

The Authority of Quality Assurance

Great Eastern University (GEU) IACUC was concerned with the increasing number of non-compliances for rudimentary issues that, in theory, should have been eliminated through their robust training program. Although the IACUC employed a full-time Post-Approval Monitor (PAM), Mr. Cooper, who was tasked with assuring adherence to IACUC-approved protocols and evaluating the proficiency of techniques being performed, the committee felt that the program needed a more proactive method for reducing non-compliance, such as a quality assurance (QA) program. In the IACUCs opinion, a QA program could reduce the occurrence of non-compliance

by reviewing programmatic expectations with animal users and evaluating lab-specific processes before the opportunity to engage in non-compliance arose.

The IACUC successfully secured additional funding from the Institutional Official and hired two QA specialists. The QA program developed quickly; by year end the QA Team completed almost 150 lab visits. As part of the initiation of the QA program, the IACUC, using the flexibility provided in Footnote 8 of the PHS Policy¹, developed a policy authorizing the QA Team to “fix” issues discovered during QA visits and periodically report back to IACUC.

The QA teams first annual report to the IACUC included a list of issues that were found in labs during QA visits and that the QA specialists fixed on the spot. Specifically, issues that didn't have a direct impact on animal welfare and/or were not a direct non-compliance. These issues, found in USDA-regulated species and non-regulated species, included:

- In the lab of a Principal Investigator (PI) who has three IACUC-approved protocols, animals were euthanized under Protocol #1 with a method listed only on Protocols #2 and #3.
- Death was confirmed (after euthanizing via CO₂ inhalation) with an appropriate (AVMA-approved) secondary method of euthanasia, but the specific method used was not included in the IACUC-approved protocol.
- A lab was performing activities in a location that wasn't included in the IACUC protocol (GEUs IACUC requires locations to be listed and IACUC-approved) but was commissioned and approved for animal activities.
- Incomplete and/or inaccurate post-operative surgical records for two cohorts of animals, but all activities were performed according to the protocol.

During GEUs most recent inspection by their Veterinary Medical Officer (VMO), the VMO questioned the legitimacy of the IACUC delegating the review (and investigation) of concerns involving the care and use of animals.

What do you (and/or your IACUC think):

- (1) Has the IACUCs policy on the authority of the QA program exceeded the flexibility provided in the PHS Policy (Footnote 8)?
- (2) Does GEUs IACUC policy create a scenario where the IACUC is disengaged from the programmatic expectations?

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Reference
 1. Public Health Service. *PHS Policy on Humane Care and Use of Laboratory Animals*. (U.S. Department of Health and Human Services, National Institutes of Health, Bethesda, MD, 2015). Page 12

COMPLIANCE CONSIDERATIONS

The Protocol Review coordinators offer the following compliance considerations:

1. Footnote 8 of the PHS Policy

Functions of the IACUC, per the PHS Policy¹, include to review and inspect, at least once every six months, the institution's program for humane care and use of animals and all of the institution's animal facilities, respectively, using the *Guide* as a basis for evaluation.

Footnote 8 directly relates to the above functions and states: “The IACUC may, at its discretion, determine the best means of conducting an evaluation of the institution's programs and facilities. The IACUC may invite *ad hoc* consultants to assist in conducting the evaluation. However, the IACUC remains responsible for the evaluation and report¹.”

2. Flexibility of Footnote 8

It is well known that Post-Approval Monitoring (PAM) is accomplished in numerous ways and include semi-annual inspections and GEUs Quality Assurance (QA) program. While all facilities must be inspected semi-annually, there is no requirement that *all* facilities must be inspected at the same time. In fact, many institutions perform semi-annual inspections on a rolling basis (e.g., a group of facilities are inspected each week vs. spending several weeks in an intense effort to visit all facilities).

Similarly, the method by which the program review is conducted can include staggered evaluations of one or more components of the program, such as a quarterly report to the IACUC of the QA

specialists PAM and other laboratory evaluations through their QA visits. The QA specialists are, essentially, ad-hoc consultants (that is, if they are not voting members of the IACUC).

On the condition that the IACUC is provided with the results of the QA activities and can perform an evaluation and review of those activities and outcomes, then GEUs IACUC is taking advantage of, and working within the scope of the flexibility provided in Footnote 8.

