliance groups seems to be intensifying

Emerging Landscape

- Contemporary animal programs are more complex
  - Traditional species without genetic manipulations are decreasing
    - CRISPR technology
    - ‘Humanized’ animal models
    - Aquatics, etc.
  - Specialization of IACUC Support Staff, e.g., Administrators
  - **Development of animal compliance offices and specialized monitoring paradigms**
  - **Fear of noncompliance: regulatory and oversight expectations have increased**

Significant dollars and effort are being spent to fund the infrastructure of the ACUP

But **Who** is primarily responsible for achieving / maintaining compliance with regulations and guidance?

- IO
- AV
- IACUC
  - Administration
  - +/- Compliance
- PI…+/-

Program Components
- Institutional Administration
- Animal Environment
- OHSP
- IACUC
- Veterinary Care
- Physical Plant

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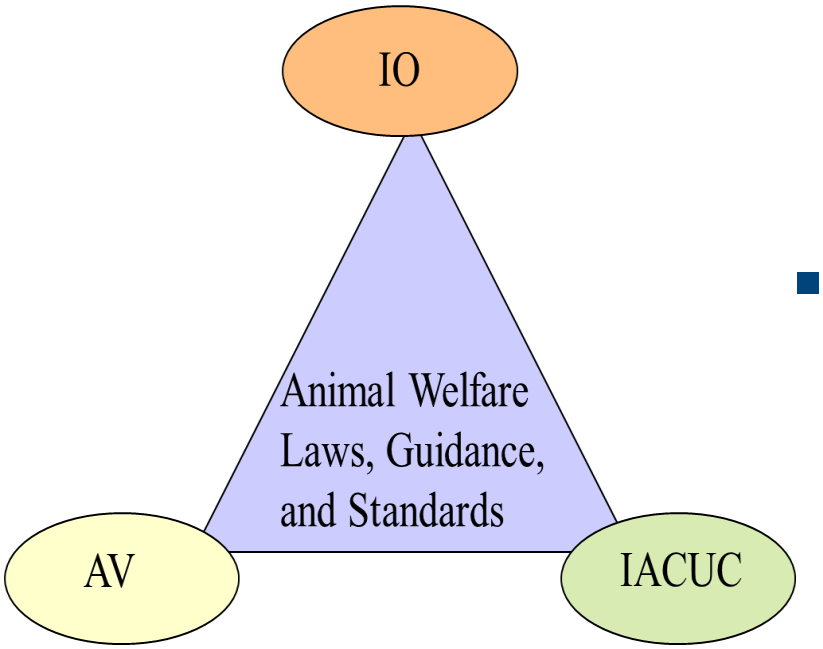
Collaboration and Effective Leadership



- The three entities must work together to provide oversight and support of researchers
- Must be an expert on regs / guidance and understand how to efficiently and effectively apply to the ACUP

Key Players in an ACUP

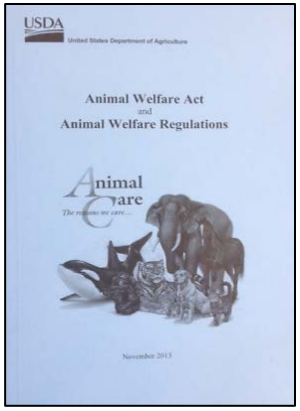
- A Program that includes these functions and **establishes a balance among them** has the best chance of efficiently using resources while attaining the highest standards of animal wellbeing and scientific quality
- Not discounting the role of the IO, but ‘day-to-day’ activities of the ACUP lie with the IACUC and AV, again working collaboratively to achieve their tasks
- Unfortunately in many programs, there has been a blurring in the lines of responsibilities and functions, which unfortunately can contribute to ‘burden’ for ACUP players (including researchers)

