Want to comment? Participants in the OLAW Online IACUC Staff Seminars have the opportunity to submit questions after the formal presentation. Your input is important, too. OLAW will accept questions and comments from viewers of this recording until March 4, 2010. After the comment period closes, OLAW will post the comments, questions and answers on the OLAW webpage. Please go to the Education Resources page and click on the seminar title for further information.

Note: Text has been edited for clarity.

IACUC Review of Proposed Animal Activities

Speakers: Brent Morse, DVM, DACLAM, Animal Welfare Specialist, Division of Compliance Oversight, OLAW and Axel Wolff, MS, DVM, Director, Division of Compliance Oversight, OLAW
Moderator: Jerry Collins, Ph.D., Division of Policy and Education, OLAW and Yale University.
Broadcast Date: December 9, 2010. A recording of the seminar can be viewed at http://grants.nih.gov/grants/olaw/Videos/OLAW_Review_of_Proposed_Animal_Activities_2010-12-09.wmv (WMP - 1 hr). A PDF version of the slides can be accessed at http://grants.nih.gov/grants/olaw/educational_resources.htm.

[Slides 1 and 2 provided information about real-time participation in the webinar and have not been included in this transcript.]

Slide 3 (IACUC Review of Proposed Animal Activities)
[Hello, welcome to the next in our series of OLAW Outreach webinars for IACUC Staff. My name is Jerry Collins. I will be the moderator for today's seminar titled "IACUC Review of Proposed Animal Activities"…] Our seminar today will be presented by Dr. Brent Morse. Dr. Axel Wolff will join him in responding to your questions. Dr. Wolff currently serves as Director of

Compliance Oversight here in the NIH Office of Laboratory Animal Welfare. At OLAW, he has also served as a Senior Assurance Officer. He is a commissioned officer in the U.S. Public Health Service and has attained the rank of Captain. Prior to joining OLAW, Dr. Wolff was the director of the Veterinary Resources Program, NIH's intramural biomedical research support program. He also directed NIH's Animal Quarantine Facility and served at the Neurology Institute. Dr. Wolff's interest in unique research animals has involved him in work with armadillos, chimpanzees, and fruit bats, as well as the more common species. He serves on the editorial board of Lab Animal and has published on various topics, including primate enrichment and PHS Policy interpretation.

Dr. Morse earned his veterinary degree from Washington State University in 1987. He served in the Army Veterinary Corps as a Veterinary Officer and was board certified in Laboratory Animal Medicine in 1996. He transferred to the U.S. Public Health Service Commissioned Corps at the National Institutes of Health in 2000 and has been at OLAW since 2006. He has held many positions including clinical veterinarian, program veterinarian, and department head. He is an Animal Welfare Program Specialist within the Division of Compliance Oversight at OLAW. It's now my pleasure to hand the microphone over to Dr. Morse.

Thank you, Jerry, and hello everyone. Glad you can participate in today's webinar. We'll spend some time reviewing the authority of the IACUC regarding the review of proposed animal activities, the requirements of the Public Health Service Policy, and then we'll transition into dealing with specific issues regarding IACUC review. We'll wrap up our session with an opportunity for you to ask some questions of myself and Dr. Wolff.

Slide 4 (Issues to be Addressed) [No comments by speaker]

Slide 5 (IACUC Authority to Review Proposed Animal Activities: HREA)
It is not unusual for investigators to inquire about the authority of the IACUC to require information about proposed animal usage. In 1985, Public Law 99-158, also known as the Health Research Extension Act of 1985, established the legal basis for the Public Health Service Policy on Humane Care and Use of Laboratory Animals by requiring that guidelines be established for the proper care of animals to be used in biomedical and behavioral research and the proper treatment of animals to be used in such research. The law states that guidelines shall be established for the "organization and operation of animal care committees" and that "guidelines...shall require animal care committees at each entity which conducts biomedical and behavioral research with funds provided under this Act to assure compliance with the guidelines established..."

Slide 6 (IACUC Authority to Review Proposed Animal Activities: PHS Policy)
The Public Health Service Policy on Humane Care and Use of Laboratory Animals, also known as the PHS Policy, promulgates the requirements of Public Law 99-158. PHS Policy Section IV.B. defines eight functions of an IACUC, two of which relate to the review of proposed animal activities.

Slide 7 (PHS Policy IV.B.)
The PHS Policy requires that IACUC's review both newly proposed animal activities and significant changes to already approved activities as part of its responsibility to approve or withhold approval of proposed animal use.

Slide 8 (PHS Policy IV.C.1.)
There are three separate but related lists of topics that an IACUC should include in its consideration of proposed animal use. For our purposes, the

first list appears in the PHS Policy, the second in the ILAR *Guide for the Care and Use of Laboratory Animals*, and the third in the Code of Federal Regulations specific to the Animal Welfare Act. It is possible that the *Guide* may not always be congruent with USDA requirements. As stated in the PHS Policy, when that happens, the PHS expects the institution to follow the Animal Welfare Act Requirements for USDA covered species.

