Troubleshooting the VVC process

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Disclaimer

- I hope everything I mention and my interpretation of the regulations and guidance is accurate.
- I do not represent the USDA, OLAW, or AAALAC International or their point-of-view.
- I do not get offended if I am verbally corrected among peers, so please speak-up.
Functions of the IACUC: review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the use of animals in ongoing activities.

Review includes determining that the proposed significant change is conducted in accordance with:
- PHS Policy
- Your OLAW Assurance
- The Guide
- Animal Welfare Act/Regulations

Approval via FCR or DMR

DMR can be used if each IACUC member is provided with a list of proposed significant change to be reviewed and full committee review is not requested.
Animal Welfare Act / Regulations

- **IACUC Functions:** Review and approve, require modifications in (to secure approval), or withhold approval of proposed significant changes regarding the care and use of animals in ongoing activities.
- Review includes determining that proposed activities are in accordance with the Animal Welfare Act/Regulations unless acceptable justification for a departure is provided.
- Approval via FCR or DMR.
- DMR can be used if each IACUC member is provided with a list of proposed significant change to be reviewed and full committee review is not requested.
**NOT-OD-14-126: Guidance on Significant Changes to Animal Activities**

- **Definition:**
  - Significant changes include changes that have, or have the potential to have, a negative impact on animal welfare.
  - In addition, some activities that may not have a direct impact on animal welfare are also considered to be significant.

- Provides guidance on significant changes which can be handled via:
  - DMR or FCR
  - Administrative with Vet (Veterinary Verification and Consultation)
  - Administrative
May be handled administratively according to IACUC-reviewed and -approved policies in consultation with a veterinarian authorized by the IACUC.

The veterinarian is not conducting DMR, but is serving as a subject matter expert to verify that compliance with the IACUC-reviewed and -approved policy is appropriate for the animals in this circumstance.

Consultation with the veterinarian must be documented.

The veterinarian may refer any request to the IACUC for review for any reason and must refer any request that does not meet the parameters of the IACUC-reviewed and -approved policies.
This includes changes in:

- anesthesia, analgesia, sedation, or experimental substances
- euthanasia to any method approved in the AVMA Guidelines for the Euthanasia of Animals; and
- duration, frequency, type, or number of procedures performed on an animal.
Seems simple ...... right?
simple is beautiful.
Duke Process for Amendments

- IACUC approved policy for amendment category and approval method
- Amendments are categorized as either:
  - Category I: SC reviewed by Full Committee Review
  - Category II: SC reviewed by the Significant Change Subcommittee (a DMR process)
  - Category III: Minor change reviewed by IACUC Leadership Review with a veterinary review (a DMR/VVC hybrid). These are changes determined by the IACUC of having a potential welfare well-being impact, but generally the outcome is more favorable and in the best interest of the animal
  - Category IV: Minor change reviewed by IACUC Leadership Review (a DMR/administrative hybrid)
  - Category V: Administrative Reviews by OAWA Staff (an other process)
- Only amendments reviewed by FCR or SCSC are sent to the entire IACUC membership for an opportunity to call for FCR
- All actions are reported to the FC
- Any amendment can be placed in a higher category by the reviewer and any amendment can be called back to the IACUC for reconsideration

https://sites.duke.edu/oawa/
Category III: IACUC leadership review that incorporates a veterinary review

- Change in anesthetic, analgesic, or sedation drug regimen which
  - Decreases the potential for pain or distress
  - Is a substitute for a protocol approved drug that is unavailable
  - Is a change from a pharmaceutical grade to a non-pharmaceutical grade
- Change in humane-endpoint which decreases potential for P/D
- Addition of a procedure which should decrease adverse outcomes
- Change in animal care/monitoring practices which increase monitoring
- Addition of a sample collection within IACUC-accepted standards
- Repeat experiments, within parameters
- Addition of a noninvasive sampling/analysis (e.g., imaging)
- Change/additional euthanasia procedure within AVMA Guidelines and Duke Policy
- Delayed weaning request within Duke’s policies
- Single housing for animal welfare within Duke’s policies
- Addition of a non-hazardous experimental substance
Why this works

- Was a VVC process before the VVC process was ‘cool’
- Meets the spirit of a VVC process
- Quicker turn-around than our DMR and FCR approval process
- The documentation and record keeping process is the same for amendments providing a sense of security
- It is familiar, historical, comfortable, and understood

http://clipart-library.com/clipart/6cr5a4Kgi.htm
What could be refined

- **Minor with vets** go through 4, possibly duplicative, reviews
  1. Administrative
  2. OAWA Vet review
  3. DLAR Vet review
  4. IACUC Chair or Vice-Chair Review for final approval

- Process could be simplified
- Turn-around could be shorter
- Not utilizing the flexibility allowed within the regulations
Implementing a new process: Troubleshooting

- **Purpose**
  AKA, why are we doing this if what we have works and everyone knows how to do it?

