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Dr. Stephen Potkay
Director of Compliance Oversight Division
Office of Laboratory Animal Welfare, NIH
6705 Rockledge Dr., Rockledge I, Ste. 1050-MSC 7982
Bethesda MD 10892-1982

Re: ILACUC-approved research techniques course at Ohio State University in Columbus, OH

Dear Dr. Potkay:

As you know, the Office of Laboratory Animal Welfare (OLAW) is responsible for ensuring that National Institutes of Health (NIH) grantee institutions comply with the Health Research Extension Act (HREA) and the Animal Welfare Act (AWA). On behalf of the Physicians Committee for Responsible Medicine, an advocacy group consisting of 5000 physician and 100,000 lay members, I would like to bring to your attention some concerns regarding NIH grantee Ohio State University (OSU).

The OSU Institutional Laboratory Animal Care and Use Committee (ILACUC) approved a National Institute of Neurological Disorders and Stroke (NINDS)-funded instructional protocol that is not in compliance with the AWA or Public Health Service (PHS) policies.

Using NINDS funds, OSU offers a three-week course each summer, titled Spinal Cord Injury Techniques, to students and professionals. According to ILACUC application documents, the grant period continues until 2007. This course teaches a technique designed to systematically injure the spinal cords of rats and mice, and various accompanying procedures related to that technique, such as microinjection, behavioral evaluation after injury, and various pathology evaluation techniques. Specifically, students will perform multiple major surgeries on 269 rats and mice that result in a crushed or severed spinal cord. After such a procedure, the animals involved develop complications ranging from impaired bladder control to paralysis. The students will then lead some of the rats and mice through a 45-minute session of forced tasks designed to evaluate neurobehavioral function, such as swimming, reflex, temperature and sensory testing, and various walking exercises on surfaces such as a treadmill, an open field, an elevated runway, an increasing inclined plane, a rotorod, and a raised wire grid. The animals are surely in a large amount of post-operative pain in addition to the complications they might experience as a result of their injury.

As OSU is a research facility that conducts biomedical and behavioral research with funds provided under the HREA, it is required to abide by PHS Policy on the Humane Care and Use of Laboratory Animals (PHS Policy) established under the HREA. As part of this required compliance, it must provide a written Animal Welfare Assurance of Compliance (Assurance) to OLAW detailing the institution's procedures for compliance with PHS Policy. Once this Assurance is approved by OLAW, the institution and all its personnel must comply with the PHS Policy, including the US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training (US Principles) and the Guide for the Care and Use of Laboratory Animals (Guide).

As further part of this required compliance, any use of live animals for testing, research, and training must be approved by the ILACUC. The approval process requires that the ILACUC "review concerns

involving the care and use of animals at the institution" and "determine that the proposed research projects are in accordance with this [PHS] Policy." Finally, the ILACUC is "authorized to suspend an activity involving animals…" including activities that have been previously approved.

A fundamental goal of the PHS Policy and the Guide is the minimization of animal pain and distress. In fact, the Policy itself states, "investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals." As the activities described above would be painful and distressing to humans, this OSU course violates efforts designed to avoid or minimize such pain and distress to the animals. These efforts, as stated in PHS Policy, include the consideration of non-animal alternatives, the design of projects that have "relevance to human or animal health…" and use the "minimum number [of animals] required to obtain valid results." To this end, Chapter One of the Guide states that considerations must be made with regard to "Availability or appropriateness of the use of less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation." Finally, the PHS Policy states "exceptions should not be made solely for the purposes of teaching or demonstration."

In the Animal Use Protocol for this course (Protocol) received by the ILACUC on June 9, 2003, the principal instructors of the course attempt to explain the rationale for using live animals, the species chosen, and of the course itself. Instructors state that the mice and rats used are "bred specifically to illustrate…the SCI response in humans," and that "Many decades of literature are available on rat injury models which make them particularly relevant for this type of research."

However, past activities do not justify current or future ones, especially when the intent of the ILACUC review process is to carefully examine the use of animals in performing the exercise needed. Past literature and breeding activities do not provide a relevant scientific justification for causing severe pain and distress in 269 rats and mice.

