



Implementing Guidance on Significant Changes: One Institution's Experience

Lon Kendall, DVM, PhD, DACLAM
Elaine Kim, BS, CPIA
Colorado State University



OLAW Online Seminar
September 8, 2016

1

Objectives

- Review NOT-OD-14-126; in particular we will outline key components of a functional VVC.
- Provide institutional and programmatic context for CSU's implementation of NOT-OD-14-126.
- Outline how CSU IACUC chose to implement VVC at our institution, including an overview of our VVC policies.



2

Objectives (cont.)

- Examine CSU's VVC review process, certain aspects of our VVC policies, and a comparison of protocol review metrics for Classic IACUC Review vs. VVC.
- Discuss CSU SOP revisions and why we made these changes
- Apply VVC in specific situations using scenarios.



3

NOT-OD-14-126: Definition of a Significant Change

“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.”

NOT-OD-14-126: Paragraph 1

- Nonsurvival to survival surgery
- Procedure results in greater pain, distress or invasiveness
- Housing location not part of the animal care program
- Species
- Study objectives
- Principal Investigator
- Impact on personnel safety

NOT-OD-14-126: Paragraph 2

Defines changes that may be reviewed administratively according to IACUC-reviewed and approved policies in consultation with a veterinarian authorized by the IACUC.

- Anesthesia, analgesia, sedation or experimental substances
- Euthanasia to any AVMA approved method
- Duration, frequency, type or number of procedures

NOT-OD-14-126: Paragraph 3

Defines changes that may be reviewed administratively according to IACUC-reviewed and approved policies.

- Increase in animal numbers

NOT-OD-14-126: Paragraph 4

Changes that may be handled administratively without an IACUC approved policy, consultation or notification include:

- Updated contact information
- Typographical and grammatical errors
- Change in personnel (not PI)

Veterinary Verification and Consultation (VVC)



“policies” = guidance documents, standard operating procedures, and drug formularies.

Institutional Context: CSU Research

- CSU ACUP: 600+ protocols
- Veterinary school
- Veterinary clinical studies
- Infectious disease
- Biomedical research
- Ag satellite facilities
- Increasing private sponsors
- FDA regulated work

Two Policies

VVC Process developed by IACUC—2 documents:

- Protocol Review Process
 - FCR
 - DMR
 - VVC
 - Administrative
- Performance of Repeat Procedures
 - Outlines what procedures can be amended under VVC

Implementation of NOT-OD-14-126 at CSU

Drugs	<i>Anesthesia, analgesia, sedation, experimental substances</i>
Euthanasia method	<i>Any method approved in AVMA Guidelines for the Euthanasia of Animals</i>
Procedures	<i>Duration/frequency/type/number of procedures performed on an animal (Diehl et al, J App Tax 21:15-23, 2001)</i>

VVC Review Process

- Amendment evaluated by IACUC Administrators to determine if it meets VVC policies.
- If the amendment falls into one of the categories under our VVC, then it gets assigned to VVC Review.
- AV verifies online with the appropriate section from the policies.
- IACUC office processes amendment approval.

VVC Review Process (cont.)

- If AV believes it does not fall under VVC, but it was assigned to VVC, then s/he comments that it needs to be sent out for DMR, usually with a rationale.
- IACUC office reroutes amendment for Classic IACUC Review in online protocol system.

Additional Considerations

VVC revisions since implementation in October 2014:

- Experimental substance administration
- Additional strains/sources of animals
- Space requirement changes
- Final disposition clarification
 - Adoption, euthanasia, transfer to other protocols

Additional Considerations (cont.)

VVC revisions (cont.):

- Examples of “duration, frequency, type of procedures”
 - Nasal, buccal, fecal collections
- Number of procedures (no increase pain, distress, or invasiveness)
- Reference materials used with the policy

VVC Review Documentation

- Veterinarian includes their rationale in their amendment review online.
- IACUC office includes this in the monthly meeting minutes, allowing the entire IACUC to review.
- Any question about DMR/FCR vs. VVC/administrative review → Goes to Classic IACUC Review.

Communication of VVC Implementation

- Quarterly Lab Liaison meetings
- IACUC Office and AV provided short Q&As at department faculty meetings
- One-on-one communications with researchers

CSU Protocol Metrics

- Classic IACUC Review vs. VVC Review: January to August 2016:
 - Average: 24 days vs. 4.5 days or fewer
 - Percentage of total amendments: about 19%
- Classic IACUC Review vs. VVC Review: January to December 2015:
 - Average: 26 days vs. 6 days or fewer
 - Percentage of total amendments: about 18%

Scenario #1

PI approved for use of ketamine/xylazine anesthesia in mice.

They want to expand the dose range listed in the protocol.

Scenario #1: Result

If change is within parameters of formulary → VVC

If change is not within parameters of formulary
→ Classic IACUC Review

Scenario #2

The PI is approved to euthanize their rats by cervical dislocation while under isoflurane anesthesia.

They would like to amend their protocol to include euthanasia by exsanguination while under anesthesia.

Scenario #2: Result

VVC—exsanguination under anesthesia is an AVMA approved method of euthanasia

Scenario #3

The PI has euthanasia followed by tissue collection procedure included on their protocol.

They want to amend it so that they can collect the tissues while the animal is under anesthesia and still alive, then euthanize after tissue collection.

Scenario #3: Result

This is an additional procedure.
Additional procedures cannot be reviewed by VVC per
OLAW guidance, therefore, referred for Classic IACUC
Review.

Scenario #4

A PI has blood collection in dogs approved at 1, 12,
and 24 hours after test article administration.

They would like to amend the protocol to include
additional blood collection time points at 4, 16,
and 20 hours.

Scenario #4: Result

VVC per CSU policy that outlines the volume of
blood that can be collected in a 24 h period based
on the blood volume of the animal.

If the volume collected exceeds the guidelines,
then it gets referred to the IACUC for review.

Scenario #5

A protocol is approved to perform cystocentesis in cats to evaluate biomarkers.

The PI would now like to amend their protocol to include blood collection at 1, 6, and 12 hours to evaluate biomarkers in the blood.

Scenario #5: Result

Although blood collection guidelines are outlined in our policy, since this is a new procedure to the protocol, it is not eligible for VVC and must be reviewed by the IACUC.

Scenario #6

PI protocol involves placing a vertebral disk fusion device in sheep followed by 8 week recovery period, then euthanasia.

They would like to transfer the animal to another IACUC approved protocol for a terminal surgical procedure.

Scenario #6: Result

This is not specifically addressed in the OLAW guidance; however, the CSU IACUC policy on VVC review has included disposition of animals as a component of VVC.

Since sheep are being transferred to a protocol that does not involve more pain/distress/invasiveness than original protocol, it is eligible for VVC.

However if transfer request was for a survival surgery, this would require IACUC review.



31

Question #1

My institution is concerned about increasing the likelihood of getting into non-compliant situations with VVC implementation. The potential risks appear to outweigh the benefits.

How did CSU handle this issue and what did their IACUC say?

32

Question #2

How has CSU navigated the documentation requirements of VVC implementation with their online protocol system?

33

Question #3

Could you please provide how the VVC process is different from veterinary care? Or are they the same thing?

34

Questions?



35



OLAW Online Seminars

December 15, 2016

Self Evaluation and Reporting:
Always Let the Guide be Your Conscience

George Babcock, PhD,
University of Cincinnati College of Medicine and
Shriners Hospitals for Children

36
