



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE  
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare  
6700B Rockledge Drive, Suite 2500, MSC 6910  
Bethesda, Maryland 20892-6910  
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare  
6700B Rockledge Drive, Suite 2500  
Bethesda, Maryland 20817  
Telephone: (301) 496-7163  
Facsimile: (301) 402-7065

September 27, 2019

Re: Animal Welfare Assurance  
#A3045-01 (OLAW Case 1Z)

Sheila L. Vrana, Ph.D.  
Associate Dean for Research  
Penn State University – Hershey Medical Center  
Office of Research Affairs, (b) (4)  
500 University Drive, PO Box 850  
Hershey, PA 17033-0850

Dear Dr. Vrana,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 26, 2019 letter reporting one adverse event and five instances of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Pennsylvania State University- Hershey Medical Center, following up on an initial telephone report on August 1, 2019. According to the information provided, OLAW understands the following about the incidents and the corresponding corrective actions:

- 1) A rat became dehydrated after the lixit failed. Also, the animal care staff failed to document the weekend health check.

Corrective action: The affected rat was moved to a working lixit and provided with veterinary care.

- 2) Two rats were in poor clinical condition and not eating. Laboratory staff provided diet gel, put sick cards on the cage, but failed to promptly contact the veterinarian.

Corrective action: The laboratory staff was retrained on how soon and for what conditions the veterinary staff is to be contacted. The staff was also counseled to adhere to the humane endpoints in the protocol.

- 3) Twenty five of 45 rats that were subjected to a femoral injury surgery exhibited wound dehiscence. The rats did not receive the full regimen of analgesics as stated in the protocol.

Corrective action: The rats with open incisions were anesthetized and the wounds were closed. All rats were given analgesics and subsequently recovered. The Principal Investigator (PI) was retrained on post-operative monitoring, on providing analgesics, and was counseled to only conduct surgery on the number of animals that can be effectively monitored by laboratory staff. The protocol was amended to clarify the anesthetic regimen and to include use of staples.

- 4) Personnel were handling animals and conducting animal activities without having been assessed by the Institutional Animal Care and Use Committee (IACUC) regarding training and experience.

Corrective action: The PI was counseled to ensure that all staff working with animals must be approved by the IACUC and was directed to submit a training protocol to the IACUC.

Obtained by Rise for Animals. Uploaded 08/31/2020

Retrieved from Animal Research Laboratory Overview (ARLO)

- 5) Lameness scoring was not documented for rats on the femoral injury study. Although the rats were observed daily, this was not being documented as described in the protocol.

Corrective action: The laboratory staff was directed to record animal monitoring and lameness scoring as per the protocol.

- 6) Rats were given a hormone to enhance breeding, but the protocol was approved for use only in mice.

Corrective action: The protocol was amended to include rats.

Based on its assessment of this explanation, OLAW understands that measures have been implemented in all situations to correct and prevent recurrence of the problem. OLAW concurs with the actions taken by the IACUC to comply with the PHS Policy. Regarding incident #1, the animal care staff should be counseled on how to fill out the room logs. Thank you for keeping OLAW apprised on these matters.

Sincerely,

(b) (6)

Axel Wolff, M.S., D.V.M.  
Deputy Director  
Office of Laboratory Animal Welfare

cc: IACUC Chair

Sheila L. Vrana, Ph.D.  
Associate Dean for Research

September 26, 2019

Brent C. Morse, D.V.M.  
Animal Welfare Program Specialist  
Office of Laboratory Animal Welfare  
Division of Compliance Oversight  
6700B Rockledge Drive, Suite 2500, MSC 6910  
Bethesda, MD 20892-6910

Re: Noncompliance events; Animal Welfare Assurance D16-00024 (A3045-01); not PHS funded

Dear Dr. Morse,

The Pennsylvania State University College of Medicine, in accordance with Assurance D16-00024 (A3045-01) and PHS Policy IV.F.3., provides this report of five noncompliance incidents, and one incident determined not to be non-compliant. These incidents were first reported to Dr. Axel Wolff on August 1, 2019 via a phone call by Dr. Ronald Wilson, and was asked to report them in one document.

- 1) Automatic water lixit malfunction and inadequate health observation/animal care staff monitoring of rats over weekend: A new shipment of rats were temporarily housed in a room that may not have been checked by animal care staff over a weekend (room log was not signed, despite verbal confirmation it was checked). Over that weekend, an automatic water lixit malfunctioned, leading to a rat becoming dehydrated. Immediately upon discovery, the rat was moved to a functioning water spout, and provided veterinary care and nutritional support.

The IACUC determined that this was not non-compliant.

- 2) Inadequate communication of sick animals to veterinarian: The morning of July 10, 2019, laboratory personnel reported to a clinical veterinarian via email that they had observed some of their experimental rats were sick on the morning of July 9, 2019: two of the rats were cold to the touch, had labored breathing, significant porphyrin staining, dull eyes, ruffled fur, and were overall lethargic. Additionally, neither of them ate any of their food from the night before but they both drank their water. Both rats were given diet gel and "sick" cards were placed on their cages the afternoon of July 10th. The rats were found dead the next morning.

Corrective action plan recommended by the IACUC:

1. Laboratory personnel were retrained in appropriate methods, timeline, and animal conditions to contact clinical veterinarians and/or veterinarians on call.
2. Laboratory personnel should review their protocol(s) in order to be familiar with the humane endpoints outlined and intervention strategies.



