Jerald Silverman, DVM, Column Coordinator

From 'Designated Member' back to 'Full Committee'?

Sean Smith and his wife Liz were both researchers at Great Eastern University. Sean, who was a member of the IACUC, was quite disturbed about an ongoing protocol review that he believed compromised the well-being of some sheep. The IACUC chairman had appointed the attending veterinarian (AV) as the sole Designated Member Reviewer for a protocol that Smith assumed would be a 'no brainer' for a veterinarian. The Principal Investigator (PI) proposed a surgical procedure utilizing appropriate anesthesia but no analgesia. Smith had done similar surgery some years earlier and acted as a consultant for the PI. He specifically reminded the PI to use an analgesic, but the PI chose not to, claiming that because the sheep were expected to be up and walking within an hour after surgery, analgesia was not needed. Smith was positive that the AV would notice this and request that an analgesic be added before the protocol could be approved.

But, when Smith asked the PI about the progress of the protocol, the latter said that he needed to respond to some small items in order for the protocol to be approved, but that the use of analgesia was not one of them. That evening, Sean related the story to Liz, and as they mulled the problem over, Liz came up with an idea. "Sean," she said, "Why don't you just ask for Full Committee Review [FCR] before the protocol is approved by the veterinarian?" "I can't," he answered, "I blew my chance when the IACUC office asked the committee members if anybody wanted FCR and nobody said that they did." But Liz was not about to give up. She read through all of the IACUC material that Sean brought home and found a passage from an Office of Laboratory Animal Welfare Notice[1] stating in part that "...any member of the IACUC may, at any time, request to see the revised protocol and/or request FCR of the protocol." "Doesn't that count, Sean?" she said. "Not really," he responded, "that's only for special circumstances." "Well," said Liz, "I didn't see anything in what I read which suggested that an IACUC member can't request a FCR before the Designated Member Reviewers have come to a decision. I think you should ask for a FCR as soon as you can, like sending an e-mail right now to the IACUC office."

Is Liz Smith right? Can an IACUC member who is not a Designated Member Reviewer request a Full Committee Review while the Designated Member Reviewers are still deliberating?

1. Office of Laboratory Animal Welfare. Guidance to IACUCs Regarding Use of Designated Member Review (DMR) for Animal Study Proposal Review Subsequent to Full Committee Review (FCR). Notice NOT-OD-09-035. (National Institutes of Health, Washington, DC, 8 January 2009). <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-035.html>

RESPONSE

Not too late for FCR

Sridhar Samineni, DVM, MS & Richard W. Ermel, DVM, MPVM, PhD, DACLAM

The Animal Welfare Act and Regulations (AWARs)[1] and PHS *Policy on Humane Care and Use of Laboratory Animals*[2] (PHS *Policy*) allow an IACUC to carry out protocol reviews by either the full committee (FCR) or a designated member (DMR)[3]. An IACUC can use DMR for a protocol if the institution has a written policy that documents the assignment criteria and the procedures for processing the protocols. The DMR process must be in full compliance with all applicable requirements of the AWARs and PHS *Policy* and the designated reviewer must use the same criteria that are applicable to protocols undergoing FCR. DMR may be restricted to protocols involving noninvasive or acute procedures or may be used for continuing and triennial reviews with no or minor changes. In DMR, the designated member has the authority to approve a protocol, require modifications to secure approval or refer it to the full committee. The intent of DMR is to reduce the workload of the IACUC at convened meetings and to enable a faster protocol review and approval process. However, any member of an IACUC can ask for a FCR at any point during the DMR process. Thus, Liz Smith is right in saying that any member of the IACUC can refer the protocol for FCR if he or she has concerns about the protocol.

In this scenario, the AV may have been satisfied with the justification to withhold analgesics or may have unintentionally missed the potential concern. If the PI provided an appropriate justification to withhold analgesics, then the animals fall into USDA category E, and the PI must have considered and described alternatives to the proposed procedure in the protocol. In either case, Sean Smith's concern about the welfare of the animals used in the proposed research and the appropriate use of an analgesic postoperatively should be addressed via a FCR. As an IACUC member, Sean Smith should express his concern to the AV and IACUC chair (request for FCR) regarding the need for appropriate pain assessment and control on this protocol.

