

**BEFORE THE UNITED STATES DEPARTMENT OF AGRICULTURE,  
ANIMAL AND PLANT HEALTH INSPECTION SERVICE,  
ANIMAL CARE DIVISION**

In re: Wayne State University

Docket No. \_\_

**PETITION FOR ENFORCEMENT**

**Submitted to:**

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**Date:**

Sept. 25, 2013

**Reply to:**

Physicians Committee for Responsible Medicine  
c/o Mark Kennedy, Director of Legal Affairs  
5100 Wisconsin Ave., N.W., Ste. 200  
Washington, D.C. 20016

**Submitted by:**

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This Petition for Enforcement is submitted on behalf of the Physicians Committee for Responsible Medicine and its membership of more than 10,000 physicians and 140,000 other medical professionals, scientists, educators, and supportive lay members. The Physicians Committee recently obtained more than 800 pages of documents from Wayne State University (WSU) through a court order, via the Michigan Freedom of Information Act. I carefully reviewed this and other documentation, which included the WSU Institutional Animal Care and Use Committee (IACUC) protocol (# 02-01-11), protocol amendments, National Institutes of Health (NIH) grant application (# 5R01-HL-055473), and WSU animal health records from January 2012 through March 2013, for the following animals: D3002 (Sally), D3000 (Linus), D3007 (Payton), D3004 (Brutus), D9030 (Ari), D9034 (Caesar), D9024 (Logan), D2001 (Betty), D2007 (Polly), D2008 (Trixie), D2006 (Rogue), D2009 (Hazel), D2011 (Holly), D3003 (No name), D3001 (No name), D3005 (Daryl), D2002 (Wilma), D2005 (Freddie), D9041 (Emma), D2000 (Hoagie), and D2010 (Hilda).

The research activities at issue in this new documentation are significantly different from the research activities at issue in the Physicians Committee's complaint dated Oct. 19, 2011. As a veterinarian involved in research for most of the past 20 years, including nearly 15 years serving on IACUCs and six years as an attending veterinarian, I have confidence that once you review the protocol and health records, you will agree with my assessment of this disturbing lack of care for the research animals. Our review found multiple significant violations of the Animal Welfare Act as detailed below.

Specifically, we found the following violations:

1. **9 C.F.R. § 2.31(d)(i)**: The IACUC shall determine that the procedures involving animals will avoid or minimize discomfort.
  - a. The approved IACUC protocol allows a second major abdominal surgery, seven days after the first major thoracic surgery. While there is no universal standard for intervals between major surgical procedures, two major surgeries within seven days is excessive and does not allow for proper recovery.<sup>1,2</sup> Appropriate veterinary and/or IACUC review should have noted this and required a change.
  - b. The approved IACUC protocol allows the principal investigator (PI) to run the dogs on a treadmill seven days after the first major thoracic surgery. Again, there is no universal standard, but a review of take-home instructions from veterinary hospitals suggested that the minimum time between major surgery and exercise is at least two weeks.<sup>3,4</sup> One week is insufficient time to allow for recovery of the surgical site and likely explains the repeated examples of incision site seromas, infections, and drainage described in the animals records, following surgical procedures. Again, veterinary and/or IACUC review should have noted the overly short interval and required a change.
  
2. **9 C.F.R. § 2.31(d)(iv)(A)**: Procedures will be performed with appropriate analgesics

