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December 1, 2011 Position Statements

Position Statements

The following Position Statements describe the ways in which OLAW expects institutions to implement the 8th Edition of the *Guide*. The public is invited to submit comments on their understanding of these Statements for a period of 60 days until February 3, 2012. In response, OLAW may further clarify the Position Statements. A link for submission of electronic comments to OLAW is provided at the end of each Position Statement.

Position Statement 1) Cost
Nearly 70% of respondents stated that they are 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. (See U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training Principle II.) Assured institutions are responsible for compliance with the *Guide*. OLAW believes compliance can be best accomplished using teamwork, professional judgment, and experience. The PHS Policy and the *Guide* define the minimum standards ("musts") and performance standards ("shoulds") that OLAW expects of Assured institutions. OLAW recognizes that there are many ways to achieve humane animal care and use. An institution may use an alternative approach if the approach satisfies the requirements of the PHS Policy as determined by OLAW. In many instances, institutions and IACUCs elect to exceed the standards. This is not required and can add expense to the program.

Position Statement 2) 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. (See *Guide* pages 50-63.) Outcome-based performance standards are paramount when evaluating cage or pen space for housing animals used for research, research training, and biological testing. While the *Guide's* space recommendations are a starting point for addressing space needs, performance standards allow flexibility to improve animal welfare and 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.

Position Statement 2a) Nonhuman Primate Housing
Like all social animals, nonhuman primates should be socially housed. (See U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training Principle VII and 9 CFR Ch. 1, Part 3, Subpart D.) Staff performing the socialization should be trained and competent in the procedure and knowledgeable about the animals. Behaviorally compatible animals must be used in socialization attempts. Group composition is critical and numerous species-specific factors should be taken into consideration when forming a group. Due to conformational differences of animals within groups, more space or height may be required to meet the animals' physical and behavioral needs. Determination of the appropriate cage size is not based on body weight alone. Professional judgment is paramount in making such determinations. (See *Guide* pages 58-60.)

When necessary, single housing of social animals should be limited to the minimum period necessary. When single housing is necessary, visual, auditory, olfactory, and (depending on the species) protected tactile contact with compatible conspecifics should be provided, if possible. In the absence of other animals, additional enrichment should be offered (as appropriate to the species or individual animal), such as safe and positive interaction with the animal care staff, periodic release into larger enclosures, supplemental enrichment items, and / or the addition of a companion animal in the room or housing area.

Institutions are encouraged to consult the Animal Welfare Act and Regulations on primate housing requirements. Compliance with the USDA regulations is an absolute requirement of this [PHS] Policy. (See PHS Policy footnote 2.) Housing of nonhuman primates in social settings (pairs or groups) is the requirement of the USDA regulations (9 CFR Ch. 1, Part 3, Subpart D) and single housing is the exception. Protected tactile contact is considered single housing by the USDA, with rare exceptions. 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.

OLAW and USDA concur on OLAW FAQ F14, "Is social housing required for nonhuman primates when housed in a research setting?" A revised version of FAQ F14 has been posted on the OLAW website. OLAW and USDA positions are further defined at the Nonhuman Primate Enrichment and Social Housing resource on the OLAW website.

Position Statement 2b) Environmental Enrichment

OLAW concurs with the *Guide's* statement, "The primary aim of environmental enrichment is to enhance animal well-being by providing animals with sensory and motor stimulation through structures and resources that facilitate the expression of species-typical behaviors and promote psychological well-being through physical exercise, manipulative activities, and cognitive challenges, according to species-specific characteristics." (See *Guide* pages 50-52.) 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.

Position Statement 2c) Rodent Housing

OLAW supports the *Guide's* approach to applying performance standards to achieve specified outcomes and expects 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.

Rodent cages of the size commonly used in the United States may be appropriate for trio breeding. The 8th Edition of the *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. Examples of these factors may include:

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

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.

OLAW's guidance on IACUC-approved departures from the *Guide* for rodent housing was first posted on September 11, 2006 in FAQ F10**, "**May the IACUC approve deviations from the *Guide* for rodent (mice and rats) cage density?" A revised version of FAQ F10 has been posted on the OLAW website.

Position Statement 2d) Rabbit Housing

OLAW concurs with the 8th Edition of the *Guide*. "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." (See *Guide* pages 51-52, 56, 59.)

