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 2, 2012. After the question and comment period closes, OLAW will post the comments, questions, and answers on the OLAW webpage. Please go to the OLAW Education Resources page and click on the seminar title for further information.

Note: Text has been edited for clarity.

NIH Adopts 8th Edition of the *Guide*: A Discussion

Speaker: Patricia A. Brown, VMD, MS, DACLAM, Director, Office of Laboratory Animal Welfare

Moderator: Jerry Collins, PhD, Division of Policy and Education, OLAW and Yale University.

Broadcast Date: December 8, 2011. A recording of the seminar can be viewed at http://grants.nih.gov/grants/olaw/12082011_nih_adopts_8th_edition_guide.wmv (Windows Media Player - 1 hr).

Slide 1 (NIH Adopts 8th Edition of the *Guide*: A Discussion)

[Text related to information for attendees and submitting questions during original broadcast of the seminar has been removed. … Hello. Welcome to the next in our series of OLAW webinars for IACUC staff. My name is Jerry Collins and I will be the moderator of today's seminar entitled "NIH Adopts the 8th Edition of the *Guide*: A Discussion."] …it's my pleasure to introduce Dr. Patricia Brown. Dr. Brown currently serves as the director of the Office of Laboratory Animal Welfare (OLAW) at the National Institutes of Health. She received her Bachelor of Science degree in Animal Science from Penn State University and her veterinary degree from the University of Pennsylvania. She served in the Air Force for eight years and, while on active duty, earned a Master's of Science degree in Laboratory Animal Medicine from Penn State. She joined the U.S. Public Health Service in 1986 and has served in a variety

of positions at the NIH, within the Veterinary Resources [Program], the National Cancer Institute, and the Office of Animal Care and Use. Dr. Brown is a Diplomate of the ACLAM and has served on the board of directors of ACLAM. She is a past president of the American Society of Laboratory Animal Practitioners and has served on the Board of Trustees of AAALAC. Dr. Brown.

Slide 2 (OLAW)

Good afternoon, Jerry. My focus today will be on the recent notice in the Federal Register [PDF] of NIH's adoption of the 8th Edition of the *Guide*. As you know, it is the responsibility of my office, OLAW, to oversee the welfare of research animals in activities funded by the Public Health Service [PHS] agencies, that is NIH, FDA, and CDC. If an institution accepts funds from the Public Health Service to conduct research with animals, then it must agree to comply with the Public Health Service Policy on Humane Care and Use of Laboratory Animals [PHS Policy] as part of the institution's Animal Welfare Assurance agreement with OLAW. The PHS Policy requires that institutions base their animal care and use programs on the *Guide for the Care and Use of Laboratory Animals* [*Guide*].

Slide 3 (NIH Adopts 8th Edition of the *Guide*)

With the announcement on December 1st, the 8th Edition of the *Guide* becomes the required edition that all Assured institutions must follow effective January 1st, 2012. To implement the new *Guide*, institutions must complete at least one semiannual program review and facilities inspection using the 8th Edition of the *Guide* as the basis for the evaluation by December 31st, 2012. It is not required that all necessary changes be completed by December 31st, 2012, but rather that an evaluation must be conducted and a plan and schedule for implementation of the standards in the 8th Edition must be developed by December 31st, 2012.

Institutions must verify to OLAW that they have met the required schedule. This will be done through the annual report to OLAW covering the 2012 reporting period and due January 31st, 2013. In addition, institutions must document the implementation in their next Animal Welfare Assurance renewal.

Slide 4 (Why Adopt?)

Why did OLAW decided to adopt the [new] *Guide*? In our judgment, the 8th Edition of the *Guide* empowers continued advancement in the humane care of research animals and in the proper conduct of research, research training, and biological testing with animals. OLAW believes that the 8th Edition of the *Guide* further develops the concept of outcome-based performance standards and advocates the use of performance standards that were a basis of the 7th Edition of the *Guide* and prior *Guide* editions.

IACUCs and institutions are better able to meet their responsibilities to ensure humane animal care and humane research with animals while advancing the quality of the scientific research through the use of the performance standards presented in the 8th Edition. We encourage the cooperative application of the diverse expertise at Assured institutions to develop outcome-based performance standards that enhance the quality of their animal programs. We expect Assured institutions to apply appropriate professional judgment and experience to the challenges inherent in developing policies and procedures to maintain a quality program that provides humane care.

Slide 5 (Impact of Implementing)

OLAW believes that implementation of the *Guide* will have a minimal impact on institutions that are currently using policies and procedures based on well-developed performance standards. These policies and procedures may not need to be revised as part of an institution's implementation of the 8th Edition of the *Guide*.

Institutions that do not currently have performance standards are expected to use the benchmarks provided by the 8th Edition of the *Guide* to develop performance-based policies and procedures.

Slide 6 (*Guide* is Guidance, Not Regulation)

As mentioned earlier, the PHS Policy requires that institutions base their programs of animal care and use on the *Guide*. The *Guide* is considered guidance, not regulation, by the federal government. A regulation is a rule that is codified in the Code of Federal Regulations. As a guidance document, the *Guide* allows an institution to use an alternative approach if the approach still satisfies the requirements of the PHS Policy. The flexibility of performance standards offered in the *Guide* allows institutions, both small and large, with a host of housing configurations and a wide range of animal models and focused areas of research, to provide the appropriate care within a common framework.