- 3) Failure to adhere to IACUC-approved protocols; failure to monitor animals post-procedurally as necessary to ensure well-being: Forty-five rats underwent femoral injury surgery over the course of two days; of those 45, 25 exhibited wound dehiscence the day following their surgery and required anesthesia and re-closure of the wounds. Although the IACUC protocol described administration of Buprenorphine HCl every 8-12 hours, the principal investigator (PI) had only delivered one dose to animals prior to surgery, with the exception of those that required incision repair receiving a second dose. Veterinary personnel treated all animals with additional Buprenorphine, and animals recovered appropriately.

Corrective action plan recommended by the IACUC:

1. The PI was retrained regarding appropriate post-operative monitoring and the analgesic regimen approved on their IACUC-approved protocol.
  2. The PI should submit an amendment to the protocol to update analgesia to remove animals "will be offered analgesics if they display signs of pain." The PI was directed to consult with a veterinarian to confirm consistent and accurate analgesia, as it was noted that there are several different analgesic procedures on the protocol that are not all consistent.
  3. The IACUC recommended submitting an amendment to the protocol to describe use of staples to close incisions and not sutures, to prevent wound dehiscence.
  4. The IACUC conveyed to the PI concern that conducting a surgical procedure of this nature on 45 animals at one time is a significant number of animals to appropriately monitor and care for post-procedurally, if there are minimal laboratory personnel available.
- 4) Participation in animal-related activities by individuals who have not been determined by the IACUC to be appropriately qualified and trained: Through review of an amendment to add new personnel to an IACUC protocol, it was determined that personnel were involved in animal handling and conducting procedures without being determined to be appropriately qualified and trained by the IACUC.

Corrective action plan recommended by the IACUC:

1. The PI should submit a Training Protocol to the IACUC for review and approval.
  2. The PI was reminded that personnel should not participate in animal activities until approved by the IACUC, as well as reminded of other federal regulations governing animal care and use and IACUCs.
- 5) Failure to adhere to IACUC-approved protocols: Rats that had undergone femoral injury were to be scored daily for lameness, and the record was to be kept in the lab for reference, so that humane endpoints could be carried out when appropriate. Laboratory personnel, animal care staff, and veterinarians were all viewing the rats daily, however, lameness scoring was not being documented as described on the IACUC protocol.

Corrective action plan recommended by the IACUC:

1. Laboratory personnel must record monitoring and lameness scoring as described in the IACUC-approved protocol. The lab immediately began recording lameness

scoring and monitoring upon notification.

6) Conduct of animal-related activities without appropriate IACUC review and approval:

A transgenic breeder rat was administered pregnant mare serum gonadotropin (PMSG) under a breeding assistance protocol held under the transgenic core. Although the protocol described use of PMSG to stimulate follicle growth and release in the ovary to attempt to increase breeding success, the protocol describes use in mice and not rats.

Corrective action plan recommended by the IACUC:

1. The IACUC recommended the PI submit an amendment to the protocol to add breeding assistance for rats. An amendment was submitted and approved by the IACUC.

The findings of the investigations were reviewed at a convened meeting of the IACUC on July 22, 2019 and August 26, 2019. The IACUC recommended to the IO that these incidents be reported to OLAW.

Please feel free to contact me if you require additional information.

Sincerely,

(b) (6)

Sheila Vrana, PhD  
Institutional Official  
Institutional Animal Care and Use Committee

**Wolff, Axel (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Thursday, September 26, 2019 12:02 PM  
**To:** Vrana, Sheila  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: Communication from Penn State College of Medicine

Thank you for this report, Dr. Vrana. I will send a response shortly.

Axel Wolff, M.S., D.V.M.  
Deputy Director, OLAW

-----Original Message-----

**From:** Vrana, Sheila <svrana@pennstatehealth.psu.edu>  
**Sent:** Thursday, September 26, 2019 11:24 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** IACUC <IACUC@pennstatehealth.psu.edu>; IACUCChair <IACUCChair@pennstatehealth.psu.edu>; Wilson, Ronald <rwilson2@pennstatehealth.psu.edu>; 'svrana@psu.edu' <svrana@psu.edu>  
**Subject:** Communication from Penn State College of Medicine

Please see attached communication from the Penn State College of Medicine.  
Thank you,  
Sheila Vrana

Sheila L. Vrana, Ph.D.  
Associate Dean for Research  
Associate Professor of Pharmacology  
Penn State College of Medicine  
500 University Drive, Box 850, (b) (4)  
Hershey PA 17033-0850  
(b) (6)  
svrana@psu.edu





## Initial Report of Noncompliance

By: aw

Date: 8/1/19

Time: 9:30

Name of Person reporting: Ron Wilson

Telephone #: (b) (6)

Fax #:

Email:

Name of Institution: Penn State Hershey

Assurance number: A3045

Did incident involve PHS funded activity? No

Funding component: \_\_\_\_\_

Was funding component contacted (if necessary): \_\_\_\_\_

What happened?

- 1) Failure to check animal room over weekend, 1 rat dehydrated & brown liquid
- 2) Cold rats after anesthesia, didn't get vet, several died
- 3) Rat on fracture study + smoking exposure. No analgesic given at correct frequency, wound dehiscence
- 4) CRO covered component, 2 people not on protocol + did animal work
- 5) Research staff didn't monitor endpoints on fracture study (#3)
- 6) PI got vet techs to help on breeding study + gave PMSB, not on protocol

Species involved: Rats + mice

Personnel involved:

Dates and times:

Animal deaths:

Projected plan and schedule for correction/prevention (if known): \_\_\_\_\_

- 1) Under investigation
- 2) Retrain lab to cold wet
- 3) Retrain on post op monitoring, amend, include staples
- 4) Amend protocol, have training protocol
- 5) Under investigation

Projected submission to OLAW of final report from Institutional Official:

- 6) Amend breeding colony protocol to include rats

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Case # \_\_\_\_\_