The instructors state that this course is necessary to train future scientists in spinal cord injury research in a consistent manner, and posit that by using animals to train students, less animals will be used in the future in this field. We believe this to be a naïve statement designed to obtain ILACUC approval for the course. Those familiar with scientific research understand that most students best learn research techniques by working on an individual basis within research projects with their faculty advisors, under close supervision, where the consequences of their actions on the project can be immediately realized. Furthermore, students typically continue to use the same methods, throughout their professional career, that they were taught early on. This course serves as an indoctrination of future spinal injury researchers to the experimental animal model, without giving students an opportunity to explore other ways to approach spinal cord injury research. Researchers participating in this course will perceive the experimental animal techniques taught by Ohio State University as the only valid methods open to them, resulting in another generation of scientists that rely heavily on animal models in spinal injury research.

As a consequence of requisite compliance with HREA and PHS policy, OSU is also required to comply with The Guide for the Care and use of Laboratory Animals (Guide), most recently published in 1996 by the National Academy of Sciences. In the section titled "Institutional Policies and Responsibilities," the Guide specifies that submissions to the ILACUC should detail, among other things, "Availability or appropriateness of the use of less-invasive procedures, other species, isolated organ preparation, cell or tissue culture, or computer simulation." Traditionally, this involves a written narrative to the ILACUC setting forth that a reasonable and good faith effort was made to determine the availability of alternatives or alternative methods, and, if a database search or other source identifies a *bona fide* alternative method (one that could be used to accomplish the goals of the animal use proposal), the written narrative should justify why this alternative was not used.

The Protocol appears to contain such a narrative. The Principal Investigator (PI) describes a MEDLINE search for "spinal cord injury, central nervous system injury, [and] experimental spinal cord injury." The PI explains that no suitable alternatives to the use of 1325 mice and rats over five years could be found. Further explanation is provided by discounting the use of tissue culture models in experimental spinal cord injury research, and an explanation of the need for "confirmation of the results [of research projects] across a number of laboratories" (page 6).

However, this search appears to be cursory, at best, and does not fulfill the intent of the guidelines it is meant to address. First, a search for alternatives to the use of animals *in this course* should include a search for alternative teaching methods, not alternative research methods. Alternatives to the course range from shadowing a researcher and the use of simulators and models to videotaped techniques demonstrations.

In addition to the perceived need for animal use in this course, the instructors have violated PHS Policy statute III in that course protocols call for more than the minimum number of animals required. In particular, the investigators proposed the use of different strains and sexes of rats and mice, based on the unconvincing justification that the observable fact that different strains and sexes of animals respond differently to spinal injuries must be illustrated to the students. Instead, instructors could simply explain these differences to the students or develop a comparative presentation, if they wished. The use of these additional animals in such painful and distressing procedures is clearly not justified.

The US Principles can be, and often are, summarized by invoking the "3R's" of animal use. The "3R's" include reduction (using the minimum number of animals to complete the protocol), refinement (ensuring all pain and distress is alleviated), and replacement (eliminating animals from the protocol). It seems that the instructors of this course did not prepare this course protocol in compliance with the US Principles. This completely unwarranted use of animals demonstrates a callous lack of concern for the welfare of animals, the 3-R principles, and the language and spirit of the law requiring that the use of animals be minimized to the greatest extent possible.

For all of the reasons listed above, the instructors who have requested approval for the use of animals in this course, the ILACUC that has approved their use, and OSU itself, is in violation of the Health Research Extension Act and its implementing regulations and policies, PHS Policy, and US Principles. My colleagues and I have attempted to discuss these issues directly with Ohio State University and its ILACUC, and have not received any response.

Accordingly, the Physicians Committee for Responsible Medicine requests that you exercise your responsibility as an OLAW official and investigate this matter and Ohio State University as a whole, in order to ensure that the institution is in compliance with the intent of these animal welfare policies as enacted.

Thank you for your prompt attention to this important issue.

Sincerely,

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