Slide 9 (PHS Policy IV.C.1.)

The PHS Policy states that: "In order to approve proposed research projects or proposed significant changes in ongoing research projects, the IACUC shall conduct a review of those components related to the care and use of animals and determine that the proposed research projects are in accordance with this Policy." It is important to remember that an institution may establish requirements that are more stringent than those in regulations and, therefore, it is important to review your PHS Assurance for any such requirements. The research project must conform to the Animal Welfare Act; the ILAR *Guide for the Care and Use of Laboratory Animals*; as well as the institution's Assurance on file with OLAW and must meet the following requirements:

a. "Procedures with animals will avoid or minimize discomfort, distress, and pain to the animals, consistent with sound research design."

b. "Procedures that may cause more than momentary or slight pain or distress to the animals will be performed with appropriate sedation, analgesia, or anesthesia, unless the procedure is justified for scientific reasons in writing by the investigator."

c. "Animals that would otherwise experience severe or chronic pain or distress that cannot be relieved will be painlessly killed at the end of the procedure or, if appropriate, during the procedure."

Congress recognized the importance of animal models in research, testing, and teaching and wanted to ensure that those animals were treated humanely. That is reflected in these first three topics listed in the PHS Policy. Avoidance or minimization of pain and distress is essential. There is a recognition that some procedures may involve pain or distress and an IACUC is charged with ensuring that appropriate measures are taken to provide each animal with the greatest level of comfort possible. Therefore, the Policy goes on to state that:

d. "The living conditions of animals will be appropriate for their species and contribute to their health and comfort. The housing, feeding, and nonmedical care of the animals will be directed by a veterinarian or other scientist trained and experienced in the proper care, handling, and use of the species being maintained or studied."

Topic **d** covers many issues relating to the living conditions of animals and is the justification for inquiry by the IACUC about any unusual requests for housing, feeding, etc. of animals at your institution. Normally questions about standard housing, feeding, etc. may not appear on a protocol form if those issues are overseen by a centralized animal program. However, if your institution has housing facilities that are operated by investigators with limited central oversight, it is appropriate for an IACUC to request specifics about housing and daily care to ensure that institutional standards are applied in all housing locations.

Slide 10 (PHS Policy IV.C.1.)

e. "Medical care for animals will be available and provided as necessary by a qualified veterinarian." In smaller programs where a veterinarian may not always be on site, it is appropriate for the IACUC to confirm that medical care for animals will be under the direction of a qualified

veterinarian. It may be appropriate for qualified non-veterinary personnel to provide care but that must be under the direction of an appropriately trained veterinarian.

f. "Personnel conducting procedures on the species being maintained or studied will be appropriately qualified and trained in those procedures."

g. "Methods of euthanasia used will be consistent with the recommendations of the American Veterinary Medical Association Guidelines on Euthanasia, unless a deviation is justified for scientific reasons in writing by the investigator and approved by the IACUC."

The PHS Policy requires that Assured institutions base their programs of animal care and use on the *Guide for the Care and Use of Laboratory Animals*. The current 1996 *Guide* lists the following topics to be considered in the preparation and review of animal care and use protocols.

Slide 11 (*Guide* Topics for Protocol Review)

So, we're now changing to *Guide* topics for protocol review. The protocol, although technical in nature, needs to be written in a way that all members of the IACUC are able to understand what it is that they are being asked to approve. A clearly written rationale and purpose section, devoid of technical jargon, will provide a sound starting point for the reviewers. Numbers justification can be challenging and some IACUC's focus heavily on this issue. The IACUC should be given a reasonable estimate of the numbers of animals that is related directly to the proposed experiments. The number of animals approved should be the minimum number required to obtain statistically valid results. It is important to ask a PI if less invasive procedures or even non-animal models can be used, since science moves

quickly and it is possible that a refinement in the procedure is available that would be in the best interest of both the science and the animals.

Slide 12 (*Guide* Topics for Protocol Review)

Many of the topics covered by the PHS Policy are also listed for consideration in the *Guide*. So we're not going to talk about the first four bullets on this slide. The issue of multiple major operative procedures can arise for legitimate scientific reasons. It is important that the IACUC not approve such procedures only for cost saving purposes. There is a philosophical issue that can arise here as well. Is it better to expose a few animals to multiple procedures or many animals to a few? The IACUC must consider the ethics of the decision and ensure that if multiple major surgical procedures are to be conducted on one animal, the scientific value of the work outweighs the ethical costs.

