

Comments of The American Association of Immunologists (AAI) to
the Association for Assessment and Accreditation of Laboratory Animal
Care International (AAALAC) Regarding the 8th Edition of the
Guide for the Care and Use of Laboratory Animals

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Rodents, and in particular laboratory mice, are of paramount importance to the members of The American Association of Immunologists (AAI) and the organization's mission to advance the field of immunology. Consequently, the interpretation by the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) of the 8th edition of the *Guide for the Care and Use of Laboratory Animals (Guide)*, as it impacts the use of these mammalian models, is of great concern to AAI. Below we have detailed specific issues regarding AAALAC's statements and additional concerns regarding the updated *Guide* for which we seek clarification of AAALAC's positions.

1) Cage Space

"At a minimum, AAALAC International expects accredited institutions to comply with all national or regional regulations, policies and guidelines, as well as conditions of funding. Additionally, AAALAC International considers performance standards paramount when evaluating cages or pens for housing animals used for research, testing or teaching. The performance criteria described in the *ILAR Guide*, *Ag Guide* and ETS 123 are used by AAALAC in assessing the adequacy of cage or pen space available to the animal(s). In those countries where regulations or guidelines do not exist or mandate cage or pen dimensions, AAALAC International suggests institutions consider the *ILAR Guide's* space recommendations as a minimum while always recognizing that performance standards also must be met."

AAI viewpoint: AAI is greatly concerned about the meaning of performance standards especially in regard to cage density of mated mice and their progeny. The strict interpretation of the updated *Guide* in this respect will have enormous negative collateral effects on biomedical research and is inconsistent with the best scientific practices. AAI notes that new scientific research published since the 7th issue of the *Guide* has shown that in many cases there are no adverse health effects to mice housed at double the current recommended density. We ask AAALAC to clarify its interpretation of Performance Standards especially in regard to cage density of mated mice and their progeny. Furthermore, AAI believes that the primary standards utilized for assessment should be appropriate for the country/nation of the institution.

2) Laboratory Animals (definition of)

“Current Position Statement on Laboratory Animals:

All vertebrate animals used or to be used in research, teaching or testing at accreditable units are to be included and evaluated in relation to the principles set forth in the *Guide*. This includes traditional laboratory animals, farm animals, wildlife, and aquatic animals.

Laboratory Animals (revised definition):

AAALAC International defines ‘laboratory animals’ as any live vertebrate animal (and any other animal considered by applicable legislation) used or intended for use in research, testing, or teaching. For accreditation purposes, the definition is broadly encompassing across species and is not limited by the type of housing enclosure (e.g., cage, pen, paddock, pasture, tank, raceway, etc.). All such animals owned by the accreditable unit are to be included in the Program Description and will be evaluated by AAALAC International according to the standards set forth in the *ILAR Guide*, *Ag Guide*, and ETS 123.”

AAI viewpoint: AAI believes that the primary standards utilized for assessment should be appropriate for the country/nation of the institution. In the United States, we should not be held to the ETS 123 standard.

3) Safety Requirements for Walk-In Cage or Rack Washers*

“The safety of walk-in type cage or rack washers must be addressed by the institution. AAALAC International has identified three key factors that must be considered when developing the safety plan for this equipment: 1) ease of egress, 2) a de-energizing** mechanism, and 3) personnel training. The possibility of entrapment must be eliminated, and ideally an emergency shut-off mechanism that is easily accessible from anywhere inside the machine and which de-energizes the washer when activated should be in place. Proper instructional signage must be posted and cage or rack washer operators must receive appropriate training so as to minimize their risk. Following risk assessment, other mechanisms and/or procedures, individually or in combination, might be determined to provide the same level of protection and eliminate possible entrapment, such as:

- **buddy system** in which at least two individuals are present when the washer is started, with the intent that one of them will always remain outside of the washer and ensure that no one is inside upon activation of the wash cycle;
- **explosion relief door latches** which open easily from the inside of the washer;

- **lock-out system** whereby the emergency stop mechanism, once activated, must be actively disengaged before the machine can be restarted.

