**OFFICE OF RESEARCH AND DEVELOPMENT**

**VETERANS HEALTH ADMINISTRATION**

**Regulatory Requirements Regarding**

**IACUC Annual Continuing Protocol Reviews**

(Summary and Clarification by the Office of the CVMO)

Date: August 11, 2015 Guidance Document: AR2015-003

**1. Summary.** The conduct of annual IACUC continuing protocol reviews can be used as an important monitoring and review activity. USDA has recently provided clarification to the VA about USDA’s current requirements regarding these reviews. VA policy currently requires application of USDA requirements to all VA animal use protocols, regardless of whether the species involved are regulated by USDA. According to current USDA requirements, “The IACUC shall conduct continuing reviews of activities covered by this subchapter at appropriate intervals as determined by the IACUC, but not less than annually.” (9 CFR §2.31(d)(5))

* Recent guidance from USDA APHIS has clarified that continuing reviews are considered compliant if they are completed within the anniversary month of the most recent previous approval or completion of a continuing review. Even if the continuing review process begins in the preceding month, as long as it is completed within the anniversary month, the anniversary date will remain unchanged. Following is an example with specific dates:
	+ March 1, 2014: A protocol is approved by the IACUC
	+ February 28, 2015: If the continuing review is completed on this date, it is compliant with USDA requirements, but the anniversary date for the next continuing review becomes February 28, 2016.
	+ March 1-31, 2015: If the continuing review is completed anytime in March of 2015 (even if the IACUC began the review in February), it is compliant with USDA requirements, and the anniversary date for the next review will remain March 1, 2015.
	+ April 1, 2015: If the continuing review is completed on this date (after March 31, 2015), it will be non-compliant with USDA requirements, and the anniversary date for the next review will become April 1, 2016.
* If an IACUC does not conduct a continuing review of a protocol in time to comply with the USDA requirement for at least annual review,
	+ USDA does not require work on that protocol to stop (The IACUC of course has the authority to suspend its approval of the protocol at its discretion, and the institution always has the authority to otherwise interrupt work on the protocol for any reason);
* Missed or tardy annual reviews are to be completed as soon as possible after their status is discovered, and are to be addressed as deficiencies in the next semi-annual IACUC program review (VA Semiannual Evaluation form, Part 1, Section A, item 169), with a plan and timetable for correction (VA Semiannual Evaluation form, Part 2);
* USDA does not consider a missed or tardy continuing review *per se* to be reportable; however, an institution may be cited if deficiencies in the continuing review process are noted during an inspection by USDA representatives. (Note: Although USDA does not require the IACUC to suspend its approval of a protocol because of a missed or tardy continuing review, if the IACUC votes to suspend and a species covered by USDA is involved, the suspension must be reported to USDA, regardless of whether it is related to a missed or late annual review.);
* OLAW requires compliance with USDA requirements, and reporting of serious or continuing noncompliance with PHS Policy, so the IACUC must determine whether to report a missed or late annual review to OLAW.
* The IACUC must determine whether to report the matter to ORO.

**2. Background.** Annual continuing reviews provide a regular opportunity for the investigator to self-declare any unanticipated results or complications, to confirm that the protocol content is still accurate, and to make any revisions that may be needed. The minimum expectations for information required from principal investigators as part of the annual continuing protocol review are found in paragraph 8.g(1) of VHA Handbook 1200.07, “Use of Animals in Research.” However, many VA programs collect more information, and a more comprehensive template form is suggested as part of joint USDA/OLAW guidance provided in 1996, available on the OLAW website (<http://grants.nih.gov/grants/olaw/references/contop96.htm>).

As noted in paragraph 8.g(1) of VHA Handbook 1200.07, all IACUC review actions should be documented in the IACUC minutes as official actions.

In the past, there has been some confusion as to how an IACUC should report missed or late annual continuing reviews, and whether protocols must be suspended if these reviews are not completed in time. This guidance document provides clarification of USDA expectations as well as the expectations of the VA Office of Research and Development (ORD), and has been acknowledged for purposes of oversight by the VA Office of Research Oversight (ORO). This should not be interpreted as hindering the IACUC from establishing more stringent local policies that it determines to be appropriate to local needs.

**3. Issue**. VA has received clarification of USDA’s expectations when the IACUC does not complete the continuing review required at least annually for each IACUC-approved protocol. Per USDA, if an IACUC does not complete the annual continuing review in time, work on the protocol may continue, and USDA does not require the IACUC to suspend the protocol. However, failure to complete the annual continuing review in time is considered non-compliance with 9 CFR §2.31(d)(5) of the USDA Animal Welfare Act Regulations (AWAR). Per the USDA Animal Welfare Act (§2144), all VA animal research programs are required to comply with the USDA AWAR, as restated in paragraph 4.b(5) in VHA Handbook 1200.07.