Slide 7 (OLAW Website: Updated to 8th Edition)

To assist Assured institutions in implementation of the 8th Edition, we have updated all of our guidance resources and sample documents. We have revised our Frequently Asked Questions section of our website to incorporate references from the *Guide* 8th Edition and we have added some new FAQs based on our 10 new position statements. Our tutorial on the PHS Policy and

the sample documents have also been updated to reflect the new *Guide* with applicable references added to specific pages in the *Guide*. The sample Annual Report to OLAW will be updated again at the end of 2012 to make it easy for institutions to verify their implementation of the new *Guide* in their 2013 annual report. The Semiannual Program Review and Facility Inspection Checklist [checklist] has been updated to cover the major topics of the new *Guide*. The checklist does not replace using the *Guide* itself in the semiannual review and inspection process, but it may be most helpful if used along with the *Guide*. We have referenced relevant pages in the *Guide* and also sections in the PHS Policy within the checklist. And we have highlighted topics that are new to this version of the checklist or are indicated as a "must" in the *Guide*. I encourage you to take a look at all of these sample documents and hopefully you'll find them useful.

Slide 8 (The *Guide* is a Living Document)

I'd now like to provide a little background about the *Guide* before discussing the OLAW Position Statements. The *Guide* was first published in 1963 and has had seven new editions leading up to the current edition. It is interesting to note the longer and longer gaps in updating the *Guide*. It is our understanding that ILAR [Institute for Laboratory Animal Research] will be considering how to keep the *Guide* current as advancements in our scientific understanding of animal care and animal behavior and in newer technologies to maintain animals are developed and reported. OLAW supports the concept of keeping the *Guide* a living document and looks forward to ILAR'S plans.

Slide 9 (*Guide* Authorship)

As just mentioned, the *Guide* is a publication of the Institute for Laboratory Animal Research of the National Academy of Sciences and the product of a 13-member committee that included scientists, veterinarians, and non-

scientists across many disciplines. NIH's role was limited to being one of the 10 funders, both federal and non-federal. NIH did not provide any specific content to the *Guide* [see Background].

Slide 10 (NIH Solicited Public Comments)

After the *Guide* was published in January 2011, NIH requested comments from the public on the adoption of the new *Guide* and a proposed implementation plan [Federal Register February 24, 2011, NOT-OD-11-042]. The comment period was open for a total of 90 days [Federal Register March 29, 2011, Federal Register May 11, 2011, NOT-OD-11-056, NOT-OD-11-066, NOT-OD-11-082]. 806 comments were received and the comments were posted on December 1st on the OLAW website. Seven duplicates and two comments not considered relevant to the questions were removed from the database. 32 comments identified as official correspondence from Assured institutions were received. 24 comments were submitted by professional organizations and four comments were submitted by animal advocacy organizations. 600 comments were received from those who identified themselves as individuals. A total of 137 institutions and organizations were represented in the database. A total of 276 comments appear to have originated from form letters authored by four organizations or individuals. Names were removed from personal comments, but organizational affiliations, where provided, are displayed in the database [see Public Comments, Background].

Slide 11 (NIH Issues Position Statements)

While a majority of respondents opposed the adoption of the 8th Edition, many of them supported many of the *Guide*'s sections. Their objections were confined to specific topics and issues. These are the subjects of OLAW's 10 Position Statements posted on December 1st on the OLAW website. The

Position Statements clarify the ways in which OLAW expects Assured institutions to implement the 8th Edition [see Public Comments]. We have also provided expanded guidance on performance standards and practice standards [see OLAW Comments]. The public is invited to submit comments on their understanding of the Position Statements for a period of 60 days from December 1st, 2011 to January 30th, 2012 [see Comment on Position Statements]. In response, we may further clarify the Position Statements. I will now explain more about performance standards.

Slide 12 (Performance Standard Criteria)

We consider performance standards the most important component of the infrastructure of our oversight of animal programs at Assured institutions. We expect Assured institutions to apply appropriate professional judgment and experience, using the teamwork of the Institutional Official, IACUC members, the veterinarian, the scientists, and the animal care staff to the challenges inherent in developing policies and procedures to maintain a quality program that provides humane care. We consider a well-established performance standard will meet the following criteria:

- it will support scientific objectives;
- it will support the health and welfare of the animal;
- it will include a justified performance index; and
- it will have associated outcome criteria.

Slide 13 (Departures from the *Guide*)

In addition to basing their animal programs on the *Guide*, the PHS Policy [IV.B.3.] also requires that an institution's IACUC identify specifically any departures from the provisions of the *Guide* and state the reasons for each departure in its semiannual report to the Institutional Official. OLAW considers a "must" statement in the *Guide* to be a minimum standard

required of Assured institutions. “Should” statements in the 8th Edition of the *Guide* often involve performance standards and we support and have a high regard for performance standards developed by the research community to meet individual program needs. We do not consider established performance standards to be a departure from the *Guide*.

Slide 14 (Alternative to *Guide* Recommendations)
We support the *Guide*’s approach to applying performance standards to achieve specified outcomes. We believe that this allows individualized applications of the standards at the local level and the flexibility to meet the unique needs of the research being conducted and still ensure the proper care of the animals. When an alternative to the *Guide* standards is necessary, it must satisfy the requirements of the PHS Policy as determined by OLAW. The Position Statements that I will now discuss emphasize our continuing support for performance standards, restate our long standing policies and guidance that have remained unchanged, and endorse several changes that we believe will improve animal welfare.

Slide 15 (Position Statement Topics)
There are 10 Position Statements covering six major topics, as you see here. So I’m going to now go into more detail about each of the Position Statement topics.

