Citizens for Alternatives to Animals Research & Experimentation
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USDA/APHIS/AC Western Region
2150 Centre Ave.
Building B, Mailstop 3W11
Fort Collins, CO
80526-8117
Via E-mail: acwest@aphis.usda.gov

Re: Use of live animals in terminal experiments to study corneal wound healing

Dear Director:

Citizens for Alternative to Animal Research & Experiments (CAARE) submits this complaint to Animal and Plant Health Inspection Service (APHIS) Animal Care to investigate the use of live animals to study corneal wound healing at the University of Missouri, Columbia.

The university has conducted a series of experiments on live dogs by inflicting wounds and chemical burns on dogs' eyes to study corneal wound healing and fibrosis. These experiments can be replaced by a number of readily available and scientifically satisfactory non-live animal methods. In addition, the dogs, if used, did not need to be euthanized as there exist adequate methods to study detailed histology without sacrificing the animals.

These experiments conflict with various sections of the Animal Welfare Act and policies under USDA which stipulate that principal investigators must research appropriate alternatives to procedures that may cause more than momentary pain and distress to animals.

Under the Animal Welfare Act, University of Missouri meets the statutory definition of a "research facility" and is therefore required to comply with the Act. As part of this required compliance, any use of live animals for research, testing, or training must be approved by University of Missouri's Institutional Animal Care and Use Committee (IACUC).

CAARE believes that the University of Missouri's IACUC failed to provide proper oversight in allowing the approval and use of live dogs in experiments to study corneal wound healing.

The specific regulatory violations are:

1. **The University of Missouri failed to conduct an adequate search of non-animal methods to study corneal wound healing**

Section 2143 of the Animal Welfare Act and CFR Title 9, Section 2.31(d)(1)(i, ii) of the Animal Welfare Act's implementing regulations require that the principal investigator (PI) consider alternatives to procedures that may cause more than momentary or slight pain or distress to any animal used for research or educational purposes.

The PI must provide a written narrative description of the methods and sources used to determine that alternatives were not available. The content of this narrative is detailed in the APHIS *Animal Care Policy Manual* (2011), which states in Policy 12: "The written narrative should include adequate information for the IACUC to assess that a reasonable and good faith effort was made to determine the availability of alternatives or alternative methods."

Further, "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 IACUC may and should ask the PI to explain why an alternative that had been found was not used."

Through a Freedom of Information request to the University of Missouri, CAARE obtained a copy of the database search and rationale for using animals as compiled by the PIs. (Attached as Appendix A, pages 31-37). We found the database search to be wholly lacking in any non-animal methods to study corneal healing, including in vitro research, clinical studies, ex vivo organ cultures, and organotypic cultures.

Despite their rationale that computer simulations or in vitro studies would not be adequate for the study, there is not a single review of a non-animal method in their database search to support this conclusion.

Having failed to provide objective evidence to support animal use in view of numerous acknowledged alternatives, this requirement of the AWA was not met.

A proper alternatives search would have revealed a range of non-animal methods to study corneal wound healing and fibrosis. See Appendix B for more information.

2. **The use of live animals to study corneal wound healing is not "unavoidable," nor was it necessary to euthanize the dogs when the study was completed.**

The Animal Welfare Act also requires that activities involving animals be designed to "assure that discomfort and pain to animals will be limited to that which is *unavoidable* for the conduct of scientifically valuable research." 9 C.F.R. § 2.31(e)(4).

We believe that this requirement was not met by the PI because of the ready availability of alternative methods to using live animals, as described above. This demonstrates that such use of live dogs is not "unavoidable."

Additionally, the dogs did not need to be euthanized at the study's completion. Killing the dogs to study microscopic and detailed cellular pathways of the cornea was simply unnecessary. The use of in vivo confocal microscopy (IVCM), in use for over twenty years, enables clinicians to non-invasively examine corneal injury and disease at the cellular level in living subjects. [1]

3. The University of Missouri IACUC failed to properly oversee animal use

Section 2143 of the Animal Welfare Act and Title 9, Section 2.31(d)(1)(i, ii) of the Act require that the IACUC enforce the requirements described above, thereby assuring that the university's animal research procedures are in accordance with the Animal Welfare Act and CFR Title 9, Section 2.31(d).

Further, Policy 12 holds the IACUC additionally responsible for assuring there are no alternatives to replace an animal experiment by stating: "The IACUC, in fact, can withhold approval of the study proposal if the Committee is not satisfied with the procedures the principal investigator plans to use in his study."

We believe that these requirements were not met by the University of Missouri IACUC because the animal use protocol was approved despite the violations described in items 1, 2 and 3 above. Thus, CAARE alleges inadequate institutional oversight by the University of Missouri IACUC.

CAARE requests that APHIS investigate this matter to find University of Missouri and the IACUC in violation of the Animal Welfare Act and regulations as detailed above, and to implement corrective action and appropriate penalties. We believe this matter is of particular importance since the PIs indicated in their publications that the initial experiments were a pilot study and part of an ongoing project.

We appreciate your serious attention this matter.

Sincerely,

Barbara Stagno, RN
President
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Attachments:
Appendix A: Copy of University of Missouri alternatives search obtained through FOI
Appendix B: Selected research on corneal wounds and healing to replace live animals

[1] Cavanagh HD, et al, Clinical and Diagnostic Use of In Vivo Confocal Microscopy in Patients with Corneal Disease, *Ophthalmology*, Volume 100, Issue 10, October 1993, Pages 1444-1454