not include one important participant in the whole process: the PI. The IACUC should communicate the two choices to the PI: (i) wait for protocol approval until IBC approval is provided, or (ii) remove the portion of the protocol that requires IBC approval so that the mouse protocol can be reviewed and approved first, then add a major amendment for the rat procedures once IBC approval is available. If the PI wants to starts her mouse work as soon as possible, she can choose the second option. If the PI doesn't mind waiting, the IACUC can choose the first option and approve the protocol pending the IBC approval.

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).
2. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2010).

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RESPONSE

PI must wait

Eva B. Ryden, PhD, DVM, DACLAM, Lois Laemle, PhD & Sharron Kirchain, DVM, DACLAM

This situation is not uncommon. The IACUC wants to assist the Principal Investigator (PI) in obtaining approval for the protocol so that she can start research while also assuring compliance with all applicable laws and policies, both federal and institutional. Both Covelli and Gordon are trying to find a way to obtain protocol approval expeditiously.

Covelli is correct in stating that there is no such thing as conditional approval. But the PHS *Policy on Humane Care and Use of Laboratory Animals* (PHS *Policy*) recognizes that a protocol can be 'approved pending modifications' (APM)[1]. In our experience, many or even most IACUC protocols are APM at the time of Full Committee Review (FCR). In these cases, the protocol is not approved, and animal research cannot start until the modifications requested by the IACUC have been received[2].

IBC approval may or may not be an administrative matter. The IBC approval number itself may be technically regarded as simply a number in the IACUC protocol, similar to a phone number. Once the missing number is received in the IACUC office, the protocol can be approved administratively by the Chair or an IACUC Administrator[3]. In our judgment, IBC review and approval is a substantive part of the protocol. If the IBC requires changes in procedures, such as the use of a biosafety cabinet that is not readily available to the PI, thus entailing 'substantive modification' prior to approval, then these changes may require modification to the IACUC protocol as well. This would necessitate a re-review of the amended protocol by the IACUC. This repeat review could be assigned to either FCR or Designated Member Review (DMR), as approved by the IACUC and in accordance with the policies described in the institution's PHS Assurance.

Can the IACUC give the PI permission to move ahead with the part of her study that does not involve IBC procedures? Although we would like do so, in agreement with the Great Eastern University IACUC, the answer is 'no'[2]. If there were some assurance that the PI could not start the IBC studies before obtaining IBC approval (e.g., if the experimental compounds that required IBC approval could only be ordered though the IBC), then this option could be considered. But Covelli is correct that the IACUC cannot give approval for Francis to move ahead with only part of her study. The idea that the rat segment can be removed and added later as a minor amendment is unacceptable. The PI cannot remove the rats without also revising the protocol, eliminating procedures, doses, experimental groups, etc. pertaining to the rats, essentially making it a new protocol. Subsequently adding rats and rat procedures to the protocol would be a major amendment requiring either DMR or FCR according to institutional policies. Although OLAW does not specify exactly what is a minor versus major amendment, it is suggested that addition of a species be considered a significant change[4]. Finally, first deleting and then adding rats and rat procedures would entail substantial amounts of extra work for the PI as well as for the IACUC. Both revisions would require either FCR or DMR review as determined by the IACUC.

In summary, the protocol should not be revised to exclude the rat work pending IBC approval. The PI must await IBC approval before her IACUC protocol can be approved and animal work started.

1. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals – Frequently Asked Questions.* Protocol Review, Question No. D-3. (US Department of Health and Human Services, Washington, DC, 2006; revised 2010). <http://grants.nih.gov/grants/olaw/faqs.htm#d3>
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals – Frequently Asked Questions.* Protocol Review, Question No. D-5. (US Department of Health and Human Services, Washington, DC, 2006; revised 2010). <http://grants.nih.gov/grants/olaw/faqs.htm#d5>
3. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals – Frequently Asked Questions.* Protocol Review, Question No. D-4. (US Department of Health and Human Services, Washington, DC, 2006; revised 2010). <http://grants.nih.gov/grants/olaw/faqs.htm#d4>
4. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals – Frequently Asked Questions.* Protocol Review, Question No. D-9. (US Department of Health and Human Services, Washington, DC, 2006; revised 2010). <http://grants.nih.gov/grants/olaw/faqs.htm#d9>

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RESPONSE

IBC approval not substantive

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Covelli's opposition to conditional or limited approval of protocols is valid. But there are other options available that will not place unnecessary restrictions on the investigators and the IACUC process. Therefore, we do not completely agree with Covelli that the IACUC could not let Francis begin any work on her protocol until the IBC approval was received.

IACUCs can approve, require modifications (to secure approval) or withhold