

**A word from OLAW**

*In response to the questions posed in this scenario, the Office of Laboratory Animal Welfare (OLAW) offers the following clarification and guidance:*

The issues raised in this scenario are matters of institutional compliance with longstanding NIH Grants Policy and with the PHS Policy. The relevant requirements are as follows:

NIH Grants Policy Statement (GPS) states “NIH will not make an award for research involving live vertebrate animals unless the applicant organization...provide[s] verification that the IACUC has reviewed and approved those sections of the application that involve the use of vertebrate animals in accordance with the requirements of the [PHS] Policy...Verification of the IACUC review may be filed at any time before award unless required earlier...the IACUC should ensure that the research described in the application is consistent with any corresponding protocols reviewed and approved by the IACUC<sup>1</sup>.”

PHS 398 Application Instructions specify “Any modification of the Research Plan section of the application, required by the IACUC, must be submitted with the follow-up [IACUC] verification<sup>2</sup>.”

PHS Policy requires the IACUC to review “those components of PHS-conducted or supported activities related to the care and use of animals” and the institution to provide “verification of approval by the IACUC of those components related to the care and use of animals.” PHS Policy reiterates the 398 Instruction “If verification of IACUC approval is submitted subsequent to the submission of the application or proposal, the verification shall state the modifications, if any, required by the IACUC<sup>3</sup>.”

After a grant is awarded, the GPS requires prior approval by the NIH funding component when an investigator wishes to substitute one animal model for another<sup>4</sup>.

In this scenario, the IACUC requested several changes to the protocol and this information was not provided in the IACUC letter of verification to the NIH. If these changes constituted a modification of the Research Plan section of the application, then they are required to be submitted to the NIH as part of the verification.

Note verification of IACUC approval is submitted by the institution to the relevant Grants Management Officer (GMO) assigned responsibility for the grant application by the NIH Institute or Center, and not to OLAW.

The scenario further describes Great Eastern findings that there were animal studies in the grant that were not described in the protocol. This situation is an obvious violation of applicable

requirements cited above. Apparently the investigator decided not to perform some of the studies, but substituted studies using a different animal model, which were approved by the IACUC. Since the PHS 398 requires identification of the species in the Research Plan, if the investigator decided to change species prior to receiving the grant award he or she should have notified the GMO. A change in animal model by the investigator post award is an action that, per the terms and conditions of the GPS, is considered a change in scope and therefore requires prior approval by the relevant GMO of the NIH awarding component (not OLAW). The 1995 OLAW guidance, referenced in two of the scenario responses, concerning criteria in determining what constitutes a “significant change” is in the context of whether IACUC review is required for changes that investigators might potentially make to approved protocols<sup>5</sup>.

NIH grantee institutions are collaborative partners with NIH; both parties have mutual obligations and responsibilities as stewards of Federal funds to ensure compliance with all Federal requirements. Institutions that rely upon statements by investigators that the grant application matches the IACUC protocol and have determined that this is an ineffective method of assuring compliance with Federal rules have a responsibility to develop and implement an appropriate system of policies and procedures to ensure compliance.

With regard to the NIH modular grant format, modular applications and awards employ a simplified process for developing and reviewing application budgets, documenting approved budgets, and making post-award budgetary changes. There are no changes regarding submission of information or policies concerning animal care and use under the Modular Grant procedures.

1. NIH Grants Policy Statement; Part II Terms and Conditions of NIH Grant Awards, Subpart A, Animal Welfare. (2003).
2. PHS 398 Grant Application, Part I, Instructions, Preparing Your Application. (2004).
3. Public Health Service. *Public Health Service Policy on Humane Care and Use of Laboratory Animals* IV.B.6; D.2 (US Department of Health and Human Services, Washington, DC, 1986; reprinted 2002).
4. NIH Grants Policy Statement, Part II Terms and Conditions, Subpart A, Administrative Requirements, Changes in Project and Budget (2003).
5. Potkay, S., Garnett, N.L., Miller, J.G., Pond, C.L. & Doyle, D.J. Frequently asked questions about the Public Health Service Policy on Humane Care and Use of Laboratory Animals. *Lab Anim. (NY)* **24(9)**, 24–26 (1995).

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form.... Institutional submission of IACUC approval, subsequent to submission of the application/proposal, must represent approval of the information originally submitted in the application/proposal, or include notification of any significant changes required by the IACUC<sup>1</sup>”. It is clear that the University had a responsibility to review all aspects of the grant involving animal use and to notify OLAW of all required changes and modifications. In this case the choice of the inves-

tigator to switch species should have been covered in the letter to OLAW along with the IACUC’s required changes and strategy for the pilot studies and how the institution would proceed if the pilots were successful.

If neither the IACUC nor Markowitz believed that the changes to the grant proposal originally submitted were significant and thus reportable, this is a strong indication that more training is necessary for both the members of the IACUC and its investigators

as to what constitutes a significant change and what is reportable to the sponsor(s) and regulatory agencies.

1. Wolff, A. *et al.* Frequently asked questions about the Public Health Service Policy on Humane Care and Use of Laboratory Animals. *Lab Anim. (NY)* **32(9)**, 33–36 (2003).

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