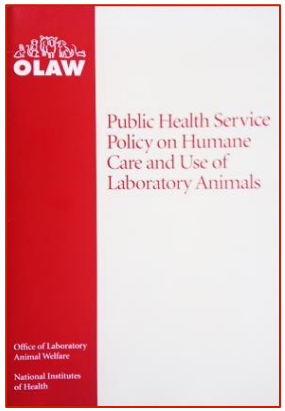
Self-Oversight

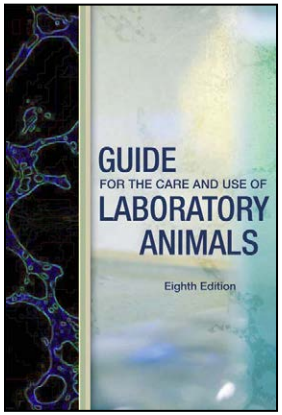
The IACUC and AV (along with the IO) must be expert on the regs / guidelines…

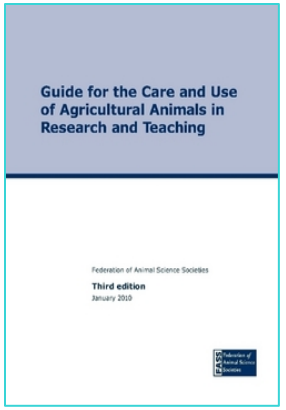
In most institutions it is the IACUC with the AV that interprets the regulations and the Guide and subsequently establishes institutional expectations and processes.

Some Level of Burden is Unavoidable









+

- Ethical principles/practices
- Sound scientific methods
- Societal mandates

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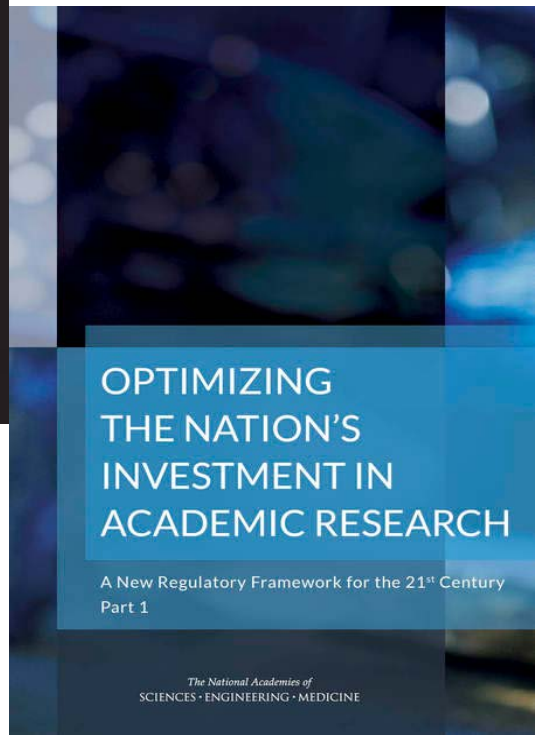
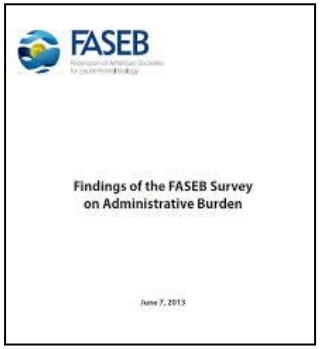
FASEB
Findings of the FASEB Survey
on Administrative Burden
June 7, 2013


NATIONAL SCIENCE BOARD
REDUCING
INVESTIGATORS'
ADMINISTRATIVE
WORKLOAD FOR
FEDERALLY FUNDED
RESEARCH


OPTIMIZING
THE NATION'S
INVESTMENT IN
ACADEMIC RESEARCH
A New Regulatory Framework for the 21st Century
Part 1
The National Academies of
SCIENCES · ENGINEERING · MEDICINE

Key Findings:

- Avoid implementing unnecessary requirements
- Disseminate information
- Review and refine IACUC processes
- IACUC to provide rapid approval of proposals
- Concerns included:
  - IACUC being overly burdensome where oversight is beyond regulations
  - IACUC is risk averse beyond regulations
  - Increasing regulations/policies



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Optimizing the Nation's Investment in Academic Research

"It takes considerable expertise to sort through the regulations, rules, guidance, and best practices that have been established and have evolved over time. Consequently, **institutions have tended to over-interpret the requirements so as to err conservatively and not be out of compliance** or inconsistent with what could be construed as grant conditions. For various reasons, many institutions have tried to maintain a zero tolerance for risk of noncompliance in their programs. In many cases, **the result has arguably been unnecessary burdens borne by institutions and investigators**."