3. Does GEUs IACUC policy create a scenario where the IACUC is disengaged from the programmatic expectations?

In this particular scenario, it is the opinion of the authors that GEUs IACUC policy on the authority of the QA program is not creating a disengaged IACUC. However, if the QA program did not report out to the IACUC, if the IACUC did not review the outcomes of the QA visits, etc., then yes, the policy could create disengagement of the IACUC from its required functions.

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Disengaged or Dynamic?

To evaluate whether the IACUC in this scenario exceeds regulatory flexibility by authorizing the Quality Assurance (QA) team to “fix” issues, it is best to first review the associated regulatory expectations of an IACUC. PHS Policy¹ requires IACUCs to evaluate the animal program and inspect all animal facilities once every six months. Footnote 8 of the PHS Policy allows IACUCs to “determine the best means of conducting an evaluation of the institution’s programs and facilities¹.” The Animal Welfare Regulations² mirror PHS Policy and, in addition, require IACUCs to involve at least two committee members in the semiannual evaluations and allow them to utilize ad-hoc consultants².

Provided that GEU includes at least two IACUC members in its semiannual program and facility reviews for USDA-regulated species and does not exclude any members from these reviews², neither PHS Policy nor the Animal Welfare Regulations prohibit IACUCs from employing QA professionals to assist in the review of the program and facilities. Rather, regulation seems to reassure the IACUC that seeking assistance is advisable.

Although the practice would be acceptable, and granted the flexibility of Footnote 8 is mentioned, the scenario presented does not explicitly state the addition of the QA program is intended to alleviate the IACUC of their semiannual duties. Instead, the scenario demonstrates an

IACUC that proactively sought assistance to ensure the research community they serve is aware of their expectations and are provided the assistance they need to satisfy said expectations. In response to question two of the scenario, GEU’s IACUC, with the added support of a policy authorizing the QA staff to identify concerns and periodically apprise the committee of their actions, seems to be the opposite of disengaged.

Furthermore, if the IACUC is comfortable with the QA staff’s actions regarding the identified issues, which they can evaluate during the required periodic updates, the committee may allow the QA staff as much or as little flexibility as they like. Provided reporting requirements to

A WORD FROM OLAW AND USDA

Response from OLAW

By extending the IACUC’s oversight using qualified and trained individuals to conduct quality assurance (QA) reviews, Great Eastern University (GEU) has begun a creditable post-approval monitoring (PAM) program to ensure compliance with the protocols that the IACUC approved¹. PHS Policy Footnote 8 supports this use of PAM and allows flexibility in the size and scope of how IACUC oversight is implemented provided that the IACUC remains responsible for the evaluation and the report to the Institutional Official².

The disconnect in this PAM program is 1) the delay in reporting findings of noncompliance to the IACUC, 2) coordination of the reporting with the IACUC’s subsequent evaluation and corrective actions, and 3) prompt reporting of any noncompliance to OLAW^{3,4}. The two examples involving use of euthanasia methods not included in the approved protocols are failures “to adhere to IACUC-approved protocols” and require prompt reporting to OLAW^{3,4}. Likewise, because of GEU’s policy requiring a list of animal activity locations in the protocol, the use of a different location deviates from the approved protocol and is reportable to OLAW⁴. Finding incomplete or inaccurate post-operative surgical records is reportable to OLAW due to the “failure to maintain appropriate animal-related records⁴.” If in doubt about whether a situation requires reporting, institutions with an

Animal Welfare Assurance should consult with OLAW⁴.

Response from USDA

The Animal Welfare Regulations (AWR) require the IACUC to review and approve significant changes in ongoing activities [§2.31(d)(1)]. Some significant changes may be handled administratively, according to IACUC-reviewed and -approved policies in consultation with a veterinarian authorized by the IACUC⁵. Provided that GEU’s IACUC has these policies in place, and the QA team collaborates with the IACUC-authorized veterinarian, the QA team’s “fix” of euthanasia methods and laboratory locations through protocol amendments is consistent with the AWR. However, the Veterinary Medical Officer (VMO) may still cite GEU for noncompliance since activities with potentially serious effects on animal welfare were not conducted in accordance with the IACUC-approved protocols. Additionally, the IACUC and GEU’s program of veterinary care must ensure appropriate post-operative care in accordance with established veterinary medical practice [§2.31(d)(1)(ix); §2.33(b)(5)]. Inaccurate or incomplete post-operative records may also lead to citations since accurate medical records are a component of established veterinary practice, and the care the animals received cannot be verified if post-operative records are inaccurate. Finally, the IACUC is required to review, and if warranted, investigate concerns involving the care and use of animals resulting from reports of

noncompliance [§2.31(c)(4)]. The QA team should report noncompliance to the IACUC in a timely manner to facilitate IACUC review and investigation of potential animal welfare concerns identified during lab visits. □