Slide 16 (Cost)
The first Position Statement is on cost. Nearly 70% of respondents stated that they were concerned about the cost of implementing the 8th Edition of the *Guide*. Cost cannot be the overriding factor in decisions related to animal welfare in PHS-funded research. This position is based on U.S. Government Principle II. Assured institutions are responsible for compliance with the

Guide. OLAW believes that compliance can best be accomplished using teamwork, professional judgment, and experience. The PHS Policy and the *Guide* define the minimum standards (the "musts) and performance standards (the "shoulds") that we expect of Assured institutions. OLAW recognizes that there are many ways to achieve humane animal care and humane research with animals. As stated previously, an institution may use an alternative approach if the approach satisfies the requirements of the PHS Policy as determined by OLAW and our guidance. In many instances, institutions and IACUCs elect to exceed the standards. This is not required and can add expense to the program.

Slide 17 (Housing)

About 60% of respondents indicated concern with changes to caging and housing specifications in the *Guide*. OLAW concurs with the *Guide* that performance standards are to be applied to housing issues and I refer you to the *Guide*, pages 50 to 63, for further details. We believe that outcome-based performance standards are paramount when evaluating cage or pen space for housing animals. While the *Guide*'s space recommendations are a starting point for addressing space needs, performance standards allow flexibility to improve animal welfare and advance scientific research. An institution's animal housing practices must be species-specific, appropriate for the animals, and in compliance with all applicable federal and local regulatory requirements.

Slide 18 (Nonhuman Primate Housing)

The Animal Welfare Act Regulations and U.S. Government Principle [VII] compel the requirement that nonhuman primates are socially housed. Exemptions to the social housing requirement must be based on strong scientific justification approved by the IACUC or for a specific veterinary

medical or behavioral reason. Lack of appropriate caging does not constitute an acceptable justification for exemption. Compliance with the USDA regulations is an absolute requirement of the PHS Policy. When necessary, single housing of social animals should be limited to the minimum period necessary. When single housing is necessary, visual, auditory, olfactory, and protected tactile contact with other compatible animals should be provided, if possible. In the absence of other animals, additional enrichment should be offered. Determination of the appropriate cage sizes for nonhuman primates is not based on body weight alone. Professional judgment is paramount in making such determinations.

Slide 19 (Environmental Enrichment)

We concur with the *Guide*'s statement that "the primary aim of environmental enrichment is to enhance animal well-being." An institution's environmental enrichment practices must be species-specific and appropriate for the animals. Devices that animals climb on or through, perch on, or nest in, contribute to, rather than detract from, the animal's living space and need not be subtracted from the floor dimensions. Some species are upset by the introduction of novel items. Animals should not be subjected to the presence of items that they find distressing.

Slide 20 (Rodent Housing)

As stated previously, OLAW supports the *Guide*'s approach to applying performance standards to achieve specified outcomes and we expect institutions to use the *Guide*'s space recommendations as a starting point. Adjustments to recommendations for primary enclosures may be made at the institutional level by the IACUC. The IACUC should critically evaluate objective measures of outcome-based performance. The *Guide* identifies examples of performance indices to assess adequacy of housing including:

- health,
- reproduction,
- growth,
- behavior,
- activity, and
- use of space.

Many institutions currently follow procedures and policies in keeping with outcome-based performance indices that meet the standards of the 8th Edition of the *Guide*. IACUCs may not need to adjust these policies and procedures.

Slide 21 (Rodent Housing: Breeding Management)

Rodent cages of the size commonly used in the United States may be appropriate for trio breeding. The new *Guide* does not add specific additional engineering standards for breeding configurations. This empowers institutions to determine appropriate housing. The IACUC must consider relevant factors when assessing the adequacy of cage space according to performance standards. These factors may include:

- average litter size of the strain(s) of rodents;
- whether multiple litters are present in the cage;
- the difference in the age of the pups of different litters;
- growth rate;
- the need for cross-fostering;
- cage dimensions; and
- the overall management and husbandry practices such as cage sanitation or frequency of bedding changes.

Blanket, program-wide departures from the *Guide* for reasons of convenience, cost, or other non-animal welfare considerations are not acceptable. Cages that might be acceptable when litters are born may have

insufficient space as pups grow. Whatever parameters are used to establish breeding configurations and weaning procedures, the IACUC must ensure that cage population does not negatively impact animal well-being and overcrowding does not occur.

Slide 22 (Rabbit Housing)

OLAW concurs with the new *Guide* that rabbits should be housed under conditions that provide sufficient space to meet physical, physiologic, and behavioral needs. The height of an enclosure can be important to allow for expression of species-specific behaviors and postural adjustments. Cage height should take into account the animals' typical posture and provide adequate clearance for the animal from cage structures, such as feeders and water devices. Space allocations should be assessed, reviewed, and modified as necessary by the IACUC considering the performance indices and special needs determined by the characteristics of the animal. IACUCs may consider the use of a rabbit cage that is 14 inches in height, if appropriate. The IACUC should establish, through performance indices related to animal well-being, that the cage provides sufficient space to meet the physical, physiologic, and behavioral needs of the animal. For example, the rabbit must be able to hold its ears in an upright position (if this is natural for the breed) and ears must not be forced to fold over by contact with the cage ceiling. OLAW recognizes that there is a necessity of cost-efficiency and the valid concerns of the community about program cost. Programs should function efficiently, but not at the cost of animal welfare.

Slide 23 (Non-pharmaceutical-grade Substances)

40% of respondents indicated concern with requirements for research use of non-pharmaceutical-grade chemicals and other substances. OLAW and USDA agree that pharmaceutical-grade chemicals and other substances, when

available, must be used to avoid toxicity or side effects that may threaten the health and welfare of animals and may interfere with the interpretation of research results. However, we do recognize that it is frequently necessary to use investigational compounds, veterinarian- or pharmacy-compounded drugs, or Schedule I controlled substances to meet scientific and research goals.