The adequacy of cage/rack washer safety is the responsibility of the institution, typically through cooperative efforts among the animal facility personnel, occupational health and safety personnel, and the IACUC (or comparable oversight body). The institution must provide the Council on Accreditation with sufficient evidence to demonstrate that issues regarding cage or rack washer safety have been addressed and will be periodically reviewed.

*This does not include bulk/walk-in sterilizers or autoclaves.

**The term 'de-energize' indicates immediate flow stoppage of water into the interior of the cage washer, along with termination of the wash cycle such that restart requires deliberate reactivation of the machine."

AAI viewpoint: This may be a major burden for some institutions. AAI requests that AAALAC include a grandfather clause for older cage-wash systems and adopt an economically realistic phase-in time for the purchase or reconfiguration of models with appropriate safety features.

4) Attending Veterinarian and Veterinary Care

"The animal care and use program is the collaborative responsibility of the Institutional Official, the Attending Veterinarian and the IACUC (or comparable oversight body). The Attending Veterinarian is responsible for the well-being and clinical care of animals used in research, testing, teaching, and production. This responsibility extends to monitoring and promoting animal well-being at all times during animal use and during all phases of the animal's life. It is expected that the program of veterinary care will uphold the highest standards of care and ethics and the veterinarian must have the authority, delegated by senior administration and the IACUC to treat, remove from the experiment, and institute appropriate measures to relieve severe pain or distress or euthanize the animal if necessary. The Attending Veterinarian must have adequate resources to manage the overall program of veterinary care. AAALAC International acknowledges that other qualified individuals may assume some of the roles and responsibilities of the Attending Veterinarian, under the oversight of the Attending Veterinarian. Important aspects of the role of the Attending Veterinarian and the program of veterinary care include:

- Veterinarians providing clinical and/or program oversight and support must have experience, training, and expertise necessary to appropriately evaluate the health and well-being of the species used, in the context of the animal use being carried out by the institution.
- The Attending Veterinarian must have access to all animals.
- There must be timely provision of veterinary medical care and emergency veterinary care must be available after work hours, on weekends, and on holidays.
- The Attending Veterinarian is expected to have oversight of several aspects of the program such as husbandry, housing, preventative medicine and health surveillance, medical treatment, establishment of sedation, anesthetic and analgesic guidelines, handling, and immobilization.
- The veterinarian is expected to provide guidance and oversight to surgery programs and perioperative care.
- Professional veterinary staff should remain knowledgeable about the latest practices and procedures to ensure that high quality care is provided to animals.
- If there is no full-time Attending Veterinarian on-site, there must be a designated person who is responsible for daily animal care and use and facility management.

In addition, the Attending Veterinarian has further responsibilities related to his/her role on the IACUC. For example:

- There should be regular, clear communication between the Attending Veterinarian and the IACUC, and animal program needs should be regularly and clearly communicated to the Institutional Official by the Attending Veterinarian.
- The Attending Veterinarian should have input in protocol review, the development of study removal criteria, and responsible conduct of research activities.
- The IACUC, in association with the Attending Veterinarian, has the responsibility for determining that personnel performing surgical procedures are appropriately qualified and trained in the procedures to be performed.
- The IACUC, along with the veterinarian, should be involved in classifying major versus minor surgical procedures.”

AAI viewpoint: AAI is concerned that the Principal investigator (PI) who is most authoritative on the scientific intent (of an animal study) seems not to be included as an active participant in fundamental decisions that can have great impact on his/her research. Although AAI recognizes that the Attending Veterinarian (AV) has ultimate responsibility for the animals’ well-being and clinical care, the AV should not have the

authority to countermand an IACUC-approved animal study unless the experimentally induced conditions have not been stated and approved. AAI is further concerned that both the updated *Guide* and the AAALAC position statement leave ambiguity regarding the oversight responsibilities of the IACUC and those of the AV.