Slide 13 (*Guide* Topics for Protocol Review)

Another area where the *Guide* places additional responsibility on the IACUC is in this first bullet on this slide. There is special emphasis on the way that an animal program defines and monitors endpoints in the presence of pain or distress. Each member of the IACUC must reach a clear understanding of the status of an animal that is not provided with a means to escape pain or distress. Once again, the IACUC is faced with a difficult cost-benefit analysis. In addition to multiple major survival surgeries, two other topics for enhanced IACUC oversight are covered by the *Guide*.

Slide 14 (*Guide* Topics for Protocol Review)

They are Physical Restraint and Food or Fluid Restriction. The main concern regarding physical restraint is *prolonged* restraint. Although this term could

apply to the restraint of any species, the *Guide* specifically states that "Prolonged restraint, including chairing of nonhuman primates, should be avoided unless it is essential for achieving research objectives and is approved by the IACUC." If the IACUC determines that restraint is essential, then other important guidelines are applicable and I refer you to the *Guide* for those other guidelines. For food or fluid restriction, the *Guide* says that "Restriction for research purposes should be scientifically justified, and a program should be established to monitor physiologic or behavioral indexes, including criteria such as weight loss or state of hydration for temporary or permanent removal of an animal from the experimental protocol." It goes on to say that "The least restriction that will achieve the scientific objective should be used" and "In the case of conditioned response research protocols, use of a highly preferred food or fluid as positive reinforcement instead of restriction, is recommended."

Slide 15 (USDA)

For the USDA, if your institution is registered as a research facility with the USDA and USDA covered species are used in research, testing, or teaching – there are additional topics that an IACUC must include in its review of proposed animal activities. And those topics are listed in 9 Code of Federal Regulations 2.31(d). I refer you to that section for those additional topics.

Slide 16 (Methods of Proposal Review)

So lets switch to the possible methods of proposal review [PHS Policy IV.B.6. and FAQ D3]. IACUC review procedures must be described in your institution's Assurance with OLAW and must comply with the PHS Policy and guidance issued by OLAW. There are only two recognized methods of review of animal activities by an IACUC: They are full committee review of protocols which requires a convened meeting of a quorum of the IACUC members and

must receive the approval vote of a majority, that is greater than 50%, of the quorum present in order to receive approval. Both full committee review and designated member review require that all members of the IACUC be provided with at least a list of the proposed research protocols or significant changes. For designated member review, all members must have the opportunity to request full committee review of any proposal. If no such request is made, then the Chair can designate the member or members to conduct the review. The designated member or members act on behalf of the IACUC and decisions rendered by the designated members carry the same weight and authority of decisions rendered during full committee review.

Slide 17 (Full Committee Review)
There are three possible outcomes of full committee review. As described in the PHS Policy, they are:

1. Approval
2. Modifications required in (to secure approval) or
3. Withhold approval

Slide 18 (Designated Member Review)
One important difference in the possible outcomes between full committee review and designated member review is that designated review may result in approval, a requirement for modifications in (to secure approval), or referral to the full committee for review. Designated review may not result in withholding of approval. Descriptors, such as conditional, provisional, or interim, when referring to IACUC approval, are not recognized by the PHS Policy and are unclear, confusing, and should be avoided. [FAQ D4]

Slide 19 (Modifications Required In (To Secure Approval))

So, lets look at “modifications required in (to secure approval).” This category is used when the proposal lacks substantive information. Substantive information is the information the IACUC needs to evaluate the proposal in accordance with:

- Requirements of the PHS Policy
- Adherence to the *Guide*
- Institution’s Animal Welfare Assurance

Although, if the committee determines that approval of a proposal is contingent upon receipt of very specific, administrative information, the IACUC may handle these clarifications as administrative details that an individual, such as the Chair, could verify. Some examples of acceptable administrative changes are: contact information, room numbers, phone numbers, confirmation of personnel training or credentials, changes in protocol personnel (other than the PI), and there are others. If the initial review of the protocol was by full committee review, and the committee wishes to allow subsequent approval of required modifications by designated member review, then that decision should be explicitly noted in the minutes. There is more information available on the requirements of this process on the OLAW website under the FAQ section. [FAQ D19]

Slide 20 (Proposed Changes)

Proposed significant changes in ongoing animal activities must be reviewed and approved by the IACUC prior to implementation. [PHS Policy IV.B.7.] IACUC approval must be by one of the two approved methods, that is either full committee review or designated member review.

Slide 21 (Examples of Significant Changes)

Examples of changes considered to be significant include, but are not limited to:

- changes in the objectives of a study;
- changes from non-survival to survival surgery;
- changes resulting in greater discomfort or in a greater degree of invasiveness;
- changes in the species or in approximate number of animals used;

Slide 22 (Examples of Significant Changes)

- changes in the Principal Investigator;
- changes in anesthetic agent(s) or the use or withholding of analgesics;
- changes in the method of euthanasia; and
- changes in the duration, frequency, or number of procedures performed on an animal.

