



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

October 15, 2019

Re: Animal Welfare Assurance  
#A4107-01 (OLAW Case 1T)

Dr. Daniel T. Jaffe  
Vice President for Research  
University of Texas at Austin  
P.O. Box 7996  
Austin, TX 78713

Dear Dr. Jaffe,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter dated October 8, 2019 following up on a noncompliant incident at The University of Texas at Austin. The incident involved deviations from the IACUC approved protocol for a PHS funded activity involving mice. In addition, there was higher morbidity than expected, which is thought to be due to poor stem cell quality causing poor engraftment following transplantation.

Corrective measures outlined in your letter dated August 2, 2019 consisted of the P.I. submitting appropriate amendments to the IACUC, which were approved. In addition, the P.I. increased the frequency of animal welfare checks to twice daily for days when pain or distress are more likely and implemented PCR testing of donor cells to determine if the quality is sufficient for the study. From your follow up letter of October 8, 2019, we understand that the funding component has been notified of the incident and the corrective actions and that no charges for unapproved activities were made to the grant. In addition, IACUC representatives met with the laboratory staff to discuss the protocol. The IACUC voted to place the protocol on the veterinary monitoring list, which is part of the institution's post-approval monitoring program. The veterinary monitoring will assess protocol compliance, evaluate pain and distress, and review recordkeeping. The activity will be removed from the monitoring list only when the IACUC is satisfied that all concerns have been resolved. Removal from the monitoring list may only occur via a vote of the full committee at a convened meeting. Any further issues of noncompliance will be promptly reported to OLAW.

Based on this explanation, OLAW understands that corrective measures have been taken to prevent recurrence of this problem, and that the IACUC has established a thorough monitoring plan to ensure that the corrective measures are instituted and are effective. OLAW appreciates your dedication to your institution's animal care and use program and commitment to compliance with the PHS Policy on Humane Care and Use of Laboratory Animals. We thank you for informing us of this matter and at this time find no cause for further action by this office.

Sincerely,

(b) (6)

*for*  
Nicolette Petervary, VMD, DACAW  
Veterinary Medical Officer  
Office of Laboratory Animal Welfare

cc: IACUC Contact



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August 13, 2019

Re: Animal Welfare Assurance  
#A4107-01 (OLAW Case 1T)

Dr. Daniel T. Jaffe  
Vice President for Research  
University of Texas at Austin  
P.O. Box 7996  
Austin, TX 78713

Dear Dr. Jaffe,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter dated August 2, 2019 regarding a reportable incident at The University of Texas at Austin. This letter had been preceded by a preliminary report to OLAW.

According to the information provided, our office understands that on May 13, 2019 a Principal Investigator (P.I.) reported unexpected morbidity in mice on a PHS funded bone marrow transplant study. Upon investigation, the IACUC discovered that protocol deviations had occurred regarding changes in radiation dosage and in the strain of mouse used. The IACUC determined that the P.I. had initiated protocol amendments but failed to follow through on submission. It was also determined that the cause of the unexpected morbidity was poor engraftment of bone marrow donor cells due to low counts of the necessary stem cells.

Corrective measures consisted of the P.I. submitting appropriate amendments to the IACUC, which were approved. In addition, the P.I. increased the frequency of animal welfare checks to twice daily for days when pain or distress are more likely, and implemented PCR testing of donor cells to determine if the quality is sufficient for the study. We understand that the Funding Component has been notified of the incident and the corrective actions. Please ensure that no charges are made to the PHS grant for any unauthorized animal activities.

Based on its assessment of this explanation, OLAW understands that measures have been taken to prevent recurrence of this problem. Please contact our office once the corrective measures have been evaluated by the IACUC to ensure that the corrections prevent recurrence. In the response please provide updates on:

- Whether the issue of morbidity has recurred with transplants after initiation of the stem cell screening to assess donor cell quality.
- Whether the enhanced welfare checks are being implemented as described.
- Whether the study procedures are being conducted in accord with the IACUC approved amended protocol.

We appreciate being informed of these matters and look forward to your response no later than **October 13, 2019**.

*Page 2 – Dr. Jaffee*  
*August 13, 2019*  
*OLAW Case A4107-1T*

Sincerely,

(b) (6)

Nicolette Petervary, VMD, DACAW  
Veterinary Medical Officer  
Office of Laboratory Animal Welfare

cc: IACUC Contact



**THE UNIVERSITY OF TEXAS AT AUSTIN**  
The Office of the Vice President for Research

P.O. Box 7996 • FAC 426, G1400 • AUSTIN, TX 78713-7996 • 512-471-2877 • FAX 512-471-2827

August 2, 2019

Axel Wolff, M.S., D.V.M.  
Director, Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health  
RKL 1, Suite 360, MSC 7982  
6705 Rockledge Drive  
Bethesda, MD 20892-7982

Subject: Report of Non-Compliance with PHS Policy on Humane Care and Use  
of Laboratory Animals

Dear Dr. Wolff:

The University of Texas at Austin (UT), Animal Welfare Assurance #A4107-01, submits this report in compliance with section IV.F.3 of the PHS Policy on Humane Care and Use of Laboratory Animals and with the published guidance document NOT-OD-05-034 "Guidance on Prompt Reporting to OLAW under the PHS Policy on Humane Care and Use of Laboratory Animals." This letter is to report one issue of noncompliance affecting animal health or welfare where animal-related activities were conducted without appropriate IACUC review and approval. The initial report of noncompliance was made June 17, 2019.

On May 13, 2019, an investigator at UT reported significant morbidity leading to euthanasia and one death in mice having undergone exposure to radiation associated with a bone marrow transplant procedure. The UT IACUC initiated a review of the protocol and procedures in an attempt to ascertain if improved technique or increased oversight would be useful in improving the welfare of the animals undergoing this work.

