

Making changes: when is VVC appropriate?

Jerry Silverman, DVM

“Why are we wasting energy trying to distinguish between a minor amendment and a major amendment?” asked Joanie Green, the new IACUC senior administrator at Great Eastern University. It seemed to her that if there was a request to add a procedure to a protocol it was to be considered an amendment, nothing more or less. “Are you saying that adding a small subcutaneous implant is as important as adding a cardiac valve replacement?” asked Bob Thorne, a clinical veterinarian. Green responded that it had nothing to do with the level of difficulty or risk to an animal, but whether or not there was a need for IACUC review.

“Look at it this way,” she said, “if you add a subcutaneous implant as an experimental procedure, it’s an amendment to the protocol and it gets reviewed by the IACUC. If you add a heart valve replacement to a study it’s also an amendment that gets reviewed by the IACUC. The first is usually a minor procedure and the second is always a major procedure, but they’re both amendments that require IACUC review.”

After some additional discussion it became obvious that the real problem was that Thorne believed a “minor” procedure could be added to a protocol via the process of veterinary verification and consultation, as described

in NIH notice NOT-OD-14-126 (ref. 1), if the IACUC had previously approved the methodology for the procedure. Green, on the other hand, was of the opinion that NOT-OD-14-126 allowed for *changes* to be made by veterinary verification and consultation, but the *addition* of a new procedure, even a “minor” one, to a previously approved protocol was not a change and required IACUC review. What is your opinion?

1. National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126. (National Institutes of Health, Washington, DC, 26 August 2014).

RESPONSE

Designated member review

Jeffrey J. Etue, BS, LATG

This situation asks, “Can a new ‘minor’ procedure, such as a small subcutaneous implant, be added to the protocol via the process of VVC if the IACUC had previously approved the methodology for the procedure, or does the procedure require IACUC review?”

The Public Health Service *Policy on Humane Care and Use of Laboratory Animals* (PHS Policy; IV.B.7; ref. 1) requires that 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.” The National Institutes of Health issued notice NOT-OD-14-126, *Guidance on Significant Changes to Animal Activities*² to help IACUCs decrease the burden for full committee review (FCR) and designated

member review (DMR) for some significant protocol changes by allowing veterinary verification and consultation (VVC).

According to NOT-OD-14-126 paragraph 2.a-c., the VVC can handle some significant protocol changes concerning “a. anesthesia, analgesia, sedation, or experimental substances; b. euthanasia to any method approved in the AVMA Guidelines for the Euthanasia of Animals; and c. duration, frequency, type, or number of procedures performed on an animal.”² NOT-OD-14-126 does not define what constitutes a procedure. Thorne could argue that VVC could handle this amendment as the number of procedures performed on this animal will change to add a small subcutaneous implant. However, OLAW’s online seminar “*Implementing Guidance on Significant Changes: One Institution’s Experience*” states that procedures exclude surgeries.³

This small, subcutaneous implant amendment is addressed in paragraph 1.b., which covers changes “resulting in greater pain, distress, or degree of invasiveness” and

possibly 1.e., which includes a “change in study objectives”, of NOT-OD-14-126 (ref. 2); each of which require traditional IACUC review. Therefore, this amendment should go to the IACUC chairperson to decide on further action. Since the IACUC approved this type of procedure before, it may not warrant FCR but instead DMR could be appropriate. For Thorne, to go any further questioning review of this amendment appears erroneous and adding it by the process of VVC could lead to citations.

Research institutions should have a comprehensive policy in place compliant with NOT-OD-14-126 (ref. 2) to address amendments and enforce consultation with the IACUC chair for review. This would prevent the argument presented and any citations from the regulatory agencies.

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).

- National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126. (National Institutes of Health, Washington, DC, 26 August 2014).
- OLAW online seminar (2016, September 8). *Implementing Guidance on Significant Changes: One Institution's Experience*. https://grants.nih.gov/grants/olaw/educational_resources/webinar_09082016.htm

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RESPONSE

Has it been approved?