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- United States Department of Agriculture. *Animal Welfare Inspection Guide* [online]. (United States Department of Agriculture, Riverdale, MD, December 2022). https://www.aphis.usda.gov/animal_welfare/downloads/Animal-Care-Inspection-Guide.pdf

external regulatory agencies are met and the semiannual reviews occur as stipulated above, IACUCs have no limitations when evaluating their programs.

To review, after identifying a concern the IACUC at GEU requested additional assistance in the form of QA staff with the stipulation the committee remains informed of the staff's endeavors. While following all regulations, the IACUC then arranged for positive, educational interactions

between the research community and the compliance office. The outcome included the identification of concerns that, gone undetected and not improved through education, could have escalated into more serious matters. The IACUC in this scenario should be applauded for their dynamic methodology. □

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2. Animal Welfare Act and Regulations, Title 9, Chapter 1, Subchapter A, Part 2, Subpart C, § 2.31.

When “Find-It-Fix-It” Goes too Far

The IACUC at Great Eastern University (GEU) is commended for developing and promoting a robust Quality Assurance (QA) program. QA programs are able to assess the animal care program through direct engagement and evaluation with active researchers. A successful QA program employs qualified and educated evaluators who are knowledgeable on animal welfare and common research techniques. This allows the evaluator to have a “find it, fix it” mentality when noting easily correctable items. During a Post-Approval Monitoring (PAM) visit, the QA personnel should be able to assess and advise on topics such as: handling techniques, injection techniques, asepsis, needle and suture size and material, and anesthetic refinement. Their recommendations can either lead to improvements in laboratory procedures, and/or may necessitate a protocol amendment to further refine the research plan. QA programs such as this can be a majorly impactful portion of an animal care program.

Although having a skillful QA team is important, ultimately the responsibility for ensuring and empowering the QA program rests with the IACUC. In providing this oversight, the IACUC must make it clear what the outcomes of a PAM session could be. The IACUC at GEU cited Footnote 8 of the PHS Policy¹, stating it allowed them flexibility to “fix” issues discovered during a PAM visit. However, Footnote 8 of the PHS Policy allows flexibility in institutions for

how they conduct semi-annual inspections and program reviews (i.e., allowing consultants to perform these reviews). It is not, in these authors' opinions, intended to allow staff members or individual IACUC members to “fix” potential non-compliance issues discovered during a PAM visit. It is, therefore, imperative that the IACUC outlines those items that may be corrected on site, those that may necessitate a protocol amendment, and finally those situations that clearly uncover protocol non-compliance. Non-compliance is something that must be reported to the IACUC for detailed evaluation at a convened meeting. The National Institutes of Health (NIH) Office of Laboratory Animal Welfare (OLAW) has provided guidance (NOT-OD-05-034)² with examples on what constitutes reportable non-compliance². The IACUC and the QA Program at GEU would do well to reference this notice in determining not only what is non-compliance, but also what should likely be reported as serious non-compliance to OLAW, if applicable.

What presents in this scenario are, in these authors' opinions, clear indications of potential protocol non-compliance. Although each instance may not have produced a negative animal welfare state, the deviation from the protocol should have been presented to the IACUC for evaluation of the situation. Once presented with the facts, the IACUC could then determine the appropriate corrective action or if serious non-compliance had occurred.

Certain activities, such as not listing the animal room appropriately on the protocol, may be considered by the IACUC as an additional item that may be correctable via amendment, not necessitating serious non-compliance and reporting to the Institutional Official (IO). Others, such as using unapproved euthanasia methods or incomplete post-operative surgical records, are likely to be serious non-compliance as referenced by NOT-OD-05-034². We recommend that the IACUC clearly defines a process for reporting potential non-compliance discovered during QA visits (i.e., PAMs) and review of those issues by the IACUC, followed by appropriate reporting of serious non-compliance to the IO. Such transparency will only enhance the QA Program at GEU. □

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