Slide 23 (Notification Procedures)

Although not specified, it is important that the notification of the investigator and the institution be made in a timely fashion. This ensures that the Institutional Official is kept aware of the status of research proposals. In many cases this requirement is met by providing the Institutional Official with a copy of the minutes of IACUC meetings. [PHS Policy IV.C.4]

Slide 24 (Proposal Review Frequency)

Although partial reviews, reports, or audits may occur on a more frequent schedule, they are not a substitute for the full *de novo* review of proposals that is required every three years. Some committees choose to require a complete review – that is a *de novo* review – on an annual basis. Although not required by the PHS Policy, this would of course count as a *de novo* review. [PHS Policy IV.C.5.]

Slide 25 (IACUC Authority)

It is not uncommon in large institutions for research proposals to require further approval by officials or other committees in addition to approval by the IACUC. However, those committees or officials may not approve an activity involving the care and use of animals, if it has not been approved by the IACUC. On the other hand, just because an activity has been approved by the IACUC, does not mean it has to be implemented by the institution. There are several reasons why an institution may not want to support a project such as monetary or a change in institutional research priorities or a change in the institution's capabilities to carry out the research. [PHS Policy IV.C.8.]

Slide 26 (Humane Animal Care)

NIH's mission is to seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce the burdens of illness and disability. Animals are critical to acceleration of biomedical discovery. Thank you for your contribution to the humane care and use of laboratory animals at your institution. Jerry.

Slide 27 (Educational Resources)
Thanks, Brent. We're now going to show you a brief list of some educational resources coming up in the upcoming year.

Slide 28 (2011 Workshops and Conferences)
You will notice that some of the dates are not yet there. As soon as we get additional information, those dates will, in fact, be updated at the OLAW website.

Slide 29 (Time for Questions)
[Dr. Collins invites participants to submit questions for Dr. Morse and Dr. Wolff. As this is a transcript of a recorded webinar, this is not an option. You may send questions to OLAWdpe@mail.nih.gov.]

Slide 30 (2011 OLAW Online Seminars)
And Dr. Axel Wolff is now going to be joining us as we begin the question session. And I've got a couple of questions that actually came in earlier, so we'll start with them and Brent, we'll have you go first.

1. What is the required length of time to allow IACUC members to call for Full Committee Review? The PHS Policy [IV.C.2.] does not specify a minimal time required for IACUC members to call for full committee review before concluding [proceeding with] the designated member review process. OLAW expects Assured institutions to have written policies that include the procedures required for designated member review and those policies should include the length of time that all members have to request full committee review. All members of the IACUC should be aware of the time requirement

and that requirement should be reasonable for their committee. You need to take into consideration the size of the IACUC, the method of communication that they use, the availability and accessibility of the non-affiliated members, especially, and other considerations.

2. Axel, a question for you. Can the Chair appoint him/herself as a designated member? Oh certainly. Yes, the PHS Policy [IV.C.2.] only requires that the designated member be appointed by the Chair and be qualified to conduct the review. If the Chair is qualified, he/she may appoint him/herself as a designated member. OLAW would question the wisdom or value of only the Chair conducting all of the reviews by this method instead of utilizing other IACUC members.

3. Next question, Brent. Can review of a proposal be conducted by the designated member method before the required time to call for full committee review has elapsed? Yes. There is no prohibition [in the PHS Policy IV.C.2.] against the designated members starting the review process before the time has elapsed, but approval of the proposed activity must not occur until the prescribed time for members to call for full committee review has expired and no member has requested full committee review, or until all members have responded without requesting full committee review. In other words, you've gotten negative responses from all of the members before the time has elapsed. If that occurs, then the designated member review process can be concluded.

4. Axel, can the Institutional Official reinstate an activity that has been suspended by the IACUC? No. [PHS Policy at IV.C.8. and FAQ B10] In this case, only the IACUC has the authority to approve, or re-approve, an

animal activity. **OK, so then the Institutional Official is not in a position to be able to say yes to something that the IACUC has said no to?** Correct.

5. Brent, should proposals that have been approved by DMR be subsequently approved by FCR at the next convened meeting of a quorum of the IACUC? No. [FAQ D3] Although that method is not prohibited, this action brings into question the IACUC's understanding of the designated member review process and authority. The IACUC can re-examine any animal activity at the institution at any time, so they certainly could go back and look at past approval by designated member review. But the members must understand that the designated member review process, as described in the PHS Policy, is equal in authority to the full committee review process and requires no further review by the committee until the *de novo* three year review time has expired.

6. Axel, can the IACUC approve more than one method of anesthesia, analgesia, or euthanasia in a single proposal? Oh yes, absolutely. In fact, OLAW encourages IACUCs to consider such options during the review process. This can be of great service to the investigators by providing more than one approved method and may prevent noncompliance such as may occur if only a single method is approved, but is not available. It is important to understand that if more than one method of, let's say, euthanasia is approved, that personnel responsible for that procedure are properly trained in those approved methods. Each of the methods should be approved individually in consideration of the protocol and not be approved as sets of blanket options.