The National Academies of Science, Engineering and Medicine (2015)

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Institutionally-induced excess burden?

- Protocol review – increasingly complex process
- IACUC workload – increased delegation of responsibilities
- Institutional risk aversion – increasingly complex compliance structures
  - Trend toward centralized, compliance offices
  - Increased compliance mechanisms
  - One-size-fits-all approach
  - Scientific disconnect?
  - Fragmented / silos?
- Institutional over interpretation – policy & expectation
- Intolerance/ inflexibility / “gotcha” mentality
- Benefit to science and animal welfare?

Researchers are feeling the weight / burden

Researcher carrying the weight of regulations, **whether external or internal**…thus, the AV and IACUC must work together

Goals of Session

- Provide scenarios for several aspects of AV and IACUC interactions that are essential within a successful ACUP
- Scenarios will target potential pitfalls that may occur without sufficient AV and IACUC interactions

Learning Objectives:
Avoiding Pitfalls in AV / IACUC Interactions

1. Planning for all animal procedures involving Pain Categories D or E (USDA Section 2.31(d) in general and section 2.31 (d)(1)(iv) through (xi) specifically. "Involve in their planning, consultation with the attending veterinarian or his or her designee."
2. Significant administrative amendments – Veterinary Verification & Consultation (VVC)
3. Training of IACUC members / research team in use of anesthetics, analgesics, sedatives, euthanasia agents, etc.

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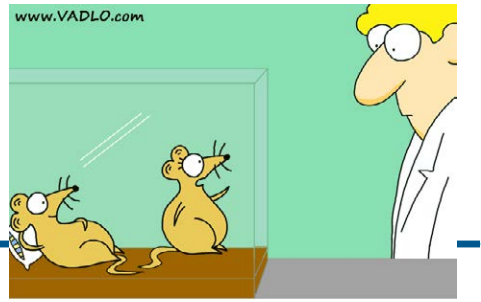
PI responsibilities (AWR's)

1) Procedures avoid or minimize p/d
2) Consider alternatives for procedures that cause more than momentary or slight p/d
3) Not unnecessarily duplicate
4) Procedures involving more than momentary p/d
   a) Appropriate anesthesia, analgesia, sedation (unless justification for withholding)
   b) Involve the AV or designee when planning
   c) Avoid the use of paralytics without anesthesia

Scenario 1 – vet review



"Do you even have a girlfriend?"

- A PI proposes to inject tumor cells (IV, IC) in p-53KO mice and study tumor progression with a novel moAB targeted to cell surface antigens….
- What are the relevant considerations for the vet?
  - Biosecurity (source of tumor cells)
  - OHSP/ biocontainment/ housing (human derived tumor cells)
  - Expertise of personnel (IC), AAT?
  - Acute effects of procedure (IC)
  - Monitoring of animals (frequency, by whom, what signs(?), methods [IVIS, etc.])
  - Experimental/ Humane endpoints
  - Options for supportive care/intervention (to achieve exp. endpoints)
  - Euthanasia

Scenario 2 – vet review

- At Big-Eastern University a veterinarian in the IACUC office routinely conducted pre-review of protocols to expedite the overall review process. Meanwhile a clinical veterinarian is called to examine several guinea pigs that are behaving strangely. Upon examination the veterinarian notes recent surgical wounds. Some animals are somewhat unresponsive and others have tremors. Members of the lab said that these signs are expected as they have induced aberrant CNS neural activity.
- What are the considerations for the vet(s)?
  - Are the clinical conditions inherent in the conduct of these type of studies? Or might these be unanticipated effects?
  - What is the appropriate course of action for the clinical vet?
  - Is there a concern about the way Big-E performs vet pre-review?