The IACUC is responsible for evaluating the potential adverse consequences of such agents when used for research. In making its evaluation, the IACUC may consider a number of factors. These are listed in the Position Statement and I refer you to that list. The IACUC may use a variety of administrative methods to review and approve the use of such agents. For example, the IACUC may establish acceptable scientific criteria within the institution, rather than on a case-by-case basis. Investigators and IACUCs should consider relevant animal welfare and scientific issues including safety, efficacy, the availability of pharmaceutical-grade compounds, and the inadvertent introduction of new variables. Cost savings alone are not an adequate justification for the use of non-pharmaceutical-grade or compounded drugs in animals.

Procedures that may cause more than momentary or slight pain or distress to the animals must be performed with sedation, analgesia, or anesthesia agents using veterinary or human pharmaceutical-grade compounds, unless the use of an investigational chemical or formulation is scientifically necessary, appropriately justified, and approved by the IACUC. The use of a non-pharmaceutical-grade euthanasia agent must meet the same standards.

Slide 24 (Food and Fluid Restriction)

Approximately 30% of respondents indicated concern with requirements regarding food and fluid restriction. Ingestion of food and fluid are requirements for proper nutrition. When food or fluid is restricted, the amount of the regulated item earned during the testing period and the amount of the regulated item freely given should be recorded to ensure each animal receives its minimum daily requirements. The IACUC must evaluate the level of restriction and the potential adverse consequences in regulating food or fluid. The IACUC must also evaluate the methods for assessing the health and well-being of animals in the animal activities that involve regulation of food or fluid. The IACUC has the authority to approve scientific justifications for departures from the recommendations in the *Guide*. For instance, using scheduled access to food or fluid sources may be justified by describing procedures based on performance standards that assure adequate maintenance of hydration, body weight, and behavioral and clinical health. It may be necessary to monitor both food and fluid intake, if regulation of one influences consumption of the other.

Slide 25 (Multiple Surgical Procedures)

Approximately 30% of respondents indicated concern regarding the number of survival surgeries to which an animal can be subjected. Surgical procedures should be defined as major or minor on a case-by-case basis and evaluated by the veterinarian and IACUC to determine their impact on the animal's well-being. Multiple procedures that may include substantial post-procedural pain or impairment may be conducted on a single animal only if justified by the PI and reviewed and approved by the IACUC. Multiple major surgical procedures on a single animal are acceptable only if they are:

- included in and essential components of a single research project or proposal;

- scientifically justified by the investigator; or
- necessary for clinical reasons.

Cost savings alone is not an adequate reason for performing multiple major survival surgical procedures.

Slide 26 (Agricultural Animals)

Approximately 1% of respondents indicated concern with the application of the 8th Edition of the *Guide* to agricultural animals. PHS Policy mandates that Assured institutions use the *Guide for the Care and Use of Laboratory Animals* as a basis for developing and implementing a program for activities involving animals. OLAW concurs with the *Guide* that, "The *Guide* applies to agricultural animals used in biomedical research, including those maintained in typical farm settings." For animals maintained in a farm setting, the *Guide for the Care and Use of Agricultural Animals in Research and Teaching*, published by the Federation of Animal Science Societies, is a useful resource. Information about environmental enrichment, transport, and handling may be helpful in both agricultural and biomedical research settings.

Slide 27 (Questions?)

Thanks, Pat. We now have an opportunity to address your questions, so please submit them using the question box at the bottom of the attendee interface screen. We will start with some questions that we received prior to the start of the webinar.

1. First one. Pat, **Is it possible that after January 30, 2012, the end of the current comment period, there will be substantial changes to the *Guide* or the ways in which the *Guide* is to be implemented?** No. The *Guide* was written by an ILAR expert committee and published by the National Academies Press. OLAW is not the author and does not have the

ability to change the *Guide*. We do know that ILAR is now considering how to maintain the *Guide* as a living document, and there may be updates in the future, but at this point in time, I believe that this is strategic planning [for the future] and still in the theoretical stage. The purpose of OLAW's Position Statements is to address the concerns raised during our public comment period. And the purpose of the current comment period is for the community to inform OLAW if they need further clarification on issues in our Position Statements. We are always willing to answer specific questions. You can write to the Division of Policy and Education at olawdpe@od.nih.gov or telephone our office at 301-496-7163.

2. Our next question: **If an institution is scheduled to conduct a facility inspection in February of 2012 and the IACUC discovers items during that inspection that were acceptable under the 7th Edition [of the *Guide*], but are now considered minor deficiencies under the 8th Edition of the *Guide*, does the IACUC have latitude in how to rate those items? In other words, do they have to be rated as "minor deficiencies" or can they simply be noted for correction and then rated as "minor deficiencies" during the next facility inspection if they are not corrected by then? Another way to say this is to ask if there is any "grace period" during the initial months under the new *Guide*?** Well, this question is asking, "How does the implementation period work?" And here is our answer: Assured institutions must implement the 8th Edition of the *Guide* during calendar year 2012. If this institution chooses to, it may conduct its February semiannual program review and facility inspection using the standards of the 7th Edition of the *Guide* and its August semis using the standards of the 8th Edition of the *Guide*. But we would encourage institutions to implement the new *Guide* as soon as possible. As I mentioned before, the Semiannual Program Review and Facility Inspection

Checklist is available for download on the OLAW website and we would hope that that would be a useful tool for the IACUCs to consider using.