- a. The approved IACUC protocol states that a 100 – 150 ug/hr Fentanyl patch will be used for analgesia. Appropriate dosage for a 20 – 30 kg dog is 75 ug/hr.<sup>5,6</sup> Thus, the dogs were being overdosed by at least 33 percent.
3. **9 C.F.R. § 2.31(e)(2)**: A proposal to conduct an activity using animals must contain a rationale for using animals, and for the appropriateness of the species and numbers of animals to be used.
  - a. The PI states in the approved IACUC protocol (Question 29d), “Based on our previous studies over the past ~25 years, we estimate that ~8 animals per experimental group are needed to arrive at statistically significant results.” This presumptive statement does not follow the letter or the spirit of the Animal Welfare Act, nor does it comply with fundamental statistical rules regarding sample sizes to achieve statistical significance. After 25 years, the PI should be able to provide a well-justified power analysis for group size.
  - b. The PI states in the approved protocol (Question 32), “Experiments will be repeated on a daily basis until we feel comfortable that we have obtained relevant control data.” Again, after 25 years of doing this research, the PI should have a clear definition of what constitutes “relevant control data” and should provide that to the IACUC.
4. **9 C.F.R. § 2.31(e)(3)**: A proposal to conduct an activity using animals must contain a complete description of the proposed use of the animals.
  - a. The approved IACUC protocol (Question 36b) states that the chest tube will be removed while the dog is sedated, about 12 hours after the end of the surgery. In every surgical case, the records indicate that the chest tube was removed prior to the end of the surgical procedure, in direct deviation from the approved protocol. In addition to this being a deviation from the approved protocol, as a veterinarian who has done hundreds of thoracic surgeries, I can attest that it is a well-established fact that premature removal of the chest tube can lead to collapsed lungs or hemothorax. Even if the thorax is “dry” at the time of closure, there is inevitable drainage after the animal recovers from surgery.
  - b. The approved IACUC protocol (Question 36b) states that during the first surgery, a flow probe is to be placed on the axillary artery and ultrasonic crystals are to be placed on the epicardium. There is no indication in the surgical record that either was ever implanted.
  - c. Dogs D2002 and D2005 had practice surgeries done using pentobarbital for anesthesia. There is no indication in the approved protocol or any amendment that pentobarbital was approved for use as an anesthetic.
  - d. Four different surgical procedures were performed on dog D2009: left thoracotomy, left retroperitoneal laparotomy, carotid artery occlusion, and thyroid artery catheterization. Careful review of the IACUC protocol and amendments

showed that neither the carotid artery occlusion procedure nor the thyroid artery catheterization was described. Thus, neither was approved to be done.

5. **9 C.F.R. § 2.32:** The research facility must ensure that all personnel involved in animal care are qualified to perform their duties.
  - a. Dog D2005 was used for an acute thoracic procedure on June 4, 2012. Only room air was used during anesthesia and a specific notation in the surgical records indicates that fluids and a heating pad were not used. This is not consistent with appropriate surgical technique, even for a nonsurvival surgery.<sup>7</sup>
  
6. **9 C.F.R. § 2.32(c)(iv):** Each research facility must ensure that all personnel involved in animal care have received training and instruction on aseptic surgical methods and procedures.
  - a. Dogs D2001, D2006, and D2007 each had notations of burns from the electrocautery pads. These dogs had surgeries done consecutive to one another, suggesting that the personnel placing the electrocautery pads were improperly trained.
  
7. **9 C.F.R. § 2.33(a)(2):** Each research facility shall assure that the attending veterinarian has the appropriate authority to ensure the provision of adequate veterinary care.
  - a. Dog D9024 was initially assigned to a protocol which allowed the dog to be used for practice for veterinary technician students. The records indicate that on Feb. 13, 2012, this dog received intravenous injections of sterile water. Sterile water is not an appropriate intravenous solution, as it can cause lysis of the red blood cells.<sup>8</sup>
  
8. **9 C.F.R. § 2.33(b)(3):** Each research facility shall establish programs of adequate veterinary care that include daily observation of all animals to assess their health and well-being; Provided, however, that daily observation may be accomplished by someone other than the attending veterinarian; Provided, that a mechanism of direct and frequent communication is required so that accurate information on well-being is conveyed to the attending veterinarian.
  - a. Throughout the animal records (Dogs: D3000, D3007, D3004, D3002, D9030, D9034, D2001, D2006, D2010, D9024, D2011, D3003, D3001, D3005, D2007, D9041, D2009, D2002, and D2005) there are multiple health issues noted, including infections, seromas, inappetence, and vomiting. Virtually none of these issues have any notation that a veterinarian was aware of or involved in the treatment of the conditions.
  - b. Dog D9034 was given Baytril (408 mg/day) after a notation was made that the dog appeared hypertensive. There was no explanation or apparent veterinary input involved in this diagnosis, nor was there evidence that an infection

responsive to Baytril was identified. Further, for no apparent reason, the dosage of Baytril was reduced to 380 mg/day for three days and then increased back to 408 mg/day before being stopped. There was no indication that a veterinarian was involved in any of these decisions.

