



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

May 15, 2019

Re: Animal Welfare Assurance
A3141-01 [OLAW Case 2D]

Ms. Candice Yekel
Associate Vice President for Research
Director, Office for Research Protection
Pennsylvania State University
330 Building, Suite 205
University Park, PA 16802

Dear Ms. Yekel,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your May 6, 2019 letter reporting the suspension of an animal activity at Pennsylvania State University, following up on an initial telephone report on April 12, 2019. According to the information provided, OLAW understands that the Institutional Animal Care and Use Committee (IACUC) took this action after determining that six mice had exceeded the humane endpoint approved in the protocol. The mice were on a holding protocol because the research protocol had expired and were noted to have necrotic tumor implant sites. Also, the mice were to be used to study tumor lung metastasis but this was not described in the protocol and the mice were not monitored daily as per protocol. A different strain of mice had been ordered prior to approval and ten mice were injected with cancer cell lines five days before protocol expiration.

The corrective actions consisted of euthanizing the sixteen mice, suspending the protocol, requiring the Principal Investigator (PI) and staff to undertake retraining, amending the protocol to clearly define the endpoints using a scoring system, identifying a key contact in the laboratory, and having the laboratory staff certify understanding of the protocol. New staff or protocol amendments must also receive certification and the PI must sign all animal use records. Upon completion of the corrective actions, the suspension will be lifted by the IACUC. The laboratory will be placed under enhanced post-approval monitoring by the IACUC and animal procedures will be monitored by the Attending Veterinarian. The grant was not charged for any unauthorized animal activities.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the IACUC to comply with the PHS Policy on Humane Care and Use of Laboratory Animals. Please also inform the NIH funding component about the suspension. Thank you for keeping OLAW apprised on this matter.

Sincerely,

(b) (6)

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

cc: IACUC Chair



PennState

Candice A. Yekel
Associate Vice President for Research
Director of Research Protections
The Pennsylvania State University
205 The 330 Building
University Park, PA 16802

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May 6, 2019

Brent Morse, D.V.M.
Office of Laboratory Animal Welfare
National Institutes of Health
RKL1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

Dear Dr. Morse:

The Pennsylvania State University, in accordance with Assurance A3141-01 and PHS Policy IV.F.3., provides this report of noncompliance regarding the suspension of activities of a Principle Investigator's (PI) for serious noncompliance with this policy. The activities were associated with a protocol that is supported by PHS funds. This incident was reviewed by the IACUC on April 10, 2019 and was reported to OLAW via telephone message on April 12, 2019.

On April 5, 2019, the IACUC was notified that six mice, which were injected with tumor cells on February 22, 2019 had been moved to a holding protocol because the PI failed to renew his application at its 3-year expiration. When examined by the veterinary staff, these animals were found to have exceeded their humane endpoints (tumor implant sites were necrotic) and needed to be euthanized. When questioned about this lapse, a lab member stated that once the tumors became necrotic the planned and approved imaging of the animals could not be completed, so they wanted to use these animals to study lung metastasis. Research on lung metastasis was not approved in the protocol.

Upon further investigation, the animal monitoring records were found to be inconsistent with what was described in the protocol (animals were only being monitored every other day after tumor size exceeded 1cm, not every day as approved in the protocol).

These items indicated a lack of attention and a more detailed audit of the lab was conducted. Items identified included:

1. A strain of mice (NOD SCID Gamma) had been ordered prior to a modification to add the strain had been approved,
2. Ten animals were injected with murine cancer cell lines 5 days prior to the protocol's expiration. The PI had no way to complete the study in this time and explained they intended to transfer these to another protocol; however, the IACUC determined that the PI's other protocols did not match this experimental treatment, the animals were euthanized.

In response to these findings, the IACUC met on Wednesday, April 10, 2019, in accordance with PHS IV.C.7 policy and AWA S2.31.d6-7, and after review of the matter at this convened meeting of a quorum of the IACUC, the majority of the quorum present voted to suspend all animal use activity for the protocol in question. The IACUC also voted to require the PI to attend the next IACUC meet, which was held on Wednesday April 17th to address IACUC questions and present a plan of corrective action.