[Dr. Collins encourages participants to send questions.]

7. Next one. Can someone other than the IACUC Chair appoint designated members, Brent? No. The PHS Policy [IV.C.2.] is very specific that the chairperson is to designate at least one member to conduct the review. There is no prohibition against the chairperson pre-approving a list of members that will be designated to perform reviews as long as those members are qualified to conduct the reviews. In this case, the administrative act of assigning the reviews to certain pre-designated members can be performed by someone other than the chairperson. So as long as the chairperson has approved a list of members to do designated member review, perhaps in the next month, then someone else can do the administrative assignment of protocols or changes as they come in.

8. Axel, is the IACUC the body required to ensure congruence between an animal protocol and a grant? Neither the PHS Policy nor OLAW requires the IACUC to perform this activity. [FAQ D10] Ultimately, the institution is responsible for ensuring that the information in the protocol and grant is congruent. And OLAW has seen several different ways where – how – institutions achieve this. Acceptable examples include having a sponsored programs officer [or] IACUC coordinator conduct this comparison. But whoever performs the activity must be qualified to do so. NIH expects that all grants using live vertebrate animals have IACUC review and approval and that's why the information in the grant application and the protocol must be congruent.

9. OK Brent, a question for you. What exactly does convene mean? Must it be in person, or does a telephone conference or Skype meeting count? Provisions for the use of telecommunications for the IACUC meetings are actually addressed in a Notice, number NOT-OD-06-052 that

was issued in March of 2006. It's available under the Notices hot link on OLAW's website. That's full of information on this topic. And it does say that although a convened meeting is – you know – convened meeting physically attended by IACUC members is optimal, through that notice OLAW recognized the value to Assured institutions of allowing other methods of conducting official IACUC business. There are specific criteria that must be met if using telecommunications for an official IACUC meeting. In general, all members have to be given notice of the meeting in advance and provided with all documents in advance that they would have received normally for a physical meeting. And there must be a quorum, of course, participating. And all members must have the ability to participate in real-time discussion. Written minutes must be maintained. These are a few of the requirements.

10. Axel, is there a minimum number of or percentage of voting members that must respond during an FCR or DMR determination? No. This response is not a majority vote procedure. The IACUC is to predetermine a time by which members are to respond to a decision to use full committee review or designated member review, even if all members have not responded by that time, the protocol can then be sent on to designated member review.

11. Brent, this is one for you. Can an IACUC defer or table the approval of a protocol to allow the investigator time to rewrite a protocol according to outstanding committee questions or should this be considered an action of approval withheld? Well, the answer to that question is yes and no. Yes to the first part of the question and no to the second part. Withholding approval may not be required in this specific case. Essentially, deferring or tabling approval is the same as the outcome of modifications required in to secure approval. You are waiting for substantive

information to be supplied by the PI. The IACUC can use that outcome from a meeting to delay approval until such time that a majority vote of the quorum at a subsequent meeting votes on a proposal; a proposal that's modified by the PI at the committee's request. On the other hand, if the review is by designated member review, the designated members can use this outcome – that is modifications required in to secure approval – to delay approval until all of the designated members are satisfied with the proposal as modified by the PI. **OK, thank you for that, Brent. I'll throw in a little comment here, keeping in mind that if the three years are up – the three years are up. We need to make sure that any work that had been contained in that protocol doesn't continue on.**

12. Axel, does DMR require majority approval or unanimous approval? Well in this case, you are assuming there's more than one designated reviewer, but it does not work the way it does with full committee review where a majority overrules or prevails in this case. So it has to be unanimous approval. If more than one reviewer is involved and one person doesn't agree with it, it needs to be sent back for full committee review.

13. Okay. Brent, when you say that there is a change in approximate number of animals in a protocol, is that a plus or a minus 10% or is there a set number? I'll just add to this as well. If there's a decrease in the number of animals, is that considered to be a change? I'll answer the first question first. Although there is no set number, OLAW has recognized that many institutions do utilize up to 10% variance in the number of animals before requiring an IACUC vote for additional animals. That only applies to mice and rats. So it does not apply to other species other than mice or rats that OLAW recognizes. Up to 10%, we have

recognized that some institutions will allow that as an administrative approval. For a decrease in number, it is important for the IACUC to be aware if a substantial number of animals have not been used on a research protocol. It needs to be assured that the statistical outcome of the experiments that the animals were used for is still valid and that all of the experiments have been carried out as they were approved. Now, if they haven't been, then the IACUC needs to be made aware of that. So they can reevaluate the outcome of that research proposal. [Contemporary Topics 36(2):47-50, 1977 #7]

