Supplementing a training procedure with the use of a cadaver

It’s hard enough for an IACUC to cope with problems directly related to the use of animals in research, education and product testing, but when an IACUC gets drawn into controversies that are tangential to its mission, its problems can quickly escalate. The Great Eastern University IACUC approved Dr. Sam Messinger’s use of pigs for training surgeons in natural orifice transluminal endoscopic surgery (NOTES) and specifically for removing the gall bladder through the mouth of the patient. In this procedure, the endoscope and associated instruments are inserted in the patient’s mouth and down into the stomach. The surgeon then makes small incisions through the wall of the stomach and eventually removes the gall bladder through the patient’s mouth. Messinger was the only surgeon at Great Eastern trained in the technique, and he was anxious to help his colleagues learn the procedure. The IACUC training protocol proposed an acute study in which the pigs would be anesthetized during the procedure then euthanized without awakening.

Before beginning the study, Messinger sent an amendment to the IACUC. With the concurrence of the Department of Anatomy, he proposed to have a human cadaver in the same room with the pigs to enable the surgeons to visualize concurrently the gross anatomical differences between humans and pigs in the areas of interest. The IACUC office did not know whether handling such an amendment was within its authority, so the office staff asked the IACUC chairman. The chairman was unsure, so he asked the Attending Veterinarian (AV) for an opinion. The AV said he had no inherent objection but suggested sending the request to the Institutional Review Board (IRB, the oversight body for human research studies that is analogous to the IACUC). The IRB was equally unsure, so it asked the Institutional Biosafety Committee (IBC) for an opinion, and the IBC said it was an IACUC issue. The IACUC then asked the Institutional Official (IO) to become involved. The IO asked the Dean for her input, and the Dean quickly arranged a meeting with herself, the AV, and the IACUC, IRB and IBC chairpersons.

Do you think that Messinger’s amendment is reasonable for the proposed training? What position would you take if you were part of the Dean’s meeting?

RESPONSE

Passing the buck

Donna L. Goldsteen, BS, LATG, CMAR, CPA, Shameen Aff-Rider, BS, LATG, CPIA, RAC & Youngmi Girard, BSN, COHN-S, MBA

Passing the buck on an issue that one doesn’t know how or want to deal with is unfortunately quite common. We elected to address this scenario by examining each committee’s responsibility.

The Institutional Review Board (IRB) is responsible for determining whether the research is in accordance with the Health and Human Services Policy for Protection of Human Research Subjects. In that policy, a human subject is defined as “a living individual.” Thus, IRB approval should have been obtained before the body was made available for use at this medical school. Hence, the IRB has no need for further action in this case.

The Institutional Biosafety Committee (IBC) is responsible for determining whether the procedure is in accordance with the institution’s biosafety program and other external requirements and guidelines to assure safe practices in handling tissues, viruses and bacteria. Personnel handling the cadaver or animals would be required to attend general occupational health and safety training in order to carry out this type of work. Unless clinical information about the cadaver indicates that there is a potential infectious exposure risk, the IBC has no need for further action in this case.

According to the Public Health Service Policy on Humane Care and Use of Laboratory Animals, “the IACUC shall conduct a review of those components related to the care and use of animals and determine that the proposed research projects are in accordance with this Policy.” The Animal Welfare Act Regulations state that a proposal to conduct an activity involving animals must contain statements identifying the species and numbers used; the rationale for involving animals; a description of the proposed use of animals, including final disposition of the animal; and descriptions of methods to alleviate or decrease pain and distress and methods of euthanasia. Animal well-being should be the primary focus of the IACUC. Most facilities try to separate animals from potentially distressful situations; for example, necropsies are not usually done in rooms that house live animals. To decrease potential distress to the pigs caused by the presence of a cadaver, the IACUC should recommend that the pigs be anesthetized sufficiently before the cadaver is brought into the room.

