



## การพิจารณาโครงการฯ — ความสำคัญของสมดุลระหว่าง สวัสดิภาพสัตว์และคุณภาพของงานวิจัย

การอบรมขั้นพื้นฐานคณะกรรมการกำกับดูแลการดำเนินการต่อสัตว์เพื่องานทาง  
วิทยาศาสตร์ที่มีประสิทธิภาพเพื่อเข้าสู่ระดับสากล



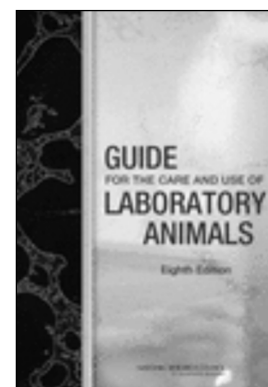
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## The Guide



- “...assist institutions in ***caring for*** and ***using*** animals in ways judged to be ***scientifically***, ***technically***, and ***humanely*** appropriate...”
- Caring for > animal welfare
- Using > research/ science
- Scientifically, technically > research/ science
- Humanely > animal welfare



## Importance of Promoting Animal Welfare



- Ethical considerations – allow laboratory animals to have the best life possible
- Scientific integrity – best life possible also means free from factors leading to unnecessary stress, which allows animals to live a normal and natural life to the greatest extent possible, which also means that any effects that are seen are due to the experimental variable and not confounding factors brought about from less than ideal factors associated with the environmental and/or handling

3

## Animal Protocol Review – Platform for Discussion



- Animal protocol review is the most important platform for discussion and debates on issues related to animal welfare and scientific integrity
- Many times, these two issues go hand in hand; however, sometimes they do not
- Examples: toxicity testing – range-finding, maximum tolerable dose (MTD)

4

## Prior to the Animal Protocol Review



- IACUC membership – scientists (with and without laboratory animal experience), statisticians, non-affiliated, non-scientist
- Animal protocol format
- Adequate time for IACUC members to review
- Opportunity for IACUC members to request clarification
- OHS review and approval

5

## At the Animal Protocol Review



- IACUC meeting quorum – policy on attendance
- Procedures – inclusive (everyone's views are taken into consideration – especially minority views), non-inhibitive (take time to explain technical issues in a non-technical way for non-scientific members), comprehensive (make sure to cover all issues), opportunity for researcher(s) to provide clarification where needed
- Veterinarian and non-affiliated/ non-scientists are responsible for representing the “animal welfare” voice
- Researchers are responsible for representing the “scientific integrity” voice

6

## Importance of the Animal Protocol Format



- A comprehensive animal protocol format allows the researcher to provide adequate information to the IACUC for review, without the need for a lot of additional explanation
- A comprehensive animal protocol format highlights key issues that need special consideration, e.g. single housing, environmental enrichment, physical restraint, unexpected outcomes, early endpoints and signs/symptoms for veterinary intervention

7

## Science vs Welfare



	Scientific Integrity	Animal Welfare
<b>I. Animal husbandry requirements</b> <ul style="list-style-type: none"> <li>• Single housing</li> <li>• Environmental enrichment</li> </ul>	<ul style="list-style-type: none"> <li>• Removing confounding factor for behavioral study, reduce chance of interfering with procedure (dermal administration)</li> <li>• Remove confounding factors; improve visibility for observation</li> </ul>	<ul style="list-style-type: none"> <li>• Social housing is ideal/standard; single housing must be enriched in other ways</li> <li>• Environmental enrichment is ideal/standard; not providing enrichment needs to be validated/defended on a per study basis</li> </ul>

8

## AAALAC Policy on Social Housing



- appropriate social interactions among members of the same species are essential to normal development and well-being
- attention **should** be given to whether the animals are naturally territorial or communal and whether they should be housed singly, in pairs, or in groups
- social housing of incompatible animals can induce chronic stress, injury, and even death
- single housing of social species **should** be the exception and justified based on experimental requirements or veterinary-related concerns about animal well-being
- where possible, visual, auditory, olfactory, and tactile contact with compatible conspecifics **should** be provided – also enrichment (staff interaction, cage items)
- need for single housing **should** be reviewed on a regular basis by the IACUC and veterinarian

9

## AAALAC Policy on Environmental Enrichment



- primary aim of environmental enrichment is to enhance animal well-being by providing animals with sensory and motor stimulation
- 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
- well-conceived enrichment provides animals with choices and a degree of control over their environment, which allows them to better cope with environmental stressors
- some items may be detrimental to well-being (e.g. injury, allergy, stress)

10

## AAALAC Policy on Environmental Enrichment (cont.)



- enrichment programs **should** be reviewed by the IACUC, researchers, and veterinarian on a regular basis to ensure that they are beneficial to animal well-being and consistent with the goals of animal use
- they **should** be updated as needed to ensure that they reflect current knowledge
- personnel responsible for animal care and husbandry **should** receive training in the behavioral biology of the species they work with to appropriately monitor the effects of enrichment as well as identify the development of adverse or abnormal behaviors
- some scientists have raised concerns that environmental enrichment may compromise experimental standardization by introducing variability, adding not only diversity to the animals' behavioral repertoire but also variation to their responses to experimental treatments – **study found this not to be true**

11

## Science vs Welfare (cont.)



	Scientific Integrity	Animal Welfare
<b>II. Route of administration</b> <ul style="list-style-type: none"> <li>• Oral gavage</li> <li>• Inhalation – nose-only</li> </ul>	<ul style="list-style-type: none"> <li>• Ability to ensure oral intake (accurately quantify exposure)</li> <li>• Ability to ensure appropriate route of administration (nasal vs oral)</li> </ul>	<ul style="list-style-type: none"> <li>• Animal handling/stress (adequate training, appropriate equipment)</li> <li>• Physical restraint (how long), heat and moisture build up in body tubes, size of body tube (risk of suffocation; frequency of observation)</li> </ul>
<b>III. Study design</b> <ul style="list-style-type: none"> <li>• Number of animals</li> </ul>	<ul style="list-style-type: none"> <li>• Statistical power</li> </ul>	<ul style="list-style-type: none"> <li>• Number of animals that undergo procedures that may increase pain/ suffering/ inconvenience</li> </ul>