Specific responsibilities of the AV
(project/ protocol review)

- Consider/anticipate potential impact to animal health and well-being (inform IACUC, PI & care staff)
- Recommend methods to minimize & alleviate p/d
  - Preemptive, multimodal analgesia regimens
- Provide guidance/ expertise on medications, dose rates, routes of administration and duration of action
- Surgery and Postop care
- Develop schedules for animal monitoring
- Establish humane endpoints (w/ PI and IACUC)
- Training – personnel expertise
- OHSP – zoonoses/ hazard control
- Preserve scientific integrity

Significant administrative amendments - Veterinary Verification & Consultation (VVC) – new category of review!

- Traditional approval of significant protocol changes – full committee review (FCR) or designated member review (DMR)
- New category – administrative – based on ***IACUC reviewed/approved*** policies in ***consultation*** with veterinarian ***authorized*** by IACUC
- Vet NOT conducting DMR – serves as expert to ***verify*** that compliance w/ approved policy appropriate for animals.

Significant administrative amendments - Veterinary Verification & Consultation (VVC)

- Veterinarian ***consultation*** must be documented!
- Includes changes in:
- anesthesia, analgesia, sedation or experimental substances
- Euthanasia approved by AVMA Guidelines for the Euthanasia of Animals
- Duration, frequency, type or number of procedures performed on animals

VVC Scenario #1

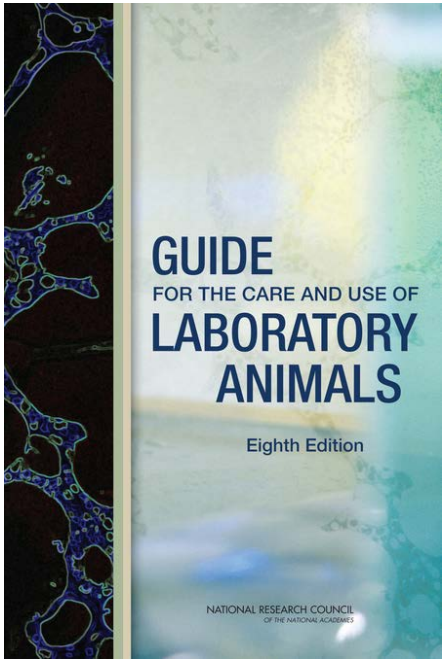
- Approved protocol allows administration of buprenorphine following trauma/hemorrhage in rats
- Principal Investigator (PI) notes pica behavior ~ 1-2 days after initial dose of buprenorphine
- PI calls AV, asks for switch to morphine
- AV ***consults*** IACUC approved formulary, ***verifies*** drug and dose
- Same day approval following note in protocol

VVC Scenario #2

- Approved protocol allows hemorrhage in conscious rabbits to study vasomotor paralysis
- PI notes sympathetic withdrawal leading to cardiovascular collapse
- PI calls veterinarian, asks for switch to less severe hemorrhage for longer duration to avoid sympathetic withdrawal
- Vet ***consults*** IACUC policy, ***verifies*** this change is allowed
- Same day approval following note in protocol

Training of IACUC members and research team in use of anesthetics, analgesics, sedatives, euthanasia agents, etc.

- The Guide states: "All personnel involved with the care and use of animals must be adequately educated, trained, and/or qualified in basic principles of laboratory animal science to help ensure high-quality science and animal well-being."



Training and Education (2011 *Guide*)

- "Institutions are responsible for providing appropriate resources to support personnel training and the IACUC is responsible for providing oversight and for evaluating the effectiveness of the training program."