3. Next question says: **Currently we don't socially house our NHPs [nonhuman primates]. How much time do we have before we will be considered to be out of compliance with the *Guide*?** Well, social housing of nonhuman primates is required by the Animal Welfare Act regulations, so this institution is currently in a noncompliant situation unless the single housing is scientifically justified and approved by the IACUC or for veterinary medical or behavioral reasons. If those conditions have not been met, then the noncompliant situation must be reported to OLAW with a plan and schedule for correction. For more information, I would refer you to the Nonhuman Primate Enrichment and Social Housing Resources. And for information about reporting noncompliance, there's also a special webpage on the OLAW website [Reporting Noncompliance].

4. Pat, the next question reads as follows: **You said that established performance standards are not departures from the *Guide*. Does that mean that if we develop new performance standards, they will be considered to be departures and therefore must be reported as such to the IO and reviewed on a regular basis?** For most institutions, operating procedures and management of the animal care program are well developed and no changes or only minor changes may be necessary to implement the new *Guide*'s standards. OLAW would not consider these changes as departures. New performance standards would also not be considered departures, but would require documentation as to the desired outcome, the performance benchmarks used, and a monitoring schedule to verify the success of the standards. And I would refer you again to the *Guide*, page 6.

5. Next one. **It seems that using locally developed performance standards could result in different decisions from different IACUCs. Is that okay?** We would say yes. The *Guide* offers that flexibility; as long as the IACUC is satisfied that there are appropriate benchmarks in place to achieve the desired outcome and that the performance standards support the health and welfare of the animals.

6. Next one is a little longer. **Our transgenic facility staff have a goal of maximizing results with minimal animal wastage. They monitor breeding success and adjust procedures based on that data. We have never officially called that a performance standard, but it sounds like it might be. Do we need to formalize it or is its very existence adequate?** Well, from the description provided, it appears that the makings of a performance standard for how rodents are bred and weaned is already available. So it should be documented through the creation of either operating procedures or policies, if they do not already exist, and with the inclusion of benchmarks and the outcomes expected for the breeding program.

7. Next question: **How do we know if the enrichment or housing that we use for our rodents are good or bad?** Well, one of the best features of the new *Guide* is the reference section. So I would refer the questioner to the reference section. Consider it as a starting point. Review the literature that's referenced in the *Guide*. And if they still have further questions, to consider getting the advice of consultants.

8. Next one, Pat, I think you will like the way it starts off. It says: **Our IACUC agrees with OLAW that we consider enrichment devices that**

animals can climb on or hide under to be part of the floor space in contrast with recommendations in the *Guide*. Do we need to contact OLAW with this position statement since it is a deviation from the *Guide* that OLAW has already issued a position statement on? Well, OLAW considers our interpretation of the *Guide* on page 56 to be in concert with the intent of the authors of the *Guide* and not a deviation from the *Guide* in that enrichment devices that can be climbed on or through, perched on, or nested in, do not actually take up floor space. So we would say there is no need for OLAW to be notified about your institution's support of OLAW's position.

9. The next one is fairly long. **Our IACUC chose to exclude rodents and shrews from the requirement that they should have freedom to rest away from urine and feces as one of the "must" statements in the *Guide* (chapter 3, page 56). I would assume that the intent of this recommendation is not to require wire caging or daily cleaning of rodent cages. But as OLAW is quite aware, rodents urinate and defecate throughout the home cage and providing a urine/feces-free location is not a "choice" of the institution when housing on solid floors. Will OLAW be issuing a position statement on this issue?** In OLAW's experience, the accumulation of urine and feces, even with species such as shrews and rodents, is most often concentrated in certain areas of the cage and the animals choose to make their bedding/nesting area removed from their toileting area. It is when a cage or pen becomes overcrowded with animals or is infrequently changed that the ability to rest away from soiled areas becomes a problem. We would consider the need for such a position statement after the comment period closes.

10. Next question is about HVAC. **Regarding HVAC failure (FAQ F6): Does the strong recommendation for electronic monitoring of temperature extend to experimental – greater than 24 hour housing – chambers within electronically monitored animal housing rooms?** Well, we would expect the institution to consider whether there's an increased risk for animals within the chambers in determining whether individual monitoring of the chambers is necessary.

11. Next one is an aquatics question: **Regarding aquatic housing (FAQ F6): Does OLAW have a specific expectation that dissolved oxygen levels be measured as a routine parameter of water quality testing? It appears that this parameter is singled out in FAQ F6.** Well, FAQ F6 lists a number of parameters that are of potential concern when HVAC systems fail and the *Guide's* pages referenced in the FAQ provide guidance to address this issue.

12. Here's another one on occupational health and safety. **With regard to the occupational health and safety program (FAQ G2): Please expand upon what is meant by pre-placement medical evaluation. Does OLAW interpret this as all individuals must be seen in person by an occupational health specialist? Or is the health history/risk assessment questionnaire evaluated by an occupational health specialist acceptable?** No. All individuals are not required to be seen by an occupational health specialist. However, an occupational health and safety program, appropriate for your institution, should be developed with input from trained professionals. The collection of a health history/risk assessment questionnaire, evaluated by an occupational health specialist, could work, if your institution determines that this meets your specific requirements. And for further information, I would recommend the OLAW webinar on

occupational medical programs – that's available in our OLAW Web resources – that was presented back in September [2011].

13. Our next question: **Can performance standards be allowed by OLAW for a "must" in the *Guide*? Departures for "must" in the *Guide* can be based** [inaudible] – well, from OLAW, as I've mentioned earlier in my presentation, departures from "musts" in the *Guide* can be based on performance standards, but they must be scientifically justified and approved by the IACUC.

