

# When is a House a Home?

**D**r. Jerry Silverman, a Principal Investigator (PI) at Great Eastern University (GEU), hypothesized that exposure to temperature extremes during the early stages of development impacts cognitive abilities. The study involved maintaining litters of rats at high and low temperatures, from birth until weaning, and then using behavioral tests to assess cognitive abilities.

To ensure accurate temperature control, Jerry proposed to use a specialized environmental chamber to house rats for periods of up to six-weeks. The environmental chamber is a large room, similar to a walk-in cooler, located adjacent to Jerry's lab, which is outside of the GEU core animal facility.

The IACUC inspected the proposed housing chamber room and noted a

number of *Guide* deficiencies. Specifically, the HVAC system fell short of the *Guide* requirements, and appropriately sanitizing the room was near impossible due to the construction design of the chamber walls and ceiling. Consequently, the GEU's IACUC disapproved the use of the chamber for housing.

Jerry, being a past IACUC Chair, appealed the IACUC's decision during a full committee meeting. He asked the IACUC to reconsider the use of the chamber and suggested identifying it as a departure from the *Guide*. Jerry continued his appeal by outlining the practices he would employ to ensure the test animals' welfare. Jerry indicated that in addition to the temperature controls, the chamber was equipped with a timer to control the light/dark cycle and that the animals would be checked daily. He said the room was on a central monitoring system that would notify him of power outages or any other emergencies. Jerry indicated the chamber would be locked, and veterinary staff would have ongoing access to the chamber.

Do you agree with Jerry that the use of the chamber can be approved as a *Guide* departure, and, if so, what would be the conditions of the approval? □

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## A WORD FROM OLAW

In this scenario, the IACUC is asked to consider use of a specialized environmental chamber to house rats for periods of up to six-weeks as an approved departure from the *Guide*. As described by one of the respondents, through a cooperative interaction with a willing PI, the IACUC was able to find solutions to allow the use of the environmental chamber that address their environmental and sanitation concerns.

The PHS Policy requires the IACUC in its oversight of animal care and use to ensure adherence to the *Guide*, identify departures from the *Guide*, and report departures in the semiannual report to the Institutional Official<sup>1</sup>. The IACUC may approve departures from the *Guide* based on scientific justification or for veterinary or animal welfare reasons<sup>2</sup>. In GEU IACUC's case, it may approve the temperature deviations as a departure from the *Guide* and allow the sanitation of the chamber based on performance standards in accord with the *Guide*<sup>3</sup>. The *Guide*'s focus on performance standards provides flexibilities that allow

for unique scientific needs within the constraints that the health and well-being of the animals are maintained<sup>4</sup>. □

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3. Public Health Service. Policy on Humane Care and Use of Laboratory Animals – Frequently Asked Questions. Institutional Responsibilities, Question No. G.10. What is OLAW's position on performance standards? (US Department of Health and Human Services, Bethesda, MD, USA). [online]. <https://olaw.nih.gov/faqs/guidance/faqs?anchor=question52960>
4. Institute for Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington DC, 2011). p. 6–7.

# Finding the balance

Finding the balance between regulations and research progress is a tight line the IACUC manages. Fortunately in this scenario, the Principal Investigator (PI) is

a previous IACUC Chair who understands the balance and is willing to work with the IACUC to achieve the goals. Now the IACUC must determine if the outcome is achievable.

In review of the space, using the *Guide*<sup>1</sup> for reference, the two standout items of concern are the air exchange frequency and the lack of ability to sanitize. The IACUC ponders: Could performance standards be used in this situation and allow an exception? More information is required to answer this question and the best way to decide is to sit down and collaborate/communicate with the PI. Leaving the PI out of the conversation creates assumptions by the IACUC, and mistrust in the IACUC by the PI (a feeling GEU is trying to alleviate at the university).

The first discussion item is the inability to sanitize the space. The IACUC had assumed that animals would be housed directly in the space in static cages on a rolling cart, which was not approved. In discussion with the PI, the IACUC learned the animals will be housed in static caging within a sanitizable isolator in the room. Additionally, the behavior equipment is enclosed and fully sanitizable. Depending on the experiment and facility manager consultation, projects will either be terminal or animals will return to the quarantine area of the vivarium.

The second discussion item is the slightly below standard air exchanges. Previously, the IACUC assumed the PI was not concerned by or did not understand the importance of managing air exchanges. In discussion with the PI, the IACUC expressed their concern of the extreme low and high temperatures with only once a day health monitoring, as the low air exchange would elevate the temperatures, heat index and humidity. An agreement between the PI and the IACUC was made to run a mock experiment (without animals) of normal, low, and high temperatures. Temperature and humidity would be monitored three times a day within the chamber and within the static cage housed in the isolator for comparison.

After receipt and review of the “mock” experimental data, the IACUC decided to approve the space based on performance standards being met and inclusion of sanitizable caging/behavioral equipment. The protocol would also include more frequent monitoring of the animals, humidity, and temperature; better defined humane endpoints; and an approved temperature range for each experimental group.