5) Social Housing

“Appropriate social interactions among members of the same species (conspecifics) are essential to normal development and well-being. An understanding of species-typical social behavior (e.g., natural social composition, population density, ability to disperse, familiarity among the animals and social ranking) is key to successful social housing. Cage complexities and important resources (e.g., perches/shelves, visual barriers, refuges, food, water, shelter, litter boxes, enrichment devices) should be provided in such a way that they cannot be monopolized by dominant animals or elicit aggression between animals.

In general, social animals must be housed in stable pairs or groups of compatible individuals, and social housing will be considered by AAALAC International as the default method of housing unless otherwise justified based on scientific necessity, social incompatibility resulting from inappropriate behavior, or veterinary concerns regarding animal well-being. In these cases, single housing of social animals should be limited to the minimum period necessary, and where possible, visual, auditory, olfactory and tactile contact with compatible conspecifics should be provided. In the absence of other animals, enrichment should be offered, such as safe and positive interaction with the animal care staff, as appropriate to the species of concern, and supplemental enrichment items or the addition of a companion animal in the room or housing area. The need for single housing should be reviewed on a regular basis and approved by the IACUC (or comparable oversight body) and/or veterinarian.”

AAI viewpoint: AAI is concerned about whether AAALAC considers mice and/or rats social animals and if so, what that means regarding husbandry and enrichment. Although many Institutions use enrichments for mice and rats, AAI believes that very few, if any, of the other considerations described apply to mice and rats. AAI therefore requests that AAALAC clarify which of those considerations it believes apply. Without adequate clarification, such statements may be subject to extreme interpretation, for example, by mandating that rodents must always be maintained in pairs or groups and that current cage formats are inadequate. Finally, the socialization mandate could be especially problematic in infectious diseases research requiring isolation of animals.

AAI is also concerned about the applicability of some further areas of the updated Guide to rodents and requests AAALAC’s interpretation in reference to rodents.

A. AAALAC position on restraint devices in rodents

Guide, p. 29: “Restraint devices..... must be justified in the animal use protocol.”
“Animals to be placed in restraint devices should be given training (with positive reinforcement) to adapt to the equipment and personnel.” “Animals that fail to adapt should be removed from the study.”

AAI Viewpoint: There should be no requirement to justify standard and acceptable (i.e., humane) methods of rodent restraint (e.g., for injection). Adaptation/training of rodents should not be required.

B. AAALAC position on food and fluid regulation in rodents

Guide, p. 31. “Written records should be maintained for each animal to document daily food and fluid consumption, hydration status, and any behavioral and clinical changes used as criteria for temporary or permanent removal of an animal from a protocol....”

AAI Viewpoint: With the understanding that animals are already required to be monitored daily, and that many studies which include food and fluid regulation are relatively innocuous, the IACUC, in discussion with the PI, should have the leeway to decide if such records are needed. Moreover, it would be impossible to monitor daily food and fluid intake for each rodent, unless they were housed at one per cage, which can have other adverse effects.

C. AAALAC position on habituating mice and rats

Guide, page 64: “Habituating animals to routine husbandry or experimental procedures should be encouraged whenever possible as it may assist the animal to better cope with a captive environment by reducing stress associated with novel procedures or people.”

AAI Viewpoint: This should not be applied to laboratory mice and rats because they have been domesticated for many years.

D. AAALAC position on IACUCs in Inter-institutional Collaborations

Guide, p. 15: “Interinstitutional collaboration has the potential to create ambiguities about responsibility for animal care and use. In cases of such collaboration involving animal use (beyond animal transport), the participating institutions should have a formal written understanding (e.g., a contract, memorandum of understanding, or agreement) that addresses the responsibility for offsite animal care and use, animal ownership, and IACUC review and oversight.”

AAI Viewpoint: Assuming that IACUCs at both institutions are operative, this seems an unnecessary regulatory burden that serves no animal welfare benefit or purpose. As it raises another barrier to timely medical research, this position is counterproductive.