- An Effective Training Program requires coordination of program components, including input from the AV

Training and Education (2011 *Guide*)

- AV input is particularly important for procedures involving animals be conducted in a manner that avoids or minimizes discomfort, pain or distress
- Selection of the most appropriate analgesic or anesthetic should reflect professional judgment as to which best meet clinical and humane requirements without compromising the scientific aspects of the research protocol

Scenario 1: Surgery in Investigator Laboratory

- During a veterinary visit to a busy investigator's lab, a student was performing abdominal surgery on a mouse located on a benchtop. Induction of anesthesia was through placing the mouse inside a bell jar containing gauze saturated with isoflurane. Although the surgery was only 3-5 minutes, the student was not monitoring depth of anesthesia after induction and no additional anesthesia was administered.
- Note: Lab personnel noted that the IACUC had conducted an inspection 2 weeks ago while a similar surgery was occurring

Scenario 1: Surgery in Laboratory

- What are the relevant considerations for the veterinarian and IACUC?
  - OHSP concerns?
  - Surgical area appropriate?
  - Expertise of surgeon?
  - Training in administration of anesthesia administration?
  - Training of animal monitoring during anesthesia?
  - Experimental/ humane endpoints
  - Sufficient analgesia
- Any concerns over IACUC members being able to recognize issues during inspections?

Scenario #2: Training of Personnel

- During a visit to the Murphy's Law Vivarium, the following items were observed:
  - Numerous cages were extremely dirty and had not been changed at the appropriate time
  - Three mice with different health problems had not been not identified
  - Some animals had not received treatments
  - Although PPE was readily available, individuals were not using it

Scenario #2: Training of Personnel

- Would the observations indicate poor performance or lack of training?
  - Could be both
- How do you differentiate between poor performance and inadequate training?
  - Do individuals have a history of performance issues?
  - Discuss the observations with individuals working in this area?
  - Are training records available for individuals?
  - Did the training address the observations?
  - Are these findings isolated to this vivarium or are similar observations occurring in other animal areas?

