

April 01, 2022

Axel Wolff, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892

Dear Dr. Wolff,

Following is the final report of the recent noncompliance at Southern Illinois University Carbondale (PHS Assurance D16-00044)

Project funded through NIH and LLNL:

NIH 1R21AI159743-01A1

LLNL Subcontract No. B644670, Prime contract No. De-AC52-07NA27344

Reporting Requirement:

PHS Policy IV.F.3. Serious noncompliance with the PHS policy, by administration of a drug treatment not approved by the IACUC

Preliminary Report:

Submitted to OLAW Division of Compliance Oversight on Wednesday, January 12, 2022

Description of Incident:

A Principal Investigator (PI) had an approved IACUC protocol 18-041 to conduct research with mice; one of the approved experiments involved dosing some mice with the immunosuppressant drug FTY720. This protocol expired on September 18, 2021. It was replaced with a new protocol, 21-025, which was approved on September 21, 2021. The new protocol contained many – but not all – of the experiments approved in the older protocol. The experiment using FTY720 was not included in the new approved protocol.

In reviewing the data from the previous experiments, the PI determined that she needed to repeat the experiment with FTY720. She entered five mice into the experiment near the end of November 2021 with surgery, which is approved in the new protocol, and began dosing them with the drug via drinking water on January 9, 2022. She told us that she did not realize that this drug treatment had been approved under the old protocol, but was not included in the new protocol.

One of the water bottles began leaking on January 11, 2022, and the animal care worker who found it reported it to the Laboratory Animal Program supervisor. The supervisor then reported it to the Attending Veterinarian (AV). Upon further inspection of the cage and water bottle, the AV realized that the drinking water contained the drug FTY720. The cage was correctly identified with a colored tag as housing animals exposed to a potential biohazard and was being handled with BSL2 precautions, so the animal caretakers were using correct PPE and handling practices to protect themselves from the biohazard.

When the AV reviewed the approved protocol 21-025, she noted that it did not contain any reference to this treatment. She informed the PI that the drug administration had to halt immediately, and that the existing new protocol would have to be amended to include the drug treatment. The drug was then removed from the animals.

The PI submitted a protocol amendment application to add the drug treatment within hours of speaking with the AV. The protocol amendment was reviewed at the SIU IACUC meeting on January 19, 2022, and some additional information was requested of the PI. The amendment was approved by designated member review on March 14, 2022.

There have been no adverse effects noted for the mice as a result of the drug treatment. The treatment was approved under the previous protocol, and no adverse effects were noted then.

Impact on PHS-Supported Activities

Neither the NIH grant nor the Lawrence Livermore grant were charged per diem for the days that the animals were off protocol. The issue was addressed before the monthly billing was finalized, so no unauthorized costs had to be removed.

Corrective Action Plan for the Principal Investigator

1. The IACUC has requested, and the PI has completed, a refresher of the CITI online training module "Working with the IACUC."
2. The IACUC requested that the PI review her approved protocol, and compare it to the older protocol, to make sure she has included all the activities that she wishes to continue. If she finds any other experiment that she wishes to conduct, she has been advised to file a protocol amendment with the IACUC before she begins a new experimental treatment. The PI completed this review, and only added the treatment with FTY720.
3. The PI, her lab staff, and the Laboratory Animal Program workers were re-trained on March 29, 2022, in the correct method of seating the sipper tube when adding a drug treatment to the drinking water. This should help prevent further leaks of water into the bedding.

Corrective Action Plan for the Laboratory Animal Program

1. The LAP has placed a form called "Husbandry by Investigator" in the room with the animals. If the PI or her students change water, change cages, or perform other husbandry, it

will be recorded on these forms. This will prompt the animal care workers to ensure that all husbandry items have been addressed, including checking for leaking water bottles.

Corrective Action Plan for the IACUC

1. The IACUC will increase post-approval monitoring visits to the PI's lab and animal rooms during the next twelve months, so that the lab and rooms are visited by IACUC representatives four times annually.

Final Notes

The IACUC has determined that this was an isolated incident, and not a programmatic failure.

The IACUC discussed the Corrective Action Plan at the regular monthly meeting on January 19, 2022, and the final version was presented to the committee and approved at the regular monthly meeting on February 16, 2022.

Southern Illinois University Carbondale is committed to protecting the welfare of animals used in research, and appreciates the guidance provided by OLAW. Should you have any questions regarding this report, please contact Sarah Kroenlein, Director of Research Compliance.

Yours truly,

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