

compromise the scientific validity of the research results; and to describe criteria for removal of animals from the study and humane endpoints. It is the responsibility of the IACUC to evaluate the procedures and objectives of the study against any potential animal welfare concerns. In addressing these issues during protocol review, Ayers was fulfilling her responsibility as an IACUC member. In this regard, she is to be commended for her attention to the welfare of Summers' animals.

1. Public Health Service. US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (US Department of Health and Human Services, Washington, DC, 2002).
2. Institute of Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2011).
3. Public Health Service. *Policy on Humane Care and Use of Laboratory Animals* IV, C, 1 (US Department of Health and Human Services, Washington, DC, 2002).
4. Animal Welfare Act and Regulations, 9 CFR, Chapter 1, Subchapter A.

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RESPONSE

Protecting animal welfare

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First, we assume that there is a strong scientific justification for housing animals at such a low temperature outside of the recommendations of the *Guide for the Care and Use of Laboratory Animals* (the *Guide*)¹. Second, although the description of "gradually adapting" mice to cold temperatures is vague, we presume that the adaptation regimen is acceptable because Ayers was impressed with the data provided by Summers who obviously has experience with the particular environmental condition as a study variable. Nevertheless, housing animals below the recommended temperature is a deviation from the *Guide* that must be approved by the IACUC on the basis of scientific justification. This deviation also will need to be included in the report of

semi-annual program evaluations to the Institutional Official. We can also assume that this study will last for at least 2 weeks on the basis of Ayers' suggestion that the body temperature be recorded weekly in order to assess stress levels of the mice. Other factors that are left unstated include whether the animals will be housed together or individually and whether nesting material will be provided in the cages. These factors definitely affect the animals' thermoregulation.

Although close monitoring of the mice is necessary, Ayers' suggestion of monitoring the body temperature of the mice weekly could add another stressor for the animals. A better option to protect the welfare of the mice is to develop a set of humane endpoints, which are both meaningful and not an obstacle to the research. Those are best developed in collaboration with the veterinarian, as the expert in animal physiology and pathology, and the principal investigator, as the expert of the study topic. Routinely monitoring the body weight of the animals; observing them for hunched posture, unkempt appearance, sunken eyes and declining activity; or creating a body condition scoring sheet are some strategies that could be used.

The question here is whether Ayers was doing her best to protect the welfare of Summers' animals; the answer in our opinion is yes. She has a responsibility as a member of the IACUC to uphold the recommendations of the *Guide* for the welfare of the animals. She is tasked not only with recognizing instances that could cause pain or distress but also with recommending and initiating changes and alternatives that can improve the outcome for the animals. Summers may feel as though Ayers' questions and suggestions are an obstruction to his research, but Ayers is trying to protect animal welfare by facilitating Summers' ability to carry out high-quality research while complying with regulatory principles.

1. Institute of Laboratory Animal Research. *Guide for the Care and Use of Laboratory Animals* 8th edn. (National Academies Press, Washington, DC, 2011).

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RESPONSE

Questioning is appropriate

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Ayers is being very judicious by questioning Summers' methods to monitor mice and identify those that may be experiencing extreme cold stress. Although Summers has provided some data from previous experiments that would support his position that mice are not experiencing high levels of stress, there is still a level of concern for animal welfare given the parameters of his experiments designed to subject mice to environmental temperatures well below their thermoneutral zone. Regardless of whether or not he gradually adapts the mice to cold temperatures, the potential stress that can ensue from being placed in this environment needs to be carefully considered by all those involved in the project.

Summers is correct in quoting the *Guide for the Care and Use of Laboratory Animals* (the *Guide*)¹, which states that mice should be housed at temperatures below their lower critical temperature to avoid heat stress (i.e., 20–26 °C). The *Guide* goes on to say, however, that animals should be provided with adequate resources for thermoregulation such as nesting material or shelter to avoid cold stress. In fact, when provided adequate nesting material, mice show a preference for a cage environment below their thermoneutral zone even when given access to an adjoining cage at or above their thermoneutral zone². Given the goal of Summers' experiments (to study the effects of cold exposure), the likelihood that mice would be provided adequate shelter to adapt to these extreme conditions is questionable.

According to the *Guide*, the IACUC is charged with evaluating scientific elements of the protocol as they relate to the welfare and use of animals¹. Therefore, as a protocol reviewer, Ayers has the responsibility of questioning the manner in which Summers will monitor the mice in this study. Although Summers presents some convincing data to suggest that mice exposed to extreme temperatures are not experiencing any greater degree of stress than mice housed at temperatures recommended by the *Guide*, his findings may have some limitations. For instance, if fecal corticosterone levels