12

## Science vs Welfare (cont.)



	Scientific Integrity	Animal Welfare
<b>IV. Study design (cont.)</b> <ul style="list-style-type: none"> <li>• Range-finding</li> <li>• Toxicity testing – lethality</li> <li>• Carcinogenesis</li> <li>• Immunotoxicology</li> </ul>	<ul style="list-style-type: none"> <li>• Identification of appropriate range of doses (non-effect and effect doses)</li> <li>• Need to confirm lethality (selected early endpoint may not be indicative of lethality)</li> <li>• Confirm cancer endpoint, e.g. tumor formation/ size</li> <li>• Need for sensitizer/ mediator (adjuvant)</li> </ul>	<ul style="list-style-type: none"> <li>• Uncertainty; difficult to pinpoint exact range and therefore how many animals will be needed</li> <li>• Avoid pain/ suffering – early endpoints</li> <li>• Tumor size (non-inhibitive of daily routine, e.g. access to food and water, early endpoints)</li> <li>• Pain and irritation, early endpoints</li> </ul>

13

## Science vs Welfare (cont.)



	Scientific Integrity	Animal Welfare
<b>V. Sample collection</b> <ul style="list-style-type: none"> <li>• Blood samples - volume</li> <li>• Blood samples - frequency</li> <li>• Urine samples – metabolic cage</li> </ul>	<ul style="list-style-type: none"> <li>• Experimental requirements – assay volumes, total number of assays</li> <li>• Need to monitor body burdens/ immune function over time</li> <li>• Urinary volume (duration of collection)</li> </ul>	<ul style="list-style-type: none"> <li>• Blood withdrawal limits (species, size)</li> <li>• Blood withdrawal limits (per day, multiple punctures at same site)</li> <li>• Animal restraint, cage size, access to food and water</li> </ul>

14

## Science vs Welfare (cont.)



	Scientific Integrity	Animal Welfare
<b>VI. Euthanasia</b> <ul style="list-style-type: none"> <li>• Decapitation, cervical dislocation</li> <li>• Blood sample/ exsanguination</li> <li>• Sample preparation/ collection - perfusion</li> </ul>	<ul style="list-style-type: none"> <li>• Anesthetic interferes with experimental endpoint</li> <li>• Need blood samples (adequate volume) for assaying</li> <li>• Require organs for assaying (appropriate organ prep)</li> </ul>	<ul style="list-style-type: none"> <li>• Animal pain/ suffering – adequate training, appropriate equipment</li> <li>• Blood withdrawal under anesthetic, monitored by veterinarian, adequate training</li> <li>• Under anesthetic, monitored by veterinarian, adequate training</li> </ul>

15

## Unexpected outcomes



- Despite the best laid plans, often times unexpected things happen – the “fail-safe switch” for this is an established and effective procedure for monitoring (including/ especially in off hours) and reporting to the veterinarian
- Procedures **must** be in place to provide emergency veterinary care both during and outside of regularly scheduled hours.
- Such procedures **must** enable animal care and research staff to make timely reports of animal injury, illness, or death.

16



## Unexpected outcomes (cont.)



- A veterinarian or the veterinarian's designee **must** be available to expeditiously assess the animal's condition, treat the animal, investigate an unexpected death, or advise on euthanasia.
- In the case of a pressing health problem, if the responsible person is not available or if the investigator and veterinary staff cannot reach consensus on treatment, the veterinarian **must** have the authority to treat the animal, remove it from the experiment, institute appropriate measures to relieve severe pain or distress, or perform euthanasia if necessary.

17

## Post-Approval Monitoring (PAM)



- Approval of an animal use protocol is only the beginning – this means that IF all animal care and use procedures are carried out as described, everything should be OK
- However, this is not always the case EVEN IF the protocol is followed
- Also, it is important that the protocol IS followed and monitoring is required for this
- Self-reporting is an important mode of monitoring BUT not the only mode
- The important eyes and ears of the IACUC are the veterinary and animal husbandry staff because they have daily hands on time in the facility

18

## AAALAC Policy on PAM



- Continuing IACUC oversight of animal activities is required
- PAM helps ensure the well-being of the animals and may also provide opportunities to refine research procedures
- PAM methods include:
  - continuing protocol review (note: e.g. annual report);
  - laboratory inspections (conducted either during regular facilities inspections or separately);
  - veterinary or IACUC observation of selected procedures;
  - observation of animals by animal care, veterinary, and IACUC staff and members (note: this is very important); and
  - external regulatory inspections and assessments

19

## Conclusions



- The IACUC (and the AV - representing vet care - on the IACUC) plays a VERY important role in a facility's animal care and use programme
- Being at the interface of animal welfare and science, the job the IACUC carries out can and is difficult
- The best approach is for the IACUC to work with researchers to improve animal welfare for the promotion of better science – this is **enabling** rather than **inhibitory**
- The researcher's main aim is to maximize the science. The IACUC's main aim is to enable the researcher to maximize the science, while taking care to assure high quality animal welfare.

20

## Conclusions (cont.)



- **Bottom line:** with the best standard of animal welfare possible, confounding factors due to sub-standard animal health and well-being are removed, thus ensuring that any experimental observation seen is due to the experimental variable (treatment) and not due to non-treatment variables such as stress and malnutrition.



21

**THANK YOU**