14. OK our next question: **Must performance standards be based on data measurements generated within the Assured institution rather than based on peer-reviewed publications?** Well, I would say that institutions and IACUCs may consider both the peer reviewed literature and their own measurements as they establish the benchmarks for performance standards. And that would also be quite a variable circumstance, depending on what performance standards they were actually looking at because there may be limited peer reviewed publications addressing that particular performance standard.

15. Our next one: **Are there situations wherein Avertin can be classified by the IACUC as a pharmaceutical-grade compound?** OLAW would not consider Avertin [2, 2, 2-Tribromoethanol] a pharmaceutical-grade compound unless it meets the definition that we've provided in our Position Statement. And that states that it's a drug, biologic, or reagent that is approved by the Food and Drug Administration or for which a chemical purity standard has been established by the U.S. Pharmacopeia-National Formulary or the British Pharmacopeia. The preparation and use of Avertin for anesthesia needs to be scientifically necessary, appropriately justified,

and approved by the IACUC, taking into consideration the side effects, stability, storage requirements, and other considerations associated with the agent.

16. Next question: **If an animal has been surgically modified by a vendor, can that animal undergo another surgical procedure at the Assured institution?** Yes. But multiple major surgical procedures on a single animal are acceptable only if they are included in and essential components of a single research project or proposal, scientifically justified by the investigator, or necessary for clinical reasons.

17. Okay, our next one: **Please define what a justified performance index entails.** Well, we would consider a justified performance index one that's based on sufficient reasons established by the institution and the performance index part of that would be the benchmarks that are used to assess the proper care, use, or treatment of the animals involved in the establishment of that performance standard.

18. Next one: **Page 61 of the *Guide* states that cage height should be sufficient for the animals to comfortably stand erect with their feet on the floor.** The question asks, **What about species that do not normally stand erect?** Well, the *Guide* expects the institution and the IACUC to consider the behavioral needs of the species in determining cage height. Species that do not normally stand erect would be considered in light of their normal behavioral repertoire – and that would be what the institution and the IACUC should consider.

19. Okay, we're becoming a little more specific here, now, in our questions, Pat. It says: **The footnote to table 3.1 on page 44 states that animals**

should be provided with adequate resources for thermal regulation, nesting materials, shelter, to avoid cold stress. Does this apply to animals housed within the recommended dry-bulb temperatures, i.e., should all mice have nestlets or shelter? Well, I would refer the questioner to the *Guide*, page 43, which has an expanded discussion of the thermoneutral zone and the need to provide animals choices in controlling their environment.

20. Another one about drugs: **According to the definition of pharmaceutical-grade compound posted at the OLAW website, if the pharmaceutical-grade compound is out of stock, is that considered a valid justification to use non-pharmaceutical compounds?** Well, in our Position Statement and our FAQ [F4], we say that the IACUC should consider the availability of the compound as one of the many factors in approving the use of a non-pharmaceutical-grade compound, including the availability of pharmaceutical-grade alternative agents.

21. These next two look like they are pretty much the same question. **What is the expected timeline for programs to implement the new caging sizes?** and **Does OLAW have any recommendations on how quickly institutions should completed any necessary changes, if needed? For example, purchasing new cages or other environmental housing, changes to IACUC policies and procedures.** Well, with regard to the timeline for new caging and sizes of caging, if a new cage is determined to be necessary, then the institution should have a specific plan and schedule developed by December 31st, 2012. And the plan and schedule would dictate a reasonable expectation for implementing new cages.

I would encourage our participants to continue to send in your questions. We have about six or seven left and we have about 15 minutes. So if you have some additional questions you want to get to us, please do send them.

22. Our next question, Pat: **Concerning the unexpected outcomes section of the new *Guide*, there is a requirement for unexpected outcomes to be reported to the IACUC. What expectations does OLAW have concerning how this information is reported and the time frame involved?** Well, we would say it depends on the impact on animal welfare. Serious problems should be reported quickly. There may be circumstances where the IACUC may need to convene a special meeting if it's something that's seriously affecting the health and well-being of the animals in ongoing studies. As stated in the *Guide*, when there are highly novel variables - when they are introduced – more frequent monitoring of the animals may be required and those negative outcomes should be promptly reported.

Our next one – our questions are coming in. We've gone from having five or six to having eight or ten, so that's great.

23. Regarding floor space. Do running wheels placed on the cage floor subtract from usable floor space? As previously mentioned, if it's something that the animal can climb in, climb on or through, then we would say that it's not impeding access to floor space. It's actually contributing to the floor space. So we would probably encourage the use of running wheels where they are appropriate for the type of housing that the animals are in.

24. Okay, our next one: **Can you please define pharmaceutical-grade?** This is available as [part of] our Position Statement and also in our FAQ [F4].

I can read it, but I think that I already did just read it in one of the prior questions.

25. Okay, our next one: **Can you give a practical example of a justified performance index?** That sounds very much like the earlier question we had with performance indices as well, Pat.
Okay, we can go on to the next one. I have nothing else to add. I think I did cover that question.
Okay, fine.

26. It says that, **Cost is not adequate justification to perform multiple surgeries on a single animal. What if someone uses the argument that they will reduce animal quantities by performing multiple surgeries on individual animals?** I think the IACUC needs to seriously consider the impact of the procedures on the animals. Using less animals may create more pain or distress than may be necessary – so it may be necessary to actually use more animals.

27. Okay, **Based on the presentation, is OLAW stating that only departures from the *Guide* are departures from the "must" statements in the *Guide*?** We're stating that changes from the "musts" are definitely considered departures, but this is not exclusive. There may be circumstances where an institution is deviating significantly from even the "should" statements in the *Guide* and we would consider those departures. If you have a question about whether what you are doing is a significant departure from the *Guide* or you are unsure, it's always better to contact us and we'll give you guidance in that area.