- **Interpretation**
  AKA, will OLAW, USDA, or AAALAC International do something to us if we interpret it wrong?
Implementing a new process: Troubleshooting

- Looked at what works and what doesn’t
- Discussed what the IACUC needs to approve to start a new process
- Reviewed
  - Who might be impacted with a change
    - IACUC Office
    - Veterinarians
    - PI’s
    - IACUC members
- Areas of concern
  - Implementing
  - Documenting
  - Notifying PI’s of change in process
  - Consistency: Crafting guidance to help with decision tree
    - IACUC Administrative personnel
    - Veterinary
Our current process
Replace or Refine

- **Input**
  - IACUC Program Committee
  - AV and Veterinary Groups
  - IACUC Office
  - Others

- **Refine**
  - Worked off our current process
  - Started with a draft policy and SOP then went from there ....
Where we were going: Policy

- **Veterinary Verification and Consultation**, the following changes will be handled via VVC if the procedure category is already approved in the IACUC animal use protocol and would not change or would decrease the potential for pain or distress. Changes in:
  - Anesthesia, analgesia, sedation, or experimental substance(s). Includes:
    - Changes in compound, dose, route, volume, frequency, or duration
    - Changes in experimental substance(s) if they are fundamentally similar compounds documented in the literature with regard to their safety and toxicity in the same species
    - Change from pharmaceutical grade to non-pharmaceutical grade compounds
  - Euthanasia to any method approved in the [AVMA Guidelines for the Euthanasia of Animals](https://www.avma.org/avi/app/avmalite/avmawebapp/search.do?op=submit&query=Euthanasia+Guidelines). Includes:
    - Acceptable
    - Acceptable with conditions, when the conditions are met
Where we were going:
Policy, con’t

- Duration, frequency, type, or number of procedures performed on an animal. Examples include:
  - Stock, strain, or genetic modification of the same species
  - Supportive care
  - Humane-endpoints
  - Peri-operative or peri-procedural monitoring
  - Survival to non-survival surgery
  - Timing of euthanasia
  - Sample collection
  - Identification or genotyping
  - Animal acquisition or disposition
Submitted like an amendment

Vet review and determination

IACUC office processes

VVC

PS: Send amendment to designated VVC veterinarian

VVC Vet: Determine if meets qualifications for a VVC review

VVC Vet: Notify IACUC@Duke.edu that this is a significant change

VVC Vet: Communicate with PI to clarify any concerns. CC IACUC@Duke.edu to capture modifications.

VVC Vet: Send Disposition to IACUC@Duke.edu
Approved, SC, or call for Full Committee Review

PS: SC - Process as described for SC

PS: FCR - Ensure that SC receives all standard reviews prior to FC meeting (OAWA pre-reviewer, AV or designee review)

PI notified, IACUC presenter identified and provided amendment and DMR/CL questions/comments/concerns. Place on agenda for future FCR meeting.

PS: Approved - Document in protocol, database, and send notification to PI
Where are we at now…
What other facilities are doing

IACUC Admin and CompMed Listserve Question

Hello CompMed,

If you currently have a VVC process for select significant change amendments as described in item #2 of Guidance on Significant Changes to Animal Activities NOT-OD-14-126<https://urldefense.proofpoint.com/v2/url?u=https-3A__grants.nih.gov_grants_guide_notice-2Dfiles_NOT-2DOD-2D14-2D126.html&d=DwIFAg&c=imBPVzF2SOB6GMVOLcstEGHo6i6YHLRSj_g74adc&r=qS XR6wvlACVp67f051nNwMekuAD7Gr9fqlNfproc0Y&m=K01- uHLLwO3RGYcSHtGlnIe9KSS8rfKKWly9GhEe4c&s=r8byuA7n-SpMfh2f73RM1ZHeEgB5AE_k-AuVYVj1HSLSw&e=> and are willing to share, I would love to:

- Hear about your process and/or have a copy of your SOP, Policy, Guideline, etc.