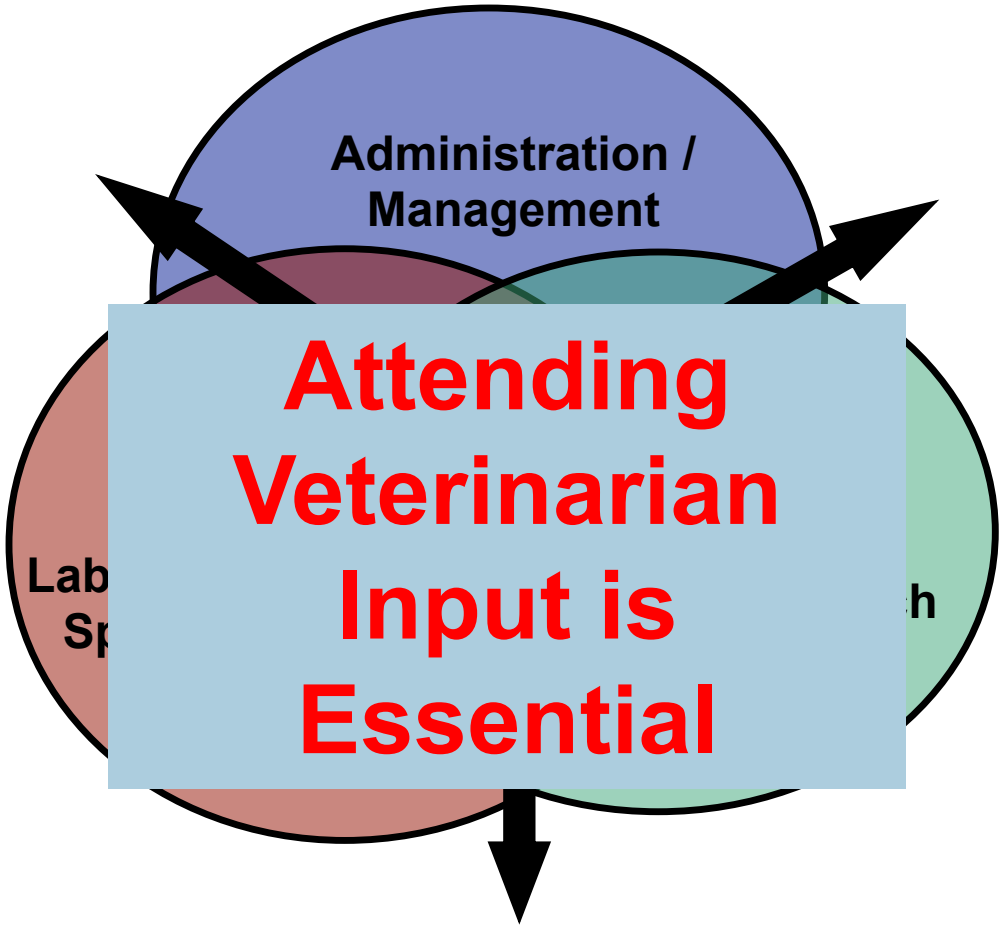
Scenario #2: Training of Personnel

- If these observations appear to stem from a training issue, what are some questions that you would ask about the training program?
  - competency of the trainer? How are other people performing that have been trained by this person?
  - Are proper SOPs in place?
  - What is the structure of the training (e.g., didactic and hands- on)?
  - Was there demonstrated competency?
  - When did individuals receive training?
  - Any refresher training and mechanism?
  - QA program? Oversight by manager or PI?

Scenario #2: Training of Personnel

- Should the AV communicate the findings / discuss the scenario with the IACUC?
  - Considerations:
    - Severity of observations, particularly if animal health issues?
    - A pattern of observations in this Vivarium?
    - Others
- Inadequate training may compromise the care of animals and the safety of personnel

Training Gradients in ACUPs



Benoit JN and Bayne K.(2005) Training the trainee: the institution's responsibility to the often forgotten. Lab Animal (34):46-50.

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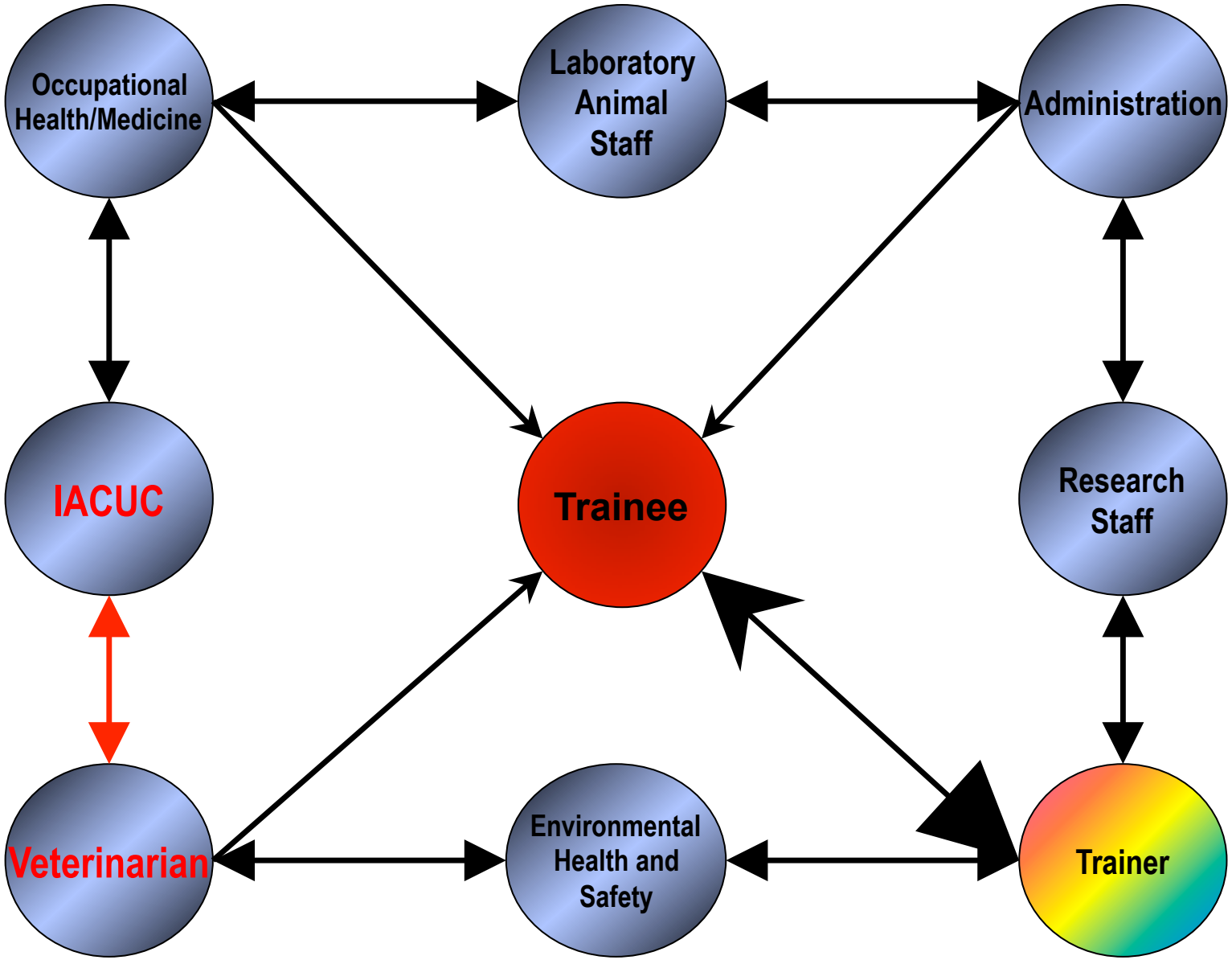