The Attending Veterinarian (AV) is responsible for the surgical procedure done on the pigs. The AV needs to assure that the cadaver bag is transferred to the facility in a manner that prevents any potential contamination of the animals.
like any bag or boxed item entering the facility. The AV may also have concerns about the requirement that the pigs be euthanized at the end of the procedure. This procedure, when done correctly, is reported to have excellent survival rates. Pigs are able to adapt to the lack of a gallbladder, as are humans. The AV may recommend that the pigs be allowed to recover and be placed back into a holding colony for future use, if possible.

If there is a possibility that the pigs may be used for another surgical procedure, the IACUC and AV may need to consider whether this surgery should be classified as major or minor. Many IACUCs classify any invasive operative procedure in which a relatively extensive resection is done (e.g. a body cavity is entered, organs are removed, or normal anatomy is altered) as major surgery. In general, if a mesenchymal barrier is opened (pleural cavity, peritoneum, meninges), the surgery is considered major. For surgical procedures that do not meet these criteria, the chance for inadvertent microbial contamination is a primary consideration. Some IACUCs classify surgeries as major or minor based on postoperative survival. Generally, the surgery is considered major if the animal is anticipated to survive longer than 24 hours. If the animal is to be terminated in less than 24 hours, the procedure may be considered minor.

The IACUC or AV may also have concerns about the reaction of the animal facility staff to the cadaver. Either party may recommend that the procedure be done in an area where access is restricted and that facility staff be notified of this unique situation.

Overall, we feel that the addition of a human cadaver in the room while the pigs are undergoing surgery requires IACUC approval, given the potential for distress and alterations to the protocol and environment.


Godbout is Senior Manager, Laboratory Animal Resources; Al-Jrrih is Associate Director - Regulatory Governance and IACUC/IBC/IRB; Administrator; and Gerard is Senior Manager, Environmental Health and Safety at MedImmune, LLC, Gaithersburg, MD.

RESPONSE

Compliance is a team effort

Harry Fyke, DVM & Thomas Lombardo, PhD

The amendment to add cadavers to this protocol is relevant. The addition of human cadavers to compare and contrast the anatomical differences between pigs and humans should enhance the learning experience for the surgeons being trained. Assuming the IACUC has reviewed and has no reason to withhold approval of the animal care and use protocol involving the pigs, the issue here becomes who is responsible for oversight of the addition of the cadavers. Because the cadavers represent a potential threat to personnel, the main concern is occupational health and safety.

Identifying potential hazards is a key component of any animal care and use program. Institutions are required to establish and maintain an occupational health and safety program (OHSP) as part of their animal care and use program. This OHSP program requires the cooperation of the Institutional Official (IO), IACUC, Institutional Biosafety Committee (IBC), Attending Veterinarian, researchers and health personnel.

The IO is ultimately responsible for health and safety in the workplace. The responsibilities may be delegated to various groups within the institution. Although the IACUC is not specifically charged with the review and assessment of every potential hazard involved with a research protocol, it is responsible for ensuring that those hazards are properly addressed by the appropriate individual or committee.

A word from USDA

In response to the questions posed in this scenario, the United States Department of Agriculture, Animal and Plant Health Inspection Service, Animal Care (USDA, APHIS, AC) offers the following clarification and guidance:

Under the Animal Welfare Act and Regulations1 (AWARs; Subpart C—Research Facilities, §2.30 (2)), the University is categorized as a research facility because live swine are used for teaching. Consequently, the AWARs (under §2.31 (B)(4)(viii)) require the University to have an IACUC whose purpose is to review animal activity and to ensure that personnel conducting procedures on a species used for study are appropriately qualified and trained in these procedures. Because the Principal Investigator presents a good case that a human cadaver is an appropriate teaching tool to help the students better understand the comparative aspects between porcine and human anatomy, it is therefore required and appropriate for the IACUC to deliberate on the amendment.

The AWARs do not cover the use of human cadavers; hence, USDA, APHIS, Animal Care has no jurisdiction in this matter. It is therefore recommended that the University check with local, state and other federal agencies on this issue.