14. Axel, here's a question I know a lot of the folks that are participating today are anxious to hear an answer to. That is, what is the status of the proposed new *Guide*? Well, we understand that it's going to be issued soon. I don't know exactly at what date. We are sticking with the guidance that we've been giving at meetings – and that is – that the *Guide* currently in use [the 1996 7th edition] is to continue to be used until directives are issued by our office. We're going to allow a phase-in period. But we're going to communicate this as soon as we know, with instructions on phase-in and expectations. So basically, just stick with the old *Guide* until further notice from our office. [NOT-OD-10-102]

15. Okay. Brent, what information is required for a final report? Well, I assume that as a final report we're talking about a report of noncompliance and that final report would need to come from the IACUC and [be] signed by the Institutional Official. The information that is required on a final report of noncompliance is covered under OLAW's guidance on prompt reporting, which, again, is available through the Notices hot link on our website [NOT-OD-05-034]. So there are some specific things. A few of the things that we always look for are, of course, the species of the animal that was involved,

the number of animals involved, dates when the noncompliance or noncompliances occurred, what were the specifics of the noncompliance? But what we really focus on are the corrective measures that were put in place by the institution. Will they prevent the noncompliance in the future? And did they correct the noncompliance that actually occurred. That's the most important thing – is to be very specific in the corrective measures.

16. Axel, how long is considered prolonged restraint? That's real case-specific. On a question like this, we put it back on the IACUC, the IACUC really needs to decide based on the type of experiment, the types of animals and – you know – the specific circumstances of that study.

17. OK. Brent, is there a requirement that the IACUC meet face-to-face? Can there be email voting? Can teleconferencing be used? I assume that question came in early in the question and answer period? We've covered that earlier. Let me just go back and say that I will refer the questioner to our website. Go to the Notices hot link and look for NOT-OD–06-052 back in March of 2006. It should answer all of those questions for you. Feel free to call OLAW [301-496-7163] anytime if you have questions about whether or not telecommunication use for a conference is appropriate. We would be glad to answer any specifics for you.

18. Axel, this is a fairly long question with at the very end – it says isn't this true? So, we thought that when doing a designated member review, you send everyone a notification to call for a full committee review, that you can – say – if you want to call for a full committee review, respond by X date. If no one replies, OLAW agrees this means they do not call for one, that is – no response means FCR is not needed in the reviewer's opinion. Is this true? I'm

not real sure that I understand that. The bottom line is an IACUC and all the members need to understand what the predetermined date is by which time they need to call for full committee review. If that date is established and the Chair or IACUC coordinator hasn't heard from everyone, then they can forge ahead and go to designated member review. They don't need to wait and wait and wait if they haven't heard from one person. That still implies that deadline has been met, the date has been arrived at, and they can then progress to designated member review. **Great answer. That actually – yeah – that actually gets to the heart of the question. Okay. Axel, thanks.**

19. Brent, does the format for the written notification of an IACUC decision to the investigator need to differ if IACUC reviews a proposal by FMR [he means FCR] **vs DMR?** Excuse me, there is nothing in the PHS Policy that talks about a difference between the notifications based on the method of review. [FAQ D3] Keep in mind – of course – that in the case of full committee review that the message to the investigator could be that approval is withheld. In that case, the investigator needs to be given some direction as to what would be required of the investigator, what changes would be required in order to make the proposal acceptable to the committee. But other than that, there's really no other difference that the PHS Policy spells out between the two methods as far as the notification to the investigator or the institution requires.

20. Axel, during DMR, may other IACUC members, not those appointed as DMRs, ask questions regarding the protocol? If so, how are these members assured that their questions are answered? Under designated member review, the rest of the members have seen the protocol, they have decided they will trust these designated members to

perform the review on their behalf. Certainly, they can contact them and give them some input, if they want. But the designated reviewers don't necessarily need to take that input. If reading the initial protocol, any of the members has a concern, they should just say, well, we want this brought up for a full committee review. So I'm not sure how they are assured that the members will answer their questions. I don't even know that they are necessarily obligated. Certainly after a protocol has been approved, any member is always welcome to discuss it at a subsequent meeting as a part of continuing review. But, in this case, the designated members are performing the review on behalf of the committee after the rest of the committee has been given the chance to say whether they want this to occur or want it to go to full committee review. **So then if somebody says that it's okay for it to go to designated member review, they are basically – they have said – our questions are not questions that have to be answered?** Right. They are trusting that reviewer to conduct the review on behalf of the committee. **Okay, great – thank you**.

