



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) 480-3387

March 23, 2020

Re: Animal Welfare Assurance
#A3213-01 (OLAW Case 2E)

Dr. Kathryn A. Moler
Vice Provost and Dean of Research
Stanford University
(b) (4) Panama Mall
Stanford, CA 94305-2061

Dear Dr. Moler,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your March 9, 2020 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Stanford University.

According to the information provided, this Office understands that the Stanford University Animal Care and Use Committee (ACUC) determined that instances of noncompliance occurred with respect to: protocol suspension. The final report states that initial report was made to this Office on October 11, 2019, the resulting IACUC determination to suspend the protocol was reported on November 4, 2019 and the follow-up determination to reinstate the protocol made at the convened meeting on December 19, 2019. The IACUC discussed an allegation of noncompliance involving mice at the October 24, 2019 convened meeting. Allegations from an unannounced walk through included the following:

- 10 cages of animals housed over two laboratory spaces (one of which was not approved for animal use).
- Cage change intervals were not adhered to during that time.
- Food and water supplies were low.
- Absence of appropriate static cage tops on some of the cages resulted in moisture build-up in each cage, and the presence of moldy food and bedding.

Under veterinary guidance, the laboratory staff returned a portion of the animals to the centralized housing facility and euthanized the animals that had reached experimental endpoints. The IACUC determined that this incident demonstrated a pattern of noncompliance based on a previous, similar determination of noncompliance by this lab, deemed at the time to not be serious or continuing, for which corrective actions were assigned and completed. Based on these facts, a vote to suspend the protocol was made, seconded and approved at the convened meeting.

As for corrective actions, all protocol activity was immediately halted, and remaining animals held under the protocol were transferred to the Veterinary Services Center (VSC) holding protocol. Additional requests by the IACUC included:

- The PI not indicate in relevant publications that these animals were housed in a manner consistent with regulatory or oversight bodies including (but not limited to) the Office of Laboratory Animal Welfare, Stanford IACUC, or AAALAC International.
- A laboratory manager be hired to oversee laboratory compliance, including implementation of the corrective action plan, and all IACUC protocols and guidelines. In addition, the newly hired laboratory manager will provide a status report monthly regarding compliance with all IACUC and VSC protocols and guidelines.
- All animal users on the protocol (including the PI) retake the online course titled *Animal Care and Use Program*.
- All animal users on the protocol (including the PI) take or retake the hands-on *Mouse Handling and Basic Techniques Workshop*.
- All animal users on the protocol (including the PI) participate in an in-person training regarding rules and regulations pertinent to animal use activities at Stanford. This will be conducted by the Research Compliance Office and the VSC.
- The PI improve the documentation of future monitoring records to include additional criteria (e.g., weight, tumor size, general status) for monitoring tumor endpoints. The records will be submitted monthly to the Research Compliance Office for six months when an IACUC protocol is in place. Thereafter, records will be available to inspectors during all announced and unannounced inspections.
- The two individuals, who had previously been trained regarding similar issues of noncompliance in 2017, cease working with animals until the PI has created a specific corrective action program for them (to be approved by the IACUC), and this program is completed.
- The laboratory be required to keep anesthetic records for all animals, even in the case of very short anesthetic procedures. These records will be submitted monthly to the Research Compliance Office for the next six months. Thereafter, these records will be available to inspectors during all announced and unannounced inspections.
- The IACUC protocol be revised to clarify the number and timing of scans that one animal may undergo.

At the convened meeting on December 19, 2019, the IACUC reviewed the progress on the required corrective actions. The Panel was confident that the PI understood the nature and severity of this incident, noted that the PI had completed the necessary corrective actions, and voted to reinstate the protocol. The PI will continue to report progress on the corrective actions to the Panel. In addition, the IACUC requested that:

- Animal work not commence until the new Lab Manager had started.
- The new Lab Manager meet twice a month for the next 6 months with the Chemistry Department Director of Finance and Operations or the Chair of the Department of Chemistry.

It is understood that the research was supported by PHS funds and no unallowable costs were made to the grant during the unapproved period. Please note, however, that the PHS funding component must be notified directly of any suspension or termination of PHS supported research. Based on the information provided, the Office of Laboratory Animal Welfare (OLAW) is satisfied that appropriate actions have been taken to investigate, correct, and prevent recurrence of the noncompliance. We appreciate being informed of these matters and find no cause for further action by this Office.

Sincerely,

(b) (6)

Jacquelyn T. Tubbs, DVM
Veterinary Medical Officer
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Contact



STANFORD UNIVERSITY

KATHRYN A. MOLER
VICE PROVOST
DEAN OF RESEARCH

Confidential

March 9, 2020

Brent Morse, DVM, DACLAM
Director of Compliance Oversight
Office of Laboratory Animal Welfare
Division of Compliance Oversight
National Institutes of Health
6705 Rockledge Drive
RKL 1, Suite 360 MSC 7982
Bethesda, MD 20892-7982

Dear Dr. Morse:

As Stanford University's authorized institutional official under its PHS Assurance (Animal Welfare Assurance #A3213-01), I am writing to notify OLAW of a reportable incident as defined in PHS Policy IV.F.3.