The *Guide for the Care and Use of Laboratory Animals* (the *Guide*)[4] expects the IACUC to use professional judgment when reviewing protocols with procedures that may cause more than momentary distress or pain and to take all necessary steps to alleviate or minimize pain and distress, unless scientifically justified. In addition, US Government Principle IV (ref. 5) states, "unless the contrary is established, investigators should consider that procedures

that cause pain or distress in human beings may cause pain or distress in other animals". In this situation, the fact that an animal may stand up and move postoperatively doesn't rule out the possibility of pain or distress and should not be used as a scientific justification to withhold analgesics. This may be viewed as a deficiency in the IACUC review process and veterinary care program at Great Eastern University. To prevent this deficiency, to meet the expectations of the *Guide*[4] and to ensure animal welfare, the institution should provide training for PIs and research staff on recognizing and treating pain and distress and should have a documented IACUC DMR process.

In summary, any IACUC member can refer a protocol for FCR during the DMR process. There is no statement in either the AWARs or PHS *Policy* to indicate otherwise.

1. Animal Welfare Act Regulations (§ 2.31, d, 2).
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* IV, C, 2 (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
3. Office of Laboratory Animal Welfare. Guidance to IACUCs Regarding Use of Designated Member Review (DMR) for Animal Study Proposal Review Subsequent to Full Committee Review (FCR). Notice NOT-OD-09-035. (National Institutes of Health, Washington, DC, 8 January 2009). <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-035.html>
4. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 10–14,60–65 (National Academies Press, Washington, DC, 1996).
5. Public Health Service. *US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training* (US Department of Health and Human Services, Washington, DC, 2002).

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A word from OLAW and USDA

In response to the questions posed in this scenario, the Office of Laboratory Animal Welfare (OLAW) and United States Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care (USDA, APHIS, AC) offer the following clarification and guidance:

For animal activities funded by the Public Health Service (PHS), the PHS *Policy on Humane Care and Use of Laboratory Animals* (PHS *Policy*; section IV.B.4) states that the "IACUC shall review concerns involving the care and use of animals at the institution"[1]. Similarly, for species covered by the Animal Welfare Act, "The IACUC shall… review, and, if warranted, investigate concerns involving the care and use of animals at the research facility resulting from public complaints received and from reports of noncompliance received from laboratory or research facility personnel or employees"[2]. Neither the PHS *Policy* nor the Animal Welfare Act Regulations limits how or when such concerns are considered. In this scenario, the IACUC member has a serious concern about the lack of analgesia for a proposed surgical procedure in a research protocol in the midst of review by a designated member of the committee. As mentioned by several of the respondents, OLAW's guidance on the use of Designated Member Review (DMR) subsequent to Full Committee Review (FCR) states that "any member of the IACUC may, at any time, request to see the revised protocol and/or request FCR of the protocol"[3]. OLAW's guidance is in accordance with USDA's regulation on designated member review[2]. The guidance can and should be interpreted broadly to apply to this particular scenario and to other circumstances where an IACUC member has concerns about a research protocol already approved by the committee or in the process of review and approval by either DMR or FCR. Administrative practices of the committee should not impede the appropriate and thorough review of concerns about proposed or ongoing animal activities. Critical to this issue is clear communication among the IACUC, the veterinarian and investigators to resolve questions and concerns about a protocol at the earliest point.

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. Code of Federal Regulations. Title 9, Chapter 1, Subchapter A – Animal Welfare: Part 2 Regulations (§2.31).
3. Office of Laboratory Animal Welfare. Guidance to IACUCs Regarding Use of Designated Member Review (DMR) for Animal Study Proposal Review Subsequent to Full Committee Review (FCR). Notice NOT-OD-09-035. (National Institutes of Health, Washington, DC, 8 January 2009). <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-09-035.html>

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OLAW, OER, OD, NIH, HHS

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RESPONSE

Sean dropped the ball

Suzanne Craig, DVM, DACLAM, Rajesh Uthamanthil, DVM, PhD, DACLAM & Peggy Tinkey, DVM, DACLAM

Designated Member Review (DMR) is one method of approving animal use proposals that is compliant with US Department of Agriculture and PHS guidelines[1,2]. The DMR process gives the designated reviewer full authority to approve the protocol but also requires that all committee members have the opportunity to look at the protocol and call for FCR prior to assignment for DMR. It appears that in this case, Sean Smith forfeited his right to call for FCR as an IACUC member during this specific pre-DMR review period. He wrongly assumed that the designated reviewer, who is also the AV, would require analgesia in this study. This case illustrates the responsibility of each committee member to play his or her role independently, irrespective of perceptions of how other members might make decisions.