21. Brent, can the IACUC adopt a policy that if the change in animal numbers is within x percent, it can be approved as an administrative change and not a significant change? I think this ties back to a question you answered earlier. Right, so I'll make the answer short and just remind the listeners that this would only apply to mice and rats used in research. And that OLAW has recognized that some institutions use up to 10% and that that can be approved as an administrative change without the vote of the IACUC or consideration by a designated member review. [Contemporary Topics 36(2):47-50, 1977 #7]

22. Axel, this question asks what is the average number of members on an IACUC? Perhaps they are asking what really is the minimum

number that's required? PHS Policy requires five. I mean, clearly states who those members are supposed to be. In USDA, it's three. But IACUCs can go above that five and have as many members as they want. But the required minimum is five. [PHS Policy IV.A.3 and FAQB1]

23. OK. Brent, is there an attendance frequency that members are expected to participate in convened meetings or activities? There's no minimum that is spelled out in the Policy or that OLAW has prescribed. Some committees only meet – of course – twice a year. We would be concerned if any particular member was not able to meet consecutive meetings. This is all spelled out – actually – in a Frequently Asked Question – again – on our website with more information. [FAQ B4] Basically, if there is a pattern of nonattendance or nonparticipation by a specific member – specific members, the chair should really look at the situation. Obviously find out if there's other types of conveniences that can be made available for that member to participate, especially if it's the non-affiliated member. If their efforts are not fruitful, then it's time to look for additional members for the committee. It's important that every member of the committee does participate at least at some level.

24. Okay, Axel, is a *de novo* review a complete rewrite of the protocol for IACUC review? A *de novo* review is a review of a pre existing protocol that's been previously approved after the three-year period. Whether that protocol needs to be completely rewritten depends on whether things have changed. After three years, usually things have changed – people have changed on it, some of the procedures have changed. Usually it's unlikely that it will be completely the same as the previous one. There's no requirement to rewrite it just for the sake of rewriting it. However, it needs to be updated to correctly reflect what's going to be going on. And

then after that, the IACUC reviews it. I have seen some breeding protocols that are pretty similar from a three-year period to a three-year period. But even there, staff changes, animal numbers change. So, you know, if you are doing it electronically, you can keep what information is the same in there and substitute what's new. But we don't say that you have to rewrite it. It just needs to be correctly reflecting what's going to occur.

25. OK. Brent, if anesthesia is provided as a paid-for service by a board certified anesthesiologist, do all of the drugs used need to be listed in the protocol or can the IACUC rely on the professional judgment of the anesthesiologist? Although it's laudable to have this type of professional available for the support of the research program, there's – the Policy and the *Guide* don't make a difference between a properly trained investigator, Ph.D., or etc. providing the anesthesia or a board-certified veterinarian anesthesiologist providing the anesthesia. The same requirements as far as the protocol and the IACUC apply. Now, as we mentioned earlier, you can use optional ways of approaching this. And that is, for certain species, you may have SOPs developed for anesthesia in those species. And to avoid having to write out the entire anesthetic procedure, it's possible for IACUCs to approve utilizing references to those SOPs within protocols. That takes into consideration that the IACUC has reviewed those SOPs on a regular basis. We also answer that in a FAQ [G1] on our website.

26. Brent, as I was listening to your answer, I was wondering if maybe the person asking the question was referring to the specific situation in which there was an emergency veterinarian intervention? Well, yes, there's – we definitely recognize a difference between a planned and approved protocol for anesthesia and one wherein a – let's say a veterinarian anesthesiologist – recognizes that there is a severe

issue with the approved regimen of anesthesia and for the sake of the safety of the animal, changes to another regimen. Now, with any kind of veterinary intervention, in this case it would – we would expect that that would be a one-time occurrence and that the investigator would notify the IACUC of the change and request reconsideration of alternate methods of anesthesia for that animal.

[Dr. Collins tells the participants that the speakers will not be able to take additional questions in the allotted time.]

27. Axel, the next one. What happens if a non IACUC member, someone else who sees the protocol during the time frame the protocol is running, sees there is something wrong with the protocol? We certainly encourage anybody that has a concern to bring it to the attention of the IACUC, that is one of their requirements – that they are to address concerns with animals. [PHS Policy IV.B.4.] In our Assurance, we ask about the ability for individuals to report concerns – that it needs to be a part of training of folks. It should be publicized as to how individuals that have a concern with a protocol or animal – how they, anonymously, if necessary – without reprisal – can report that to the IACUC. If someone sees something going wrong, they don't have to be an IACUC member to report that to the IACUC.

28. OK. Brent, when an institution is performing work at another institution, under the authority of their IACUC, is the date of IACUC approval required prior to the grant award as part of the institutional agreement? Or is written assurance that the work will not proceed without IACUC approval sufficient? I'm going to try to answer this in a little different way – that the grant will not be awarded

without IACUC approval. And in other words – if we're talking about – I assume it's an NIH grant – we're talking about work performed at an Assured institution. Although OLAW sees great value and encourages institutions that collaborate to develop Memoranda of Understanding – you know – the existence of that memorandum would not be sufficient in order to award the grant. It requires IACUC approval.