28. Next question relates to euthanasia. **How is non-pharmaceutical-grade potassium chloride used for euthanasia for animals under anesthesia viewed by OLAW? Would this be acceptable?** Well, if the animal is appropriately anesthetized by a pharmaceutical-grade drug, then we would say it would be acceptable to give KCl, because at that point in time, the animal is already under anesthesia.

29. Our next one: **It can be challenging to explain to investigators the difference between reagent- and pharmaceutical-grade materials. Do you have any advice on how to make it clearer to them?** Well, I would refer them to our Position Statement and the definition that we've provided.

30. Okay. And we have about four questions left. **What is the reason for the increase in recommended macroenvironmental temperature for rodents, 68° to 79° rather than 64° to 79°?** It's my understanding that this is based on the scientific review of the literature by the *Guide* committee. And I would refer you to the references provided in that section of the *Guide*.

31. Okay, three questions remaining. **Do approved departures from the *Guide* need to be reported repeatedly in the semiannual inspection report to the IO or do they just need to be reported once?** At a minimum, they need to be listed at least once in the semiannual inspection report to the IO. If they are an ongoing departure, it would probably be advisable to list them as a way to document what are ongoing approved departures from the *Guide*. That would be considered a best practice by the institution to continue to list them over the period of time that those departures are in place.

32. Pat if I could add my own sort of question to that one, **Is there also an expectation that the IACUC is going to be on an ongoing basis reviewing those departures to make sure that, in fact, they are appropriate?** Most definitely. That should be part of the ongoing semiannual program review of the animal care and use program.

33. Next to the last one: **Please provide the specific reference of the Animal Welfare Act that actually requires social housing for nonhuman primates.** Well, we had someone here in the office looking this up for me and it's 9 CFR Chapter 1, 3.81 (a) Environment enhancement to promote psychological well-being.
You should pretend that you took that right out of the top of your head rather than telling that somebody looked it up for you.
Oh right, yes, absolutely.

34. Our last question – unless folks have more coming in and they're going to be getting them to us in the next minute or so **– How are appropriate benchmarks determined and by whom?** Well, again, I would refer back to our Position Statements where it – this is an institutional responsibility, but it necessarily includes the expertise of the team. That's the IACUC, the animal care staff, the veterinarian, the scientists, can all play a role in the development of the benchmarks that would be most appropriate to provide for the health and welfare of the animals. But also keep in mind the specific scientific objectives as they may affect or be influenced by those particular performance standards. And the IACUC is the determining factor or the determining entity that would approve a performance standard, but the input, as I said, would be coming from those within the institution in terms

of policies and procedures that document and are incorporated into the performance standard.

Pat, thank you very much. We will now begin to close our webinar. If there are other questions that are coming in and they haven't gotten to us in time, we will make sure that they are also included in the material that goes to the website – and even as I speak, I'm being handed some more questions.

35. So Pat, if you have got your microphone back on, the first one asks: **Can enrichment devices add to the floor space? That is if a high hanging perch is provided, can the area it provides as a resting space be added to the total floor area?** It's my understanding that the Animal Welfare Regulations do not accept the addition of the floor space – of the use of a perch as a floor space. But the USDA will consider for vertical housing considerations, the use of perches for unique circumstances, so it is something that's worth considering, but it's not routinely acceptable to just add the floor space from a perch as the total floor space for the animal.

[AWAR 3.80 (b) *Minimum space requirements*. Primary enclosures must meet the minimum space requirements provided in this subpart. These minimum space requirements must be met even if perches, ledges, swings, or other suspended fixtures are placed in the enclosure. Low perches and ledges that do not allow the space underneath them to be comfortably occupied by the animal will be counted as part of the floor space. And AWAR 3.80 (c) Innovative primary enclosures not precisely meeting the floor area and height requirements provided in paragraphs (b)(1) and (b)(2) of this section, but that do provide nonhuman primates with a sufficient volume of space and the opportunity to express species-typical behavior, may be used

at research facilities when approved by the Committee, and by dealers and exhibitors when approved by the Administrator.]

Okay, and now it looks like in fact we will have more questions that we will be able to answer. So, again, if we don't get to them now, the questions and answers will be on the website when we post this.

36. Our next question: **Our Assurance expires in May 31st of 2011, so it is due for renewal January 31st of 2012.** Not sure if those numbers [dates] are correct. **Are we required to use the new template dated 12/1/2011 or is the previous template okay?** We would say that to ensure efficient and effective review of your renewal Assurance, we would find it advisable for you to use the new sample document.
Okay, and in looking at this again clearly, **they are saying it's expiring in 2012; not that's it's already expired.**
Right.
I apologize for that.

37. The next one: **Do performance standards need to be formally defined by the IACUC?** We would say yes.

38. Okay, and in some ways, a related question: **I am always a little confused by the statement "appropriately justified." What exactly does this mean?** Well, within the context of scientific justification, we would say that there's a genuine scientific reason for the departure or the reason why something is being requested that deviates from either the *Guide* or some other activity within the animal program.

39. Okay, our next question relates to rabbits. **Does OLAW consider adult rabbits to be a social species and be housed in groups?** I've answered this question in previous forums and if you review the literature, you will see that rabbits are considered a social species. We would encourage institutions to consider – when they can house animals in groups, rabbits included, if they are put into compatible groups, just like with nonhuman primates, they can do quite well in a social setting.

40. Our next question: **Are field studies specially addressed in the new *Guide*?** Yes, there's – I've been given the page numbers. You can refer to page 18, page 32, and page 155 in the *Guide*.