The Office of Laboratory Animal Welfare guidance that Liz used to support her contention that any IACUC member could request FCR of a protocol was taken out of context. The guidance that Liz quoted is specific to the use of DMR subsequent to FCR[3] and does not apply in this scenario. The specific wording in the guidance refers to the situation that could arise if a committee had voted to allow use of the DMR process to review modifications required for approval that were stipulated by members during a convened meeting of the full committee. In that case, PHS allows for required modifications to be reviewed by the DMR process under two

conditions: (i) all IACUC members agree in advance in writing that the quorum of members present at a convened meeting may decide by unanimous vote to use this method, and (ii) any member of the IACUC may, at any time, request to see the revised protocol or request FCR of the protocol. As stated previously, one required element of the DMR process is that all IACUC members must be given the opportunity to call for FCR. In our opinion, the provision presented in this guidance was stipulated specifically to allow members not present at the meeting the opportunity to call for FCR of any protocols sent for subsequent DMR during the FCR process. There is no provision in this guidance or in others that allows members more than one opportunity to call for FCR if they have second thoughts prior to approval. After approval, however, any member may request additional review of any protocol if he or she has concerns about animal welfare.

In summary, an IACUC member (Sean) cannot intervene during the DMR process once the process has begun (which happens only if no IACUC member calls for FCR). Sean now has two options: (i) contact the designated reviewer, mention his concerns and request that they be considered, with the full knowledge that the designated reviewer has the authority to reject the comments, or (ii) wait for approval of the protocol by DMR and then immediately request FCR of the protocol, citing his concerns.

1. Animal Welfare Act Regulations, 9 CFR (Chapter 1, Subchapter A, Part 2).
2. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* (US Department of Health and Human Services, Washington, DC, 1986; amended 2002).
3. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals – Frequently Asked Questions*. Protocol Review, Question No. D-19. (US Department of Health and Human Services, Washington, DC, 1986; amended 2002). <http://grants.nih.gov/grants/olaw/faqs.htm#d19>

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RESPONSE

Talk to the veterinarian!

Diane J. Gaertner, DVM, DACLAM

In my opinion, Liz Smith is correct that, as an IACUC member, Sean Smith can ask for a FCR of the protocol until the protocol is approved through the normal DMR process. This does not require "special circumstances" as asserted by Sean Smith.

In addition, even after the IACUC DMR process has approved a protocol, the IACUC has the responsibility to review any concerns brought to it regarding the use of animals at the institution. If the PI's protocol has already been approved by the IACUC DMR process, Sean Smith or any other member of the University community can bring his or her concern for the adequacy of analgesia for these sheep to the attention of the IACUC with the expectation that the concerns will be discussed at a convened IACUC meeting. Sean Smith's concerns would not overrule the AV's opinion during this discussion, but the IACUC members may be convinced that supplemental analgesia for these sheep is warranted and the IACUC discussion may require modification of the protocol. In general, when in doubt, most IACUCs will rule that postoperative analgesics shall be provided to research animals unless the PI can show scientific proof that the provision of these analgesics will alter the data to be obtained or endanger the animals' recovery.

This scenario and the processes described above also illustrate how people's convoluted efforts to avoid confrontation can waste time with political maneuvering. I question why the IACUC member, Sean Smith, didn't simply express his concerns directly to the AV and discuss this issue. I am optimistic that an honest and respectful discussion regarding the need for analgesics to supplement anesthesia could allow for the best outcome for the sheep without the need for convoluted political maneuvering or a potentially heated IACUC discussion. If Sean Smith has useful references or personal experience that convince the AV that postoperative analgesics are needed, then this recommendation can be conveyed to the PI by the AV as the Designated Member Reviewer as part of the DMR process, without the need for a confrontational discussion at the IACUC meeting. If the AV has a solid basis for not requiring postoperative analgesics, then she or he can explain that basis; for example, some 'balanced' or 'multimodal' anesthetic protocols include drugs that provide substantial continued analgesic effects after animals awaken. If the AV continues to believe that postoperative analgesics are not needed, then Sean Smith can take the next step by requesting FCR (if the protocol is not yet approved) or by conveying his concerns as a member of the University community, resulting in a full discussion of the approved protocol by the IACUC at the next convened meeting.

In my opinion, Sean Smith should take the direct approach of discussing his concerns with the AV rather than expressing his distress to his wife Liz, other IACUC members or other colleagues!

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