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 the 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.

Position Statement 3) Non-Pharmaceutical-Grade Substances

Approximately 40% of respondents indicated concern with requirements on the research use of non-pharmaceutical-grade chemicals and other substances.

OLAW and USDA agree that pharmaceutical-grade[1] chemicals and other substances, when available, must be used to avoid toxicity or side effects that may threaten the health and welfare of vertebrate animals and / or interfere with the interpretation of research results. However, it is frequently necessary to use investigational compounds, veterinarian- or pharmacy-compounded[2] drugs, and / or Schedule I[3] 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 factors including, for example:

- grade,
- purity,
- sterility,
- acid-base balance,
- pyrogenicity,
- osmolality,
- stability,
- site and route of administration,
- compatibility of components,
- side effects and adverse reactions,
- storage, and
- pharmacokinetics.

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, 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.

Although the potential animal welfare consequences of complications are less evident in non-survival studies, the scientific issues remain the same. The principles and need for professional judgment outlined above apply to non-survival studies.

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.

OLAW's guidance on the use of non-pharmaceutical-grade substances was first published in 2003 (Lab Animal. 2003; 32(9):33-36) and posted on the OLAW website on September 11, 2006. The USDA's position on non-pharmaceutical-grade substances may be found in the Animal Care Manual Policy [3]. OLAW provided additional guidance on use of non-pharmaceutical-grade substances in FAQ F4, "May investigators use non-pharmaceutical grade compounds in animals?" A revised version of FAQ F4 has been posted on the OLAW website.

[1] A pharmaceutical grade compound is a drug, biologic, or reagent that is approved by the Food and Drug Administration (FDA) or for which a chemical purity standard has been established by the United States Pharmacopeia-National Formulary (USP-NF), or British Pharmacopeia (BP) .

[2] Veterinary compounding is the customized manipulation of an approved drug by a veterinarian, or by a pharmacist upon the prescription of a veterinarian, to meet the needs of a research study. IACUCs considering the use of veterinary compounding for research purposes are advised to consult: http://www.avma.org/issues/drugs/compounding/veterinary_compounding_brochure.asp for more information about federal regulations.

[3] United States Department of Justice Drug Enforcement Agency controlled substances Schedule I and II-IV drugs may be used in biomedical research according to the standards of the Code of Federal Regulations 1301.13.

Position Statement 4) Food and Fluid Restriction / Use of Preferred Foods
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 testing and the amount of the regulated item freely given should be recorded to ensure each animal receives its minimum daily requirements. (NRC 2003, Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research, Washington: National Academies Press) The IACUC must evaluate the level of restriction and 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.

Position Statement 5) 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. (See *Guide* page 30, 117.) Multiple procedures that may induce 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 investigator; or
- necessary for clinical reasons.

Cost savings alone is not an adequate reason for performing multiple major survival surgical procedures. (See *Guide* page 30.)

Note that under USDA regulations (AWR 2.31 (x) A-C), “No animal will be used in more than one major operative procedure from which it is allowed to recover, unless: (A) Justified for scientific reasons by the principal investigator, in writing; (B) Required as routine veterinary procedure or to protect the health or well-being of the animal as determined by the attending veterinarian; or (C) In other special circumstances as determined by the [Animal Care] Administrator on an individual basis. Written requests and supporting data should be sent to the Animal and Plant Health Inspection Service, Animal Care, 4700 River Road, Unit 84, Riverdale MD 20737-1234”.

OLAW's guidance on use of multiple surgical procedures was first published in 1997 (*Contemporary Topics*. 1997; 36(2):47-50) and posted on the OLAW website on September 11, 2006 as FAQ F9, “Are major multiple survival procedures permitted on a single animal?” A revised version of FAQ F9 has been posted on the OLAW website.

Position Statement 6) 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. (See PHS Policy IV.A.1.) 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*, (FASS 2010) [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." (See *Guide* page 33.)

The USDA position on regulation of agricultural animals may be found in the Animal Care Policy Manual Policy 17. OLAW's guidance on using standards for agricultural animals was posted on September 11, 2006 as FAQ G7, "May institutions utilize the *Guide for the Care and Use of Agricultural Animals in Agricultural Research and Teaching* if their programs include traditional farm animals?" A revised version of FAQ G7 has been posted on the OLAW website.