29. OK, Axel, another question for you. Can the IACUC suspend activities without previously notifying the PI? The IACUC may suspend any activity that it has previously approved if it determines that it's not being conducted in accordance with the Animal Welfare Act, the *Guide*, or the Assurance or the Policy. [PHS Policy IV.B.8.] So, if something goes wrong and the IACUC meets and votes on the matter with a convened quorum, that protocol is suspended. I'm sure somewhere in the mix, there, the IACUC is going to inform the PI, if the PI doesn't already know in advance. But if there is a problem, the IACUC – it's incumbent upon them to suspend the protocol. And when the PI is notified, it's really up to the committee.

30. OK. Brent, if there are substantive changes made during the DMR, does one need to report those changes back to the IACUC at a future meeting or in some other manner? There's no requirement in the Policy that – that those changes be reported back to the full committee. Although, the normal best practice is that they are read into the minutes of the next convened meeting of the IACUC. And in that way, it's – the rest of the members are made aware of what occurred during designated member review. Remember, when this review method is used, it is agreed upon that the – that by all of the other members – that this one or multiple other designated members can conduct the review and ask whatever questions

they want and make or require what other changes be make in the proposal that they think is needed in order for them to approve the protocol. [PHS Policy IV.C.2.]

31. Axel, how long can you have the same members be DMRs? Do the DMRs need to change periodically? The PHS Policy, as far as DMR goes, just indicates that the Chair needs to pick this person or persons and that they need to be qualified. So let's say that you get three protocols in a row that have to do with some kind of neuroscience and one member is especially knowledgeable about that. Most likely that person will be reviewing those three. You don't need to change them periodically, you just need to be sure that they are qualified to conduct that review. So it's dependant on the type of protocol and that person's expertise. [PHS Policy IV.C.2.]

32. OK. Brent, next to the last question. It was suggested that minutes be given to the IO to keep him or her informed of IACUC decisions on proposals. Two part question: What's the regulatory reference for this, and, secondly, what other methods are commonly used or may be used? Sure, the answer to the first one, what's the regulatory reference. This is specified in the PHS Policy where it says that the IACUC has to keep – has to notify the investigator and the institution of the decisions from its review of proposals. [PHS Policy IV.C.4.] And the answer to number two – what other methods are commonly used? It – one of the other things that are – that is – asked for in the PHS Policy [IV.B.5.] or in your Assurances – how does the IACUC communicate with the Institutional Official? So there – you have to have another way besides just minutes to be able to communicate with the Institutional Official. That can be face-to-face communication. It can be email. Meetings between the chair

and the Institutional Official on a regular basis. And there are institutions where the Institutional Official actually sits in or participates as an *ad hoc* member in the IACUC proceedings, often during semiannual program reviews and facility inspections. It's a good way for the Institutional Official to get firsthand look at what the IACUC does and what the program entails and what the – what status the facilities are in.

33. OK. Axel, what is the requirement of the IACUC to review the scientific merit of a protocol? We have answered that in some Frequently Asked Questions. [FAQ D12] But the bottom line is that scientific merit is usually judged by a peer review panel. However, scientific merit, in the context of animal welfare, does fall under the purview of an IACUC. These things are sort of intertwined, but in general peer reviewers make the decision that this work is meritorious and should be conducted based on the science. Then the IACUC takes a look at how this plays into animal care and use issues. And so, if the scientific merit is involved in that, they can certainly take a look at it and question it as per additional information. But that's how it's divided.

34. OK. Axel you have the last question. And it is – can the IACUC designate a subcommittee to make changes in anesthetics and other drugs without going to the full committee for approval? Okay. Changes in anesthetics and other drugs constitute a significant change. [FAQ D9] So as mentioned in this whole presentation, significant changes need to go to one of the approved methods of review. Either full committee review or designated member review. [FAQ D3] The subcommittee, if it's a designated member review committee can do it, but no, you can't just bypass either one of the approval methods if you want to make changes,

you know, significant changes, to a protocol including anesthetics and changes in other drugs.

Okay and with that – there's one more point being raised. Axel? What? No, I thought there was an additional comment that was being handed to you to be presented. Just says – a note says here all subcommittee members can act as designated member reviewers. Okay. Great, thank you. We still have additional questions here. And obviously, we are not going to have time to answer all of them. So we would encourage you to send your questions to OLAW [olawdpe@mail.nih.gov], they will be answered, or you can also attend the workshops listed in your screen and there will be an OLAW representative at each of those workshops who will be there to answer questions as well.

As always, we want to thank you for your participation in this seminar series and really would be grateful for feedback from you. [Asks the participants to send in questions and comments…share with us ideas for future topics…and provide feedback about technical problems.] As we have done with previous webinars, this session for IACUC staff is being recorded and will be available on the OLAW website in the near future. We certainly hope to see you in – have you participate with us in the OLAW seminars scheduled for 2011. Finally from all of us here at OLAW, thank you for what you do to ensure humane care of animals used in research, teaching, and testing and we hope you find peace and joy during this holiday season. Goodbye.