41. Okay, our next question: **How would you advise an institution to proceed with renewing its AWA by the end of January of 2012?** Do you have a sense of what that is, Pat?
I think they are asking about their Animal Welfare Assurance. So if they are already renewing their Assurance within the current time frame [2011], then they should be using – they can continue to use the standard Assurance document that we've had in place in the past. For any institutions that would be moving forward into the next year [2012] and the following year [2013], then we would be expecting them to use our new Animal Welfare Assurance document.

42. Okay, our next one reads: **Our facility conducts testing on materials, chemical and biological, that are not pharmaceutical-grade. Does our IACUC need to approve each product tested in the protocols as an approved deviation to the *Guide*?** Well, what we've already said is that the IACUC can develop its own administrative methods and scientific criteria for when they would find it acceptable for this kind of

special need or special use of chemicals and biologicals that are not pharmaceutical-grade. As I said before, in our Position Statement, we recognize that that is the basis for many scientific endeavors – is the use of investigational compounds – so there's certainly flexibility in how IACUCs choose to approve those and ensure that the toxic side effects or other things to consider in terms of stability and the other factors that are listed in our Position Statement are considered.

43. Pat, the next question may, in fact, be a little too far down in the weeds but it asks, **Is USP phenobarbital compounded for injection at a pharmacy considered pharmaceutical-grade?** Well, by definition, if it's a compounded material, I believe it no longer is considered pharmaceutical-grade because it's been further manipulated. But would we consider it something that IACUCs should consider as acceptable? Most likely, yes.

44. Okay, and let's see, we probably have time for maybe two or three more questions. **What do you do when you know that your institution has overcrowding issues?** Well, this is up [to] the IACUC to assess the situation and ensure that it is resolved. And if it's a chronic situation, it would need to be reported to OLAW as noncompliance [Reporting Noncompliance].

45. Okay, this one – we've gone through so many, we may have asked you this already, but **Is OLAW stating that the only departures from the *Guide* that need to be reported to the IO as departures are those "must" statements in the *Guide*, i.e., departures from the "must" statements?** I think I really already did answer this question.

46. Okay and then one final quick one: **How long will it be before a transcript of today's session is available? This is somewhat more urgent than most of the OLAW webinar topics.** I'm actually going to turn to Susan Silk who is responsible for all of the things running as smoothly as they do.
We're happy to tell you that a transcript will be posted as soon as possible.

And with that, we do have some additional questions that we will make sure are posted along with those transcripts, as well as the answers to them. Again, Pat, thank you. And to all of you that participated, we, as always, thank you for your participation and really would appreciate feedback from you. You will receive a follow-up message from us tomorrow. Please use that as an opportunity to share with us your ideas for future topics and to provide feedback on any technical problems that arose during this seminar. As we have done with previous seminars, this session for the IACUC staff has been recorded and, as obviously answered by the last question, will be up on the OLAW website as soon as possible. There will be a PDF of the slides as well as the transcript.

We hope that you will be able to join us for our 2012 webinars. We have not yet finalized topics for 2012 because we realize that one webinar may, in fact, not be adequate to address issues relating to OLAW's adoption of the 8th Edition of the *Guide*. It's likely that the March 2012 webinar will also be focused on that topic, but we are awaiting input from you to help us determine what issues we should address in 2012. 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. We hope that you have a peaceful holiday season.

Additional Submitted Questions Not Addressed During the Webinar

47. If Avertin is being used in an approved protocol not due to expire for three years, does the protocol need to be re-reviewed to ask for a justification? Assured institutions must implement the 8th Edition of the *Guide* during calendar year 2012. The IACUC should develop a plan and schedule for changes that are needed to maintain compliance with the *Guide*.

Toxicities of Avertin have been reported in the literature. Avertin is no longer in common use, so it is likely that IACUCs at Assured institutions have required scientific justification before granting approval for the use of this anesthetic.

In situations where the IACUC has approved the use of Avertin or other substances formulated by the research team without a scientific justification, the specific situations should be identified. The investigator should submit an amendment for review and approval by the IACUC. The amendment should provide a scientific justification for this departure from the *Guide* or describe a compliant modification to the animal activity.

48. Is the addition of saline to a pharmaceutically defined drug such as ketamine for dilution for administration to mice considered compounding? No, diluting stock solutions is not compounding.

49. Is the use of Avertin as an agent for anesthesia for terminal procedures considered a deviation from the new *Guide*? Yes.

50. Extrapolating from your answer to the question regarding KCL, would OLAW consider the use of any non-pharmaceutical compound acceptable in an animal under surgical anesthesia in a nonsurvival procedure? It depends on the substance and reason for its use. OLAW's Position Statement on use of pharmaceutical-grade agents and OLAW FAQ F4 is applicable in most instances but there may be situations when a non-pharmaceutical-grade product is needed such as when conducting a terminal perfusion or fixation under deep anesthesia. (See also question 28.)

51. Page 139 of the *Guide* indicates (in regard to HVAC): They should be capable of adjustments in and ideally maintain dry-bulb temperatures of plus or minus 1°C (2°F)." It is challenging to maintain temperature at such a tight set point. Can the IACUC approve a deviation to this requirement based on historical facility records? Assured institutions must develop a plan and schedule for compliance with the standards of the 8th Edition of the *Guide*. Historical records are not an adequate justification for a deviation from the *Guide*. The *Guide* recognizes that minor changes in temperature and humidity can occur during the day including variation outside of the established parameters and states on page 140 that "moderate fluctuations in temperature and relative humidity outside suggested ranges are generally well tolerated by most species commonly used in research as long as they are brief and infrequent".