The PI attended this meeting and accepted responsibility for the items discovered. After the PI left the meeting, the IACUC voted on the following corrective actions which must be met before the suspension would be lifted:

- The PI and all members of the lab group listed on the IACUC protocols must retake the CITI IACUC training.
- The PI must submit an amendment to the protocol to make clear that animals that develop tumor ulceration with bleeding/oozing and those with tumors that become necrotic will have met their endpoint and will be euthanized.
- The PI must develop a scoring system, whether visual or descriptive, to be added to the protocol which allows the PI and staff to clearly identify when endpoints have been met.
- The PI must assign a PI Proxy to the CATs IACUC protocols. This must be someone responsible in the lab to those projects and who can serve as a key contact.
- The PI must review the current protocol with all personnel listed on it and keep record of this review. The record should include sign off by both PI and the lab member that they understand the protocol and their responsibility. This record must be updated anytime a new lab member is added to a protocol, a new protocol is approved, or a modification to a protocol is approved. The PI must review and sign off on animal experimental records (surgery, postsurgical monitoring) to ensure personnel are maintaining appropriate record keeping in accordance with the protocol. These records will be subject to IACUC audit.

Once these actions are completed, the IACUC will review and vote to lift the suspension. After the suspension is lifted, the following conditions will be in place:

- The research group will be on a probationary period of 1 year with the IACUC. During this time the lab, the animals and the records will be subject to random and unannounced audit by the IACUC.
- The Lab AV will observe the current procedures and work with the team to overcome any technical issues the group may be having. This will continue until the Lab AV is satisfied that all procedures are accomplished as intended.

The PI, his Department Head, Research Dean and grants office have been notified that no unallowable costs may be charged to the NIH grant at issue in this incident of noncompliance. The Pennsylvania State University is committed to protecting the welfare of animals used in research and appreciates the guidance and assistance provided by OLAW in this regard.

Dr. Brent Morse
May 6, 2019
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Should you have any questions regarding this report, please contact Jeremy DeRicco, IACUC Compliance Director.

Sincerely,

(b) (6)

Candice A. Yekel
Institutional Official

cc: AAALAC International Main Office

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, May 7, 2019 7:23 AM
To: Dericco, Jeremy Saul
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Final report to OLAW

Thank you for this report, Mr. DeRicco. We will send a response soon.

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

From: Dericco, Jeremy Saul <jzd237@psu.edu>
Sent: Monday, May 6, 2019 4:19 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Yekel, Candice <cay3@psu.edu>; (b) (6) <accredit@aaalac.org>
Subject: Final report to OLAW

Dear Division of Compliance Oversight,

Please find attached a Final Report from The Pennsylvania State University Institutional Official. If you have any questions or concerns, please let me know.

Thank you,
Jeremy

Jeremy DeRicco, MBA, CPIA
ABI Program Director
Office for Research Protections
The Pennsylvania State University
(b) (4) *The 330 Building*
University Park, PA 16802
Direct Line: (b) (6) */ Fax:* (b) (6)
www.research.psu.edu/orp

The pilot release of CATS IACUC, replacing PRAMS, is underway (details: <https://www.research.psu.edu/iacuc>).



Initial Report of Noncompliance

By: [Signature]Date: 4/12/19Time: VoicemailName of Person reporting: Jeremy DiRiccoTelephone #: (b) (6)Fax #: [Redacted]Email: [Redacted]Name of Institution: Penn. St. U.Assurance number: A3141Did incident involve PHS funded activity? Yes, + NSFFunding component: NIAMSWas funding component contacted (if necessary): Not yet

What happened? 10 mice injected w/ tumor cells + left past humane endpoints. Not monitored as required. Euthanized by Am. Care staff.

Species involved: mousePersonnel involved: ResearcherDates and times: Animal deaths: Projected plan and schedule for correction/prevention (if known):

PI to meet w/ IACUC next week. Protocol suspended until then at least.

Projected submission to OLAW of final report from Institutional Official:

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Case #