As a point of clarification, according to the AWARs ($1.1), a major operative procedure is defined as "any major surgical intervention that penetrates and exposes a body cavity or any procedure which produces permanent impairment of physical or physiologic functions". Post-operative survival time is therefore not a recognized criterion for categorization, as one comment stated.


Chester Gipson, DVM
Deputy Administrator
USDA, APHIS, AC

www.labanimaleurope.eu

Volume 12, No. 6 | JUNE 2012 33
The Institutional Review Board is not responsible for oversight of the use of cadavers because the Protection of Human Subjects act defines only living individuals as human subjects. The use of cadavers may be governed by other federal, state, and local laws. The Department of Anatomy may already be following the appropriate regulations; this should be verified by the IACUC.

IBC review is required to ensure that proper preventive procedures are in place. These include routine precautions such as adequate ventilation and the use of nitrile gloves, respirators and safety glasses to minimize risks from embalming chemicals such as formaldehyde and phenol. Although the risk of contracting infectious diseases from properly preserved cadavers is low, special precautions should be taken to prevent any chance of exposure to a contagion such as Creutzfeldt–Jakob disease, mycobacterium tuberculosis, human immunodeficiency virus and hepatitis B or C.

This scenario is a good example of the need for close collaboration and cooperation of all academic oversight bodies. This will help to ensure not only the health and welfare of research subjects, whether they are laboratory animals or humans, but also the health and safety of research personnel.


Copyright 2012© by Nature America, Inc.

Fyke is Attending Veterinarian and Lombardo is Director of the Division of Research Integrity and Compliance and Associate Professor in the Department of Psychology, IACUC and IRB member at the University of Mississippi, University, MS.

### RESPONSE

Amendment is reasonable

Jeff Stanton, DVM & Lorraine Hill, DVM, DACLAM

The question posed by this scenario is whether IACUC oversight is appropriate for an animal protocol involving a training procedure that utilizes live, anesthetized pigs in conjunction with a human cadaver. When addressing this question, Great Eastern University needs to consider both the welfare of the animals and the safety of the people involved in the training procedure. Since the experimental protocol was previously approved by the IACUC, the welfare of the animals has been assured. However, the Guide for the Care and Use of Laboratory Animals (the Guide)1 and the Public Health Service Policy on Human Care and Use of Laboratory Animals2 require that institutions establish and maintain an occupational health and safety program (OHSP). Specifically, the Guide states, “The institutional OHSP should identify potential hazards in the work environment and conduct a critical assessment of the associated risks.” In order for institutions to establish an effective OHSP, there must be coordination between the research program, the animal care and use program, the environmental health and safety program and occupational health services. Although the IACUC is not the sole institutional body charged with the responsibility of administering the OHSP, it is positioned to facilitate the collaboration between all of the groups that deliver the OHSP, specifically within the animal care program.

Submission of an amendment to the IACUC is reasonable, though not required, for the proposed training because the IACUC does have oversight responsibility related to occupational health and safety issues associated with animal protocols. In reviewing the amendment, the IACUC will be alerted to the presence of a human cadaver, which represents a potential infectious disease and chemical hazard risk in the work environment, and can then work with other institutional bodies, such as environmental health and safety, to ensure a safe work environment. None of the major institutional regulatory bodies—IACUC, Institutional Review Board (IRB) or Institutional Biosafety Committee (IBC)—has direct oversight of procedures involving the human cadaver. With respect to IRB function, federal regulations specifically define a human subject to be a “living individual”3; therefore, the IRB does not have oversight of a cadaver. The scope of IBC oversight is limited to research involving recombinant DNA4 and, therefore, does not apply to this human cadaver.