Reflection of this scenario reminds us that communicating and collaborating

## COMPLIANCE CONSIDERATIONS

The Protocol Review coordinators offer the following compliance considerations:

### What is considered “housing”?

The regulatory definitions of housing facility, study area, and animal facility provide context around the type of structure (indoor, outdoor) and whether the animals are outside of a core vivarium space (e.g., an area that houses animals for greater than 24 hours is considered a satellite facility<sup>1</sup> that requires inspection by the IACUC<sup>2</sup>). The PHS Policy<sup>1</sup> and *Guide*<sup>3</sup> are silent on the definition of “housing”; consequently, it is up to the IACUC to define this term in context of, and in adherence to, all other regulations.

### What are departures from the *Guide*?

Any IACUC approved deviation from “must” (i.e., a minimum standard required) or “should” (where performance standards are not applicable<sup>4</sup>) statements is a departure from the *Guide*<sup>5</sup>.

### What are performance standards?

Performance standards are alternate methods of achieving outcomes delineated in the *Guide* through data-driven metrics; they:

- are clearly defined and regularly monitored;
- support scientific objectives;
- support the health and welfare of the animal;
- include a justified performance index; and
- have associated outcome criteria.

### What are the sanitization requirements?

The *Guide* provides guidance for the cleaning and disinfection of:

- Microenvironments: “enclosures and accessories, such as tops, should be sanitized at least once every 2 weeks.”
- Macroenvironments: “components of the animal facility, including animal rooms and support spaces (e.g., storage areas, cage-washing facilities, corridors, and procedure rooms) should be regularly cleaned and disinfected as appropriate to the circumstances and at a frequency based on the use of the area and the nature of likely contamination.”

### Can performance standards be applied to Jerry’s chamber?

- The *Guide* allows for laboratory housing if the purpose meets scientific aims.
- The chamber is a macroenvironment for performing research activities in which the temperature of the animals’ environment is purposefully manipulated.
- GEU’s IACUC could require Jerry to provide data showing whether the cleanliness (or lack thereof) of the macroenvironment negatively impacts the welfare of the animals for the duration of the research activity in the chamber.

### What about Jerry’s study is a *Guide* departure?

- The manipulation of the animals’ environmental parameters (i.e., temperature), with IACUC approval, is considered a departure from the *Guide*.
- The *Guide* permits performance standards to determine the cleaning and disinfection of the macroenvironment, which, even with IACUC approval, would not be a departure from the *Guide*.

### If the IACUC approved the *Guide* departure, would there be any conditions of the approval?

While the IACUC cannot grant any “conditional approvals”; any application of performance standards would require regular monitoring to verify continued success of the outcomes. □

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with stakeholders of the IACUC is essential to understanding the full picture. Hearing the word “IACUC” may not bring up fuzzy, warm feelings. To bridge the gap between the IACUC and those who must follow the regulations, both sides must learn to collaborate,

educate and be open to communication. Transparency is key.

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# Too Many Variables: The IACUC Should Care About the Science

The environmental chamber, as described in the scenario, appears to be little more than a cold room, with poor ventilation and issues impacting the ability to perform proper sanitation. As such, an assumption can be made that there is no (or inadequate) built-in dehumidification. The IACUC should not grant exceptions to *The Guide* for the use of this room as a housing facility. Even with appropriate SOPs, monitoring, and humane endpoints in place, there are factors accompanying the use of such a space that may impact the health and welfare of the animals in both anticipated and unanticipated ways, and may thereby introduce uncontrolled variables into the scientific design.

Cold rooms are typically subject to elevated relative humidity (RH), due to the differential of external to internal air temperatures. Such rooms are notoriously prone to the growth of mold, and in this case, the inability to appropriately sanitize the room would likely increase the possibility for mold growth. Indeed, it has been demonstrated that the presence of elevated RH promotes the growth of mold or other pathogens<sup>1</sup>, and can also impact bacterial propagation and ammonia production<sup>2</sup>. The room's limitations for air handling, sanitation and humidity control

could impact animal health, and may possibly also become an occupational health concern for animal care staff.

Additional concerns arise from considerations of the rodent thermoregulatory system. Multiple studies have demonstrated that reduced temperatures may lead to myriad and complex physiological shifts, including the suppression of the immune system and increased susceptibility to pathogens, activation of the sympathetic nervous system, the progress of tumor development, and numerous other changes in physiology<sup>3</sup>. Even using sophisticated climate-controlled animal housing, there are numerous variables that would need to be controlled for in the experimental design. Without the ability to adequately regulate airflow, RH and any associated effect of pathogens, as would appear to be the case in this scenario, the number of variables would only increase.

Why does this matter? One of the responsibilities of the IACUC is to ensure that the use of animals is scientifically justifiable. While the IACUC does not review for scientific merit *per se*, ensuring that the use of animals in a study is likely to result in a sound scientific outcome is an essential component of protocol evaluation, as indicated by the U.S. Government

Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training:<sup>4</sup> “Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.” The number of unknown variables introduced by the housing situation in this circumstance undermines the assurance that the IACUC would typically have from the PI that the merit of the science justifies the use of the animals. □

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