- c. Dog D2006 was found to be lethargic, with cold extremities on Oct. 8, 2012. Bloodwork done on that day revealed anemia (hematocrit: 21.7), thrombocytopenia (platelets:  $157 \times 10^3/\text{ul}$ ) and elevated white blood cell count ( $18.1 \times 10^3/\text{ul}$ ). On Oct. 9, 2012, the dog was noted to still be lethargic, with a capillary refill time of 4+ seconds (versus 1 second normally), have pale mucous membranes, and her red blood cell morphology showed Howell-Jolly bodies, target cells, and hypochromasia (all signs of active blood loss and concurrent red blood cell formation). By Oct. 10, 2012, the hematocrit had decreased to 19. The dog was euthanized on Oct. 10, 2012, whereupon a hemothorax was found on necropsy. With abundant evidence that this dog had active blood loss, the only therapy given was Baytril for the increased white blood cell count. There was no indication the veterinarian was involved in the diagnosis or treatment of this dog.
9. **9 C.F.R. § 2.33(b)(5)**: Each research facility shall establish and maintain programs of veterinary care that include adequate post-procedural care in accordance with current established veterinary medical and nursing procedures.
- a. Throughout the records, multiple dogs had draining wounds treated with sugar. While the literature does suggest that application of sugar may prevent infection in draining wounds, this therapy is not consistent with any modern veterinary standards of care.<sup>9</sup>

The violations described above demonstrate a systemic failure of IACUC oversight and review, inadequate regard for animal health and welfare, and a disturbing lack of veterinary oversight. The haphazard approach to following the study protocol not only violates the Animal Welfare Act, but also compromises the reliability of the results in a manner that may have precluded IACUC approval if known in advance.

Based upon the above findings, we request that you immediately investigate and appropriately cite Wayne State University.

## References

1. <http://www.petsurgerytopics.com>: ACVS-boarded surgeon describes timing of multiple orthopedic surgeries. Spacing is one to two months apart.
2. <http://surgery.about.com/od/beforesurgery/f/BetweenSurgery.htm>: Article written by a RN about intervals between human surgeries. Recommendations for spacing of elective procedures are one to two months to allow for complete recovery from the previous procedure.
3. <http://www.vscdsurgerycenters.com/library/docs/Thoracotomy.pdf>: Post-operative client sheet describing that minimal exercise should be allowed for two weeks after a thoracotomy.
4. <http://www.swvetsurgery.com/downloads/Thoracotomy%20Handout.pdf>: Postoperative client sheet describing minimal exercise for three weeks after a thoracotomy.
5. <http://www.ahc.umn.edu/rar/documents/StdPostOpAnalgesia.htm>: University of Minnesota Research Animal Resources post-operative analgesics. Recommendation for a 20 – 30 kg dog is a 75 ug/hr patch.
6. [http://www.vasg.org/perioperative\\_pain\\_management\\_part\\_ii.htm](http://www.vasg.org/perioperative_pain_management_part_ii.htm): Veterinary Anesthesia and Analgesia Support Group. Transdermal fentanyl dosage recommendation is 2.5 ug/kg/hr. Dogs described in the obtained records were all 20 – 25 kg body weight.
7. Guide for the Care and Use of Laboratory Animals, 8<sup>th</sup> ed. p.119: While it is recognized that USDA does not follow the Guide, the Guide does state that maintaining body temperature minimizes cardiovascular fluctuations during surgery. As this research depends upon stable cardiovascular measurements, the value of any data collected from these animals should be questioned by the IACUC in its review of reduction of animal use.
8. <http://www.drugs.com/pro/sterile-water-for-injection.html>: Information about the use of sterile water, showing the label which clearly states that sterile water without the addition of solutes will cause hemolysis.
9. A.N.G. Mphande, C. Killowe, S. Phalira, H. Wynn Jones, W.J. Harrison. Journal of Wound Care, Vol. 16, Iss. 7, 01 Jul 2007, pp 317 - 319: Article describing sugar usage for wound care. States that nearly 40 percent of patients experienced wound infection after sugar therapy.