**4. Reporting Requirements**. Failure of the IACUC to complete the annual continuing review in time (per 9 CFR §2.31(d)(5)) is not *in and of itself* considered by USDA to be reportable, but the following apply:

a. If a VA animal research program is inspected by a USDA Veterinary Medical Officer (VMO), the incident is grounds for citation of the program for non-compliance with 9 CFR §2.31(d)(5).

b. If the IACUC votes to suspend approval of the protocol for any reason, the suspension must be reported to USDA.

c. Compliance with the PHS Policy requires compliance with the USDA AWAR (IV.A.1, Footnote 2), so a missed or tardy annual review is also non-compliance with PHS Policy. OLAW requires reporting of “any serious or continuing noncompliance” with PHS Policy (NOT-OD-05-034), so the IACUC must determine whether a given instance of a missed or tardy annual review is “serious”. If an institution chronically fails to conduct the annual continuing review or is routinely late, the issue becomes continuing programmatic non-compliance, and must be reported to OLAW. VA programs are encouraged to consult with OLAW in these matters.

d. AAALAC Rules of Accreditation specify that protocol suspensions are to be reported to AAALAC in the next Annual Report, and “OLAW/USDA investigations” are to be reported promptly to AAALAC. The Rules of Accreditation do not specifically require reporting of missed or tardy annual reviews of protocols. VA programs are encouraged to consult with AAALAC in case of questions about specific incidents.

e. Compliance with VHA Handbook 1058.01 requires that the IACUC must be notified of any failure to complete an annual continuing review in time. The IACUC must then determine whether the matter is a “reportable incident” (e.g., serious or continuing noncompliance with PHS policy). If so, the IACUC must notify the VA facility Director and ACOS/R&D of the reportable incident (VHA Handbook 1058.01, par. 7.f(2)), and the Director must report the incident to ORO (VHA Handbook 1058.01, par. 7.f(3)).

f. Item 8.g.(1) in Handbook 1200.07 requires the VA IACUC to perform annual continuing review of all protocols, no matter what species is involved, but does not establish any VA-specific policies about reporting late or missed reviews. The regulatory requirements that apply to VA with regard to reporting of missed or late annual reviews are those of USDA, OLAW, AAALAC, and ORO, and are summarized in this document (4.a – 4.e, above).

**5. Anticipated Questions.**

**a. What does the IACUC have to do to meet the deadline for an annual continuing review of a protocol based upon USDA’s interpretation of “annual”?**

Paragraph 9 CFR §2.31(d)(5) states, “The IACUC shall conduct continuing reviews of activities covered by this subchapter at appropriate intervals as determined by the IACUC, but not less than annually.”

Meeting the deadline requires that the IACUC complete a review of the protocol.  The review can be conducted by the full IACUC or by a subcommittee, but all members must be aware of the review and have the opportunity to participate (USDA Animal Welfare Inspection Guide, Chapter 7, p. 7-41).  The completion of the review does not require reinstatement of the “approval of the protocol”, as the approval of the protocol does not automatically expire on the deadline for the annual review (see 5.b and 5.e, below). Completion of the annual review involves determination by the IACUC that all deficiencies and necessary modifications of the protocol have been identified (it is not required that all deficiencies be resolved before the review may be considered “complete”, see 5.d, below), and is to be documented in writing. The regulatory language does not identify any specific method for documenting completion of annual continuing reviews, but completion can easily be included in the IACUC minutes. It is a best practice to include documentation for easy reference in the protocol file as well.

Note that the IACUC has an obligation to monitor local compliance and program quality, and the *lack of adherence* to annual continuing review requirements is to be reported in the VA Semiannual Evaluation Form (Part 1, Section A, “Review of the Program”, item 169), with any actions needed and taken to prevent future problems in Part 2, “Table of Deficiencies and Departures.”

**b. If the IACUC fails to meet the deadline for an annual continuing review of a protocol, must animal use under the protocol cease until the IACUC completes its continuing review?**

As a matter of quality control, programs may voluntarily adopt local policies that require previously approved animal research to be suspended or otherwise temporarily interrupted until the annual review is completed, but this is not required by Federal regulations, as discussed above.

**c. What are the consequences for failure of the IACUC to meet the deadline for completing an annual continuing review of a protocol?**

To summarize the guidance above, if an annual review is missed or late, the IACUC must:

* Complete the missed or tardy continuing review as soon as possible.
* Document the incident in the next semi-annual IACUC program review, with a plan and timetable for correction as needed; and
* Determine whether the matter is reportable to ORO or OLAW, and act accordingly.