IACUC determination	Protocol Suspension
Funding	DP1 NS105737

Overview:

To meet reporting requirements, Stanford's Research Compliance and Research Administration offices provided preliminary and ongoing information to NIH and OLAW officials via phone and email of actions taken during the period of protocol suspension. An initial report of the matter was promptly communicated to OLAW on October 11th, 2019, the resulting IACUC determination to suspend the protocol was reported on November 4th, 2019, and the follow-up determination to reinstate the protocol made at the convened meeting on December 19th, 2019 when corrective actions had been met has also been reported. The NIH Program Officer was also notified of the suspension and reinstatement on November 5th, 2019 and January 9th, 2020 respectively. No unallowable costs were made to the grant during the unapproved period. More details of the matter follow.

Description of Animal Care Issue:

At the October 24th convened meeting, the IACUC discussed an allegation of noncompliance involving mice. During an unannounced walk-through, it was noted that 10 cages of animals (containing approximately 20 animals) had been housed over two laboratory spaces (one of which was not approved for animal use) for an extended period of time. During this time, cage change intervals were not adhered to and food and water supplies were low. The absence of appropriate static cage tops on some of the cages resulted in moisture build-up within each cage, likely elevating the CO₂/ammonia levels and the presence of moldy food and

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Dr. Brent Morse
March 9th, 2020

bedding. Under veterinary guidance, the laboratory staff returned a portion of the animals to the centralized housing facility and euthanized the animals that had reached experimental end-points.

IACUC Determination:

The IACUC determined that this incident constituted a failure to adhere to the PHS "Policy on Humane Care and Use of Laboratory Animals". Additionally, The IACUC determined that this incident demonstrated a pattern of noncompliance that indicated a deficiency likely to result in further noncompliance. This was based on a previous, similar determination of noncompliance by this lab, deemed at the time to be not serious or continuing, for which corrective actions were assigned and completed. Based on these facts and that the protocol was not being conducted in accordance with applicable provisions of the Animal Welfare Act, the *Guide*, and Stanford University's current policy, a vote to suspend this protocol was made, seconded and approved at the convened meeting.

Corrective Actions:

All protocol activity was immediately halted and remaining animals held under this protocol were transferred to the Veterinary Services Center (VSC) holding protocol. In addition, the IACUC requested that:

1. The PI not indicate in relevant publications that these animals were housed in a manner consistent with regulatory or oversight bodies including (but not limited to) the Office of Laboratory Animal Welfare, Stanford IACUC, or AAALAC International.
2. A laboratory manager be hired to oversee laboratory compliance, including implementation of the corrective action plan, and all IACUC protocols and guidelines. In addition, the newly hired laboratory manager will provide a status report monthly regarding compliance with all IACUC and VSC protocols and guidelines.
3. All animal users on the protocol (including the PI) retake the online course titled *Animal Care and Use Program*.
4. All animal users on the protocol (including the PI) take or retake the hands-on *Mouse Handling and Basic Techniques Workshop*.
5. All animal users on the protocol (including the PI) participate in an in-person training regarding rules and regulations pertinent to animal use activities at Stanford. This will be conducted by the Research Compliance Office and the VSC.
6. The PI improve the documentation of future monitoring records to include additional criteria (e.g., weight, tumor size, general status) for monitoring tumor endpoints. These records will be submitted

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monthly to the Research Compliance Office for six months when an IACUC protocol is in place. Thereafter, records will be available to inspectors during all announced and unannounced inspections.

7. The two individuals, who had previously been trained regarding similar issues of noncompliance in 2017, cease working with animals until the PI has created a specific corrective action program for them (to be approved by the IACUC), and this program is completed.
8. The laboratory be required to keep anesthetic records for all animals, even in the case of very short anesthetic procedures. These records will be submitted monthly to the Research Compliance Office for the next six months. Thereafter, these records will be available to inspectors during all announced and unannounced inspections.
9. The IACUC protocol be revised to clarify the number and timing of scans that one animal may undergo.

Reinstatement

At the convened meeting on December 19th, 2019, the IACUC reviewed the progress on the required corrective actions. The Panel was confident that the PI understood the nature and severity of this incident, noted that the PI had completed the necessary corrective actions, and voted to reinstate the protocol. The PI will continue to report progress on the corrective actions to the Panel. In addition, the IACUC requested that:

1. Animal work not commence until the new Lab Manager had started.
2. The new Lab Manager meet twice a month for the next 6 months with the Chemistry Department Director of Finance and Operations or the Chair of the Department of Chemistry.

Concluding Remarks:

The IACUC has carefully reviewed this incident with all parties involved. Stanford believes that a recurrence of an incident of this nature is unlikely as all lab members have received appropriate training, and the PI and laboratory staff are committed to preventing a future occurrence. Please contact me or (b) (6) (b) (6) if you have any questions or need additional information.

Sincerely,

(b) (6)

cc: Kathryn Bayne, MS, PhD, DVM, DACLAM, DACAW, CAAB, Global Director AAALAC International

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, March 18, 2020 6:54 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: OLAW Notification for PHS Assured Institution #A3213-01

Thank you for this report, (b) (6) We will send a response soon.

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

From: (b) (6)
Sent: Tuesday, March 17, 2020 2:49 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: OLAW Notification for PHS Assured Institution #A3213-01

Dear Dr. Morse -

On behalf of Stanford University's Institutional Official, I am writing to notify OLAW of a protocol suspension. Please see the attached document.

Feel free to contact me if you have any questions or concerns.

Best,
(b) (6)

(b) (6)

As part of an on-going effort to improve our services, we invite you to complete a post-approval survey regarding your APLAC experience.

Please use this link: https://stanforduniversity.qualtrics.com/jfe/form/SV_e5694IPKNqUvDM1