- Get your feedback on how it is working: Pros, Cons, etc.

If you don't have a VVC process and are willing to share your reason(s) why one hasn't been implemented that would be great as well.

Full disclosure, I am speaking about the VVC process at the ACLAV forum and want to get a sense of what is going on in the community and what are the pros/cons of this process. Any information provided will be anonymous and generalized.

Thanks,
Anna
This includes changes in:

- anesthesia, analgesia, sedation, or experimental substances
- euthanasia to any method approved in the AVMA Guidelines for the Euthanasia of Animals; and
- duration, frequency, type, or number of procedures performed on an animal.
Responses

HELP
About the respondents

- 12 process like amendments
- 6 outside amendment process (vet approves)
  - 3 - 30 days to get into the protocol
  - PI or Veterinarian Responsibility
- 1 was industry
- Did they like it?
Anna’s Comments

- Term change vs. addition varied
- Most had stipulations
  - Safety approval
  - Max number (injections, location, et.)
  - Other Policies, SOP, Guideline, etc.
- One had a checklist
- A universal theme = could not increase the potential for pain or distress or have an negative animal welfare impact
Summary for IACUC approved references

Personal Communications
Websites
IACUC Formularies
Book Formularies
Journals
Professional Judgement
Summary for
Anesthesia, analgesia and sedation
Summary for Experimental substances

Administration

Concentration/Dose/Volume

Safe

Non-pharmaceutical

PathogenType

SameClass

ContractAgents

NewTumorCellLine

Route

Innocuous

NoSideEffects

Antimicrobials

VeterinaryDrug
Summary for Euthanasia

AVMA Guidelines
IACUC Policy
Professional Judgement
Other things approved by VVC

- Animal Numbers
- Funding
- Personnel
- Annual Reviews
- Training
- Title
The VVC Policy with the least amount of burden:

- Any Veterinarian can approve:
  - Any change/addition of anesthesia, analgesia, sedation, or experimental substances.
  - Any change/addition of euthanasia, and
  - Any change/addition of procedures that are welfare neutral or positive.

Reference: Professional Judgement

PI or Vet has to provide documentation for protocol

Take Home Message...
Before you “assume” try this crazy method called “asking”.
What is a new procedure?

- The definition can be broad
- The determination needs to be inline with the IACUC approved policy
- Rule-of-thumb: no increase in pain, distress, or negative animal welfare
- When in doubt go up the ladder of scrutiny
- Where people go wrong: okay to approve via VVC if approved in another protocol
REMEMBER

- FCR
- DMR
- VVC
- Administrative

ALL ARE REAL METHODS OF APPROVAL
True/False about VVC
The IACUC

- A list of the proposed activity needs to be sent to the membership
  - False
- Any IACUC member can call it for FCR?
  - True
- The IACUC needs to be provided a list after approval?
  - False
- An IACUC member can call a VVC approved activity back for reconsideration by the IACUC?
  - True
True/False about VVC
The IACUC

- IACUC approval of the VVC policy/SOP/practice includes
  - Voting for approval at a FC meeting
    - True, if an IACUC practice
  - Presenting at a FC meeting with no objections
    - True, if an IACUC practice
  - Distribution to the membership with no objections
    - True, if an IACUC practice
  - Approval by an IACUC subcommittee
    - True, if an IACUC practice
  - Approval by a designated member
    - True, if an IACUC practice

- The IACUC needs to re-approve the VVC process every 3-years
  - False, re-review
True/False about VVC
The Veterinarian

- The IACUC has to approve the Veterinarian
  - True
- The veterinarian has to be the Attending Veterinarian or designee
  - False
- The veterinarian has to be a clinical Veterinarian
  - False
- The veterinarian cannot be a Research Veterinarian
  - False
- The veterinarian must be a subject matter expert
  - False
- The veterinarian has to be employed by the institution
  - False
- The veterinarian has to be on the IACUC
  - False
True/False about VVC
The Veterinarian

1. IACUC should know and trust the vet
2. The vet should be named by position, title and in policy
3. Avoid COI (e.g., is personally involved in the activity)
4. Avoid vet shopping
Will online systems restrict the VVC process?
Animal Welfare
Will they care who approves?
My 2-cents

- Interpret the regulatory guidance
- Create a simple process that works for your program
- Have institutional backing
- Implementing it well
- Re-review (≤ every 3-years) and check for additional guidance
- Avoid reactive, one-off changes