aspects of the study. This monitoring could include an observation form that is completed by IACUC members, a facility veterinarian or animal care and technical staff. The monitoring forms would then be reviewed by the IACUC prior to approval of each phase of Holmes' study. By approving the protocol with these requirements, the IACUC could satisfy the interests of their members as well as the interests of the individuals within the institution.

1. 9 CFR Chap. 1, Subchapter A, Subpart C, Section 2.31(d)(5).
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* – Frequently Asked Questions. Institutional Responsibilities, Question No. 6. (US Department of Health and Human Services, Washington, DC, 2006; revised 2008). http://grants.nih.gov/grants/olaw/faqs.htm#instresp_6.
3. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
4. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* (National Academies Press, Washington, DC, 1996).

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RESPONSE

Approve and monitor

Erin Daugherity, DVM

Approval of the entire protocol is appropriate. Institutions receiving support from the Public Health Service (PHS) for research or teaching involving vertebrate animals must implement an animal care and use program that includes procedures for self-monitoring. This function is described in the *Guide for the Care and Use of Laboratory Animals*[1] (the *Guide*), which states that the IACUC is responsible for the "establishment of a mechanism for receipt and review of concerns involving the care and use of animals at the institution." If the entire protocol is approved, Holmes is required to terminate the study if Phase II is not successful. It is the responsibility of the IACUC to ensure that these conditions are followed.

Post-approval monitoring is accomplished in several ways. The *Institutional Animal Care and Use Committee Guidebook*[2] suggests that research, veterinary and husbandry staff should be aware of approved procedures and the conditions of the approval. The IACUC can establish a climate of compliance and encourage prompt reporting of departures from the approved protocol. The IACUC may choose to employ a compliance specialist to ensure that procedures are consistent with protocol approval. Additionally, the PHS *Policy on Humane Care and Use of Laboratory Animals*[3] (the PHS Policy) requires that the IACUC "inspect at least once every six months all of the institution's animal facilities." During this semi-annual inspection, IACUC members must note any deviations from the approved protocol. Regardless of the mechanisms used to accomplish post-approval monitoring, I assume that Best America Pharmaceuticals has competent self-monitoring mechanisms in place and that if Holmes is observed conducting elements of Phase III without the establishment of an ED_{90}, this deviation will be observed and the IACUC would then be allowed to suspend the activity in accordance with the PHS Policy.

Some IACUC members wanted Holmes to report Phase II results prior to the initiation of Phase III. Because the *Guide*[1] requires that the IACUC meet only every 6 months, however, Holmes' research may be delayed inappropriately if the IACUC requires additional information prior to proceeding. Additionally, because the Phase III studies are dependant on the ED_{90} data, there seems to be little motivation for Holmes to continue with Phase III if an ED_{90} is not established in Phase II. Furthermore, the results from Phases I and II of the study will not alter the total number of animals utilized. Therefore, there seems to be little rationale for not approving the entire protocol.

Finally, although the presented scenario does not specify whether this is a true or modified LD_{50} study, and the posed question does not hinge upon this specification, my institution would require a modified LD_{50} study with defined intervention points unless there is strong scientific justification requiring a true LD_{50}.

1. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* (National Academies Press, Washington, DC, 1996).
2. Office of Laboratory Animal Welfare. *Institutional Animal Care and Use Committee Guidebook* 2nd edn. (US Department of Health and Human Services, Washington, DC, 2002).
3. 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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