John A. Salig, M.S., LATG, CPIA

In this scenario, Green, the IACUC administrator, is basically correct. According to *Guidance on Significant Changes to Animal Activities*¹, any of the following changes must be approved by one of the valid IACUC approval methods described in the PHS Policy (IV.C.2; ref. 2), that is, by either Full Committee Review, or Designated Member Review:

- “a. from non-survival to survival surgery;
- b. resulting in greater pain, distress, or degree of invasiveness;
- c. in housing and or use of animals in a location that is not part of the animal program overseen by the IACUC;
- d. in species;
- e. in study objectives;
- f. in Principal Investigator (PI); and
- g. procedures that impact personnel safety.”

Adding either of the procedures described by Green would fit under either situation a, b or e above. As minor as a procedure may be, if it is a new procedure being added to a protocol, according to the Guide, it has to be approved by the IACUC.

The Veterinary Verification and Consultation process (VVC) which Dr. Thorne refers to can be used to make significant changes to animal activities that are already part of a protocol which was previously reviewed and approved.

No matter what classification the amendment is given, the animal's welfare should prevail.

A Word from OLAW

In response to the questions posed in this scenario, the Office of Laboratory Animal Welfare (OLAW) provides the following clarifications.

Veterinary verification and consultation (VVC) is a method for approving significant changes to a previously approved protocol.¹ It may not be used to add a new procedure that was not previously approved on the protocol. Such a change should be reviewed and approved by full committee review (FCR) or designated member review (DMR).

There are two parts to approving a significant change by VVC. The first part is when the IACUC approves a policy, SOP or guidance that describes the significant changes acceptable to the IACUC. The second part is when a veterinarian authorized by the IACUC, in consultation with the research team, verifies that the requested change is in compliance with the IACUC-approved policy and appropriate for the specific situation and animal(s). The veterinarian is not conducting DMR, but is verifying compliance with the IACUC policy and that the change is appropriate for the animals in this circumstance. The consultation with the veterinarian must be documented.¹

An example of when VVC is appropriate is as follows. The IACUC has a VVC policy that describes acceptable parameters of blood collection. The IACUC approved a protocol to use one of the approved methods of blood withdrawal in its policy. The IACUC may use VVC to permit the research team to make a significant change, such as collecting additional samples or changing the location of the blood withdrawal, providing it is within the parameters specified in the policy. However, VVC may not be used to add blood collection for a protocol that was not approved for blood collection.

1. National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126. (National Institutes of Health, Washington, DC, 26 August 2014).

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- National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126. (National Institutes of Health, Washington, DC, 26 August 2014).
- Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).

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RESPONSE

New procedure requires IACUC review

Deyanira Santiago, MBA, RLatg and Ann Marie Dinkel, MBA, RLatg

The disagreement between Green and Thorne is not whether the procedure should be approved by the IACUC, but when it should be approved. Green believes

that an additional procedure versus a change in procedure will require FCR or DMR for approval. Thorne believes that Veterinary Verification and Consultation (VVC) is appropriate in this instance. *Guidance of Significant Changes to Animal Activities*¹ states that the VVC may be used for “review and approval of proposed significant changes to animal activities.”

The investigator has requested an additional procedure to the protocol, which was not in the original submission. The VVC guidance was meant to alleviate administrative burden on both the IACUC and the researcher. However, it does not remove the IACUC's responsibility to review procedures added to a protocol, regardless of whether the procedure is being viewed as major or minor. If the investigator wanted to change the method of implant from a small incision to say an injectable method, and the IACUC has an already approved policy for these types of procedures, than the significant change in procedure could be administratively handled via the VVC

process. However, this does not appear to be the case. Ms. Greene is correct in insisting that the new procedure should be reviewed by the IACUC via either DMR or FCR.

In the future, these questions and gray areas might be avoided by the development and approval of guidance documents or SOPs to address these matters in a more standardized way. It may benefit the institution if

within their VVC policy, the IACUC clearly defines what they consider to be a change in protocol and what types of specific procedures can be handled via the VVC process. Once the IACUC has determined these procedures, SOPs or other guidance documents should also be developed and approved for the specific procedures, i.e. blood collections, genotyping, dosing methods, etc.

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1. National Institutes of Health. *Guidance on Significant Changes to Animal Activities*. Notice NOT-OD-14-126. (National Institutes of Health, Washington, DC, 26 August 2014).

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