**d. What if the continuing review identifies a deficiency or determines that a modification of the protocol is needed?**

If the continuing review results in identification of a deficiency in the conduct of the protocol, the IACUC is responsible for addressing the deficiency, and may determine that suspension of IACUC approval or other corrective action is necessary. All of the usual regulatory requirements apply to such determinations and their reportability, but there is no requirement that the deficiencies be resolved before the continuing review may be considered complete.

If the continuing review results in IACUC recognition that a modification of the approved protocol is needed, the process of reviewing and approving the modification does not have to be completed by the deadline for continuing review. The important distinction is that the “review” of each IACUC-approved protocol must completed annually (as defined by USDA, see 5.f, below) by the IACUC, but any additional submissions for modification of the protocol by the Principal Investigator, and review and approval of the modification by the IACUC do not have to be completed by the deadline for the annual continuing review, for the annual continuing review to be “complete”. Of course, none of the proposed modifications may be implemented until after they are approved by the IACUC.

Similarly, if an investigator includes a modification to a protocol as part of an annual review submission, the IACUC is not required to complete the review and approval of the modification before the deadline for the annual review, but the review of the annual review information must be completed before the deadline.

Acceptable mechanisms for IACUC review and approval of modifications of approved protocols include not only full committee review (FCR) and designated member review (DMR), but also Veterinary Verification and Consultation, as described in recent guidance from OLAW and USDA (<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-126.html>).

**e. What is the difference between the annual “continuing review” required by USDA (9 CFR 2.31(d)(5)) and the “complete *de novo* review … required at least every three years” by PHS Policy (PHS Policy IV.C.5, and FAQ D.1)?**

It is very important to distinguish between the “annual continuing review” required by USDA and the “triennial complete *de novo* review” required by PHS policy.   OLAW considers the approval of any protocol by the IACUC to expire on the third anniversary date of the original approval.  Therefore, failure of the IACUC to complete the triennial complete *de novo* review and grant renewed approval by the third anniversary date *does* result in a lapse in IACUC approval of the protocol.  Consequently, if the triennial review is not completed on time, *animal use must stop* until the new protocol is granted approval by the IACUC.   If no work on the protocol is conducted while the approval is lapsed, there is no non-compliance involved, but if work on the protocol is carried out during the lapse in IACUC approval, this is work done without IACUC approval, which must be reported to OLAW, ORD, and AAALAC. ORO requires that this matter be reported to the IACUC and that the IACUC notify the medical center Director and ACOS/R&D of its determinations, with subsequent notification to ORO as required (VHA Handbook 1058.01, par. 7.e and 7.f). USDA does not require reporting of such an incident, but it is grounds for citation of the program for non-compliance with the AWAR (§2.31(d) and other sections), during an inspection, if USDA species are involved.

**f. How is the deadline for completion of the next annual continuing review calculated?**

The first anniversary date of an IACUC-approved protocol is one year after the date on which it was granted full approval by the IACUC. If an annual continuing review is completed by the IACUC any time during the first anniversary month, the anniversary date does not change. If an annual continuing review is completed outside of the anniversary month, the anniversary date is to be revised according to the date of actual completion of the continuing review. An example with specific dates is as follows:

* + March 1, 2014: A protocol is approved by the IACUC
	+ February 28, 2015: If the continuing review is completed on this date, it is compliant with USDA requirements, but the anniversary date for the next continuing review becomes February 28, 2016.
	+ March 1-31, 2015: If the continuing review is completed anytime in March of 2015 (even if the IACUC began the review in February), it is compliant with USDA requirements, and the anniversary date for the next review will remain March 1, 2015.
	+ April 1, 2015: If the continuing review is completed on this date (after March 31, 2015), it will be non-compliant with USDA requirements. In addition, the anniversary date for the next review will become April 1, 2016.

 (Note: Calculation of the expiration date of the protocol, which is the date by which the triennial complete *de novo* review and re-approval of the protocol must be completed for IACUC approval not to lapse, is based solely on the date on which IACUC approval of the protocol was last granted, and is independent of any changes in the deadlines for the annual continuing reviews.)

**6. Additional questions.** For questions on this guidance, please contact the CVMO’s Office (Alice.Huang@va.gov or Michael.Fallon@va.gov). Questions related to reporting of animal welfare incidents under VHA Handbook 1058.01 should be referred to the Research Safety and Animal Welfare team in ORO at AskORO@va.gov. Questions about the PHS Policy and the USDA AWAR should be referred to the NIH Office for Laboratory Animal Welfare and the APHIS Animal Care Office, respectively.