Occupational Health/Medicine
Laboratory Animal Staff
Administration
IACUC
Trainee
Research Staff
Veterinarian
Environmental Health and Safety
Trainer

AV and IACUC working together to pull the researcher through the regulatory process

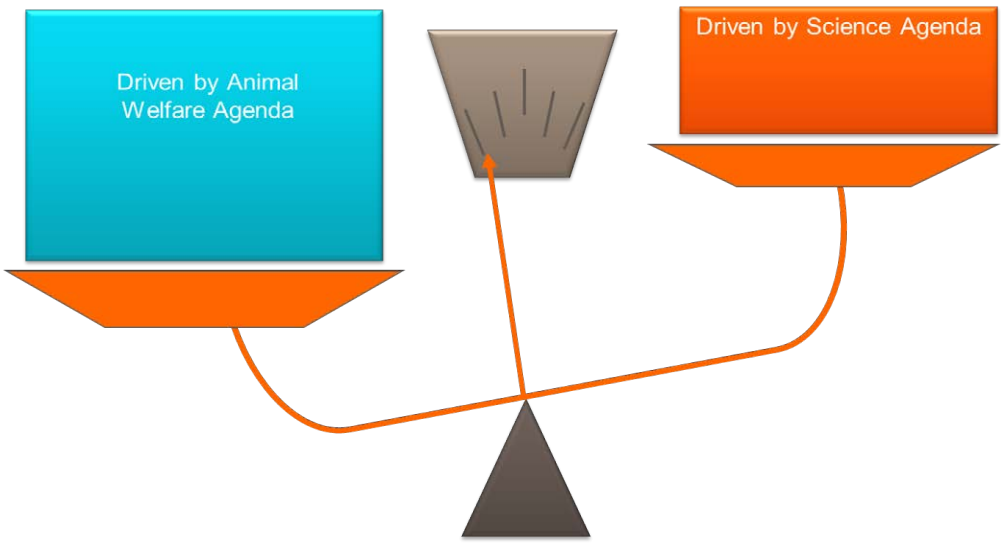
Punitive effect on researchers

Summary

Take home points:

- Some aspects of regulatory burden are immutable, but institutions play a significant role in excessive regulatory burden

- Essential AV and IACUC communication must occur for efficient and effective ACUPs
- Reducing unnecessary administrative burden is a benefit for all animal programs



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Questions?

Thank you!