Officials at Great Eastern University should consider any federal, state or local laws that would apply to the cadaver. At our institution, the Anatomical Board of the State of Texas regulates cadaver specimens utilized by the Department of Anatomy. Reviewing the state statutes, we find no regulations regarding the use of a human cadaver, but section 691.034 of the Texas Health and Safety Code5 does state that authorized individuals utilizing human remains will “conduct all activities related to such dissection with respect and dignity.” Of note, there are no clear federal regulations that provide oversight for the use of deceased humans in research, but the Animal Welfare Act6 mandates federal oversight for the use of deceased animals in research.


Stanton is Resident in Laboratory Animal Medicine and Hill is Attending Veterinarian at Baylor College of Medicine, Houston, TX.
Applying mouse genetics expertise to research

Carol Linder, PhD, Associate Professor of Biology, Department of Biology and Chemistry, New Mexico Highlands University, Las Vegas, NM.

Dr. Linder discusses her transition from providing mouse models to researchers to conducting mouse research herself.

After completing post-doctoral research in biochemistry at Washington State University, you worked in the Genetic Resources department at The Jackson Laboratory. What inspired this career decision?

I learned that The Jackson Laboratory had a Technical Services Advisor position opening when I was looking for academic positions after my post-doc. The position seemed to fit my personality, requiring a combination of scientific expertise and the ability to communicate with a wide variety of people. I was thrilled to move to Bar Harbor, ME, and Acadia National Park. I attended conferences and gave talks all over the US and Europe. I also had the opportunity to work on bioinformatics databases and development of mouse model information to assist scientists in choosing the best mouse for their research.

One of the most important things I learned in that position was to work with a broad spectrum of people with a wide variety of educational experiences. I worked with incredible scientists, veterinarians, customer service representatives and other professionals. I was humbled by the extensive knowledge of the animal caretakers and colony managers. I also learned how important good training and education are to success. I had an exceptional mentor in Dr. Muriel Davison, and this has helped me tremendously in eventually running my own research laboratory.

You now hold an academic position at New Mexico Highlands University, where you conduct research on the regulation of spermatogenesis. How did you become interested in this topic?

I became interested in cell and developmental biology during my doctoral training, conducting my dissertation research on metabolic activation following fertilization in sea urchins. For my post-doctoral research, I was lucky enough to find a wonderful opportunity in the laboratory of Dr. Michael Griswold at Washington State University. My position at The Jackson Laboratory did not allow me the time to continue this research, but when I accepted a position in academia after 10 years away from the bench, I decided to combine my acquired mouse genetics expertise with my interest in the regulation of spermatogenesis. I managed to do this with funding from a NIH NM-INBRE grant and the support of two mentors, Mike Griswold and Mary Ann Handel.

I think that spermatogenesis is the perfect developmental biology system: within a single organ you can find 19 different stages of development from spermatogonial stem cells to elongated spermatids. Spermatogenesis is regulated by endocrine, paracrine and autocrine signaling pathways; there is still so much to discover about this process that it will keep me busy throughout my career.

In your experience, how can one benefit from holding both academic and nonacademic positions in the course of one’s career?

I have learned so much from both environments. The Jackson Laboratory is a unique institution, combining research with the business of supplying mice from one of the largest repositories of mouse models for biomedical research. My position allowed me to greatly expand my knowledge base in areas ranging from basic animal care and husbandry to experimental design in almost every field of research. As I moved into administration, I was lucky enough to receive some professional training and experience in management, finance, leadership and team building.

Returning to academia has been incredibly rewarding and has presented a number of new opportunities and challenges. In a comprehensive university, one has three areas of responsibility: teaching, service and research. I enjoy all three areas, but I seem to spend a great deal of time on teaching and service while research often has to be fit in the cracks. I serve as an academic advisor for several student clubs, and this past summer I led a group of students on a Habitat for Humanity trip to Honduras. I have been fortunate to have some excellent students in my laboratory, currently including six undergraduates, two graduate students and a new research associate, so I am definitely in the laboratory on a daily basis. It is great to be part of the academic community and interact directly with other faculty and with students in the classroom and lab.