In the process of this investigation, the IACUC identified that the researcher had increased the radiation dosage and changed the strain of mouse without approval from the IACUC. It appears the researcher did attempt to amend the protocol, but failed to follow through with the approval process. Therefore, the change was never presented to the committee for consideration. Through an investigation of the incident, it was determined that the high death rate was a result of poor bone marrow engraftment, which was confirmed by flow cytometry analysis. Therefore, this incident was due to bad quality (i.e. low counts of blood-forming stem cells) of bone marrow donor cells.

The researcher submitted a protocol amendment to the IACUC on June 10, 2019 in order to add a new strain of mouse and change the total body irradiation dosage. The researcher

Axel Wolff, Director, Division of Compliance Oversight  
August 2, 2019  
Re: PHS Assurance Number A4107-01  
Page 2

indicated that he would be using a lower radiation dosage than the one involved in the incident, and that this would be adequate for his study. Animal welfare checks have been increased to twice daily on days where signs of pain and distress are more likely. Through literature searches and pilot studies, the amount of irradiation proposed is adequate for the new strain of mouse. The researcher confirmed that appropriate cell line testing (PCR) will be conducted on all human and/or rodent cells that will be transplanted into these animals. The protocol amendment was approved by UT IACUC on July 23, 2019.

The project involved in this report is funded by NIH/NCI, project number 5K24CA198315-05 entitled "*Mentoring and Research in Cancer Stem Cells*". The grant officer has been copied on this notification.

Sincerely,

(b) (6)

Daniel T. Jaffe  
Vice President for Research  
University of Texas at Austin

DTJ:aem

cc: Kathryn Bayne, Global Director, AAALAC  
S. John Mihic, Chair, Institutional Animal Care and Use Committee  
(b) (6)  
Sergey Radaev, Program Official, NIH/NCI

## Morse, Brent (NIH/OD) [E]

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Monday, August 12, 2019 7:43 AM  
**To:** (b) (6) OLAW Division of Compliance Oversight (NIH/OD)  
**Cc:** Jaffe, Dan; (b) (6) Mihic, S J; (b) (6) Radaev, Sergey (NIH/NCI) [E];  
(b) (6)  
**Subject:** RE: noncompliance report NIH award #5K24CA198315-05

Thank you for providing this final report (b) (6). We will send an official response soon.

Best regards, Brent Morse

Brent C. Morse, DVM, DACLAM  
Director  
Division of Compliance Oversight  
Office of Laboratory Animal Welfare  
National Institutes of Health

Please note that this message and any of its attachments are intended for the named recipient(s) only and may contain confidential, protected or privileged information that should not be distributed to unauthorized individuals. If you have received this message in error, please contact the sender.

**From:** (b) (6)  
**Sent:** Friday, August 09, 2019 5:11 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** Jaffe, Dan <dtj@austin.utexas.edu>; (b) (6) Mihic, S J  
<mihic@austin.utexas.edu>; (b) (6) Radaev, Sergey (NIH/NCI) [E]  
<sradaev@mail.nih.gov>; (b) (6)  
**Subject:** noncompliance report NIH award #5K24CA198315-05

To Whom it Concerns,

On behalf of Dr. Daniel Jaffe, Vice President for Research at the University of Texas at Austin, please find the attached final report involving an issue of non-compliance with NIH Grant award 5K24CA198315-05. Please feel free to contact me with any further questions.

(b) (6)



**Morse, Brent (NIH/OD) [E]**

**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Tuesday, June 18, 2019 8:12 AM  
**To:** (b) (6) OLAW Division of Compliance Oversight (NIH/OD)  
**Cc:** Jaffe, Dan; (b) (6) Mihic, S J; (b) (6)  
**Subject:** RE: initial report of non-compliance

Thank you for this initial report (b) (6) We will open a case file and await further information.

Best regards, Brent Morse

Brent C. Morse, DVM, DACLAM  
 Director  
 Division of Compliance Oversight  
 Office of Laboratory Animal Welfare  
 National Institutes of Health

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**From:** (b) (6)  
**Sent:** Monday, June 17, 2019 4:57 PM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Cc:** Jaffe, Dan <dtj@austin.utexas.edu>; (b) (6) Mihic, S J  
 <mihic@austin.utexas.edu>; (b) (6)  
**Subject:** initial report of non-compliance

Axel Wolff, MS, DVM  
 Deputy Director OLAW  
 Office of Compliance

Dear Dr. Wolff,

On behalf of Dr. Daniel Jaffe, VP of Research, please accept this initial report of non-compliance for NIH/NCI project number 5K24CA198315-05, under Assurance number A4107-01.

On 5/13/2019 an investigator at the University of Texas at Austin reported significant morbidity leading to euthanasia and one death in mice having undergone exposure to radiation associated with a bone marrow transplant procedure. The University of Texas IACUC initiated a review of the protocol and procedures in an attempt to ascertain if improved technique or increased oversight would be useful in improving the welfare of the animals undergoing this work.

In the process of this investigation the IACUC has identified that the researcher had increased the radiation dosage without approval from the IACUC. It appears the researcher did attempt to amend the protocol, but failed to follow through with approval process. Therefore the change was never presented to the committee for consideration. The investigation of the incident has also noted that the dosage of radiation given to the mice may be considered borderline high for the strain involved.

As per NOT-OD-05-034, conduct of animal-related activities without appropriate IACUC review and approval is reportable.

The IACUC will continue to review the matter. After finishing the review a final report of its conclusions and actions will be submitted to the Office of Laboratory Animal Welfare. In the meantime please let me know if you have any questions.

Sincerely,

(b) (6)