



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

September 16, 2021

Re: Animal Welfare Assurance
#A3226-01 (OLAW Case 2T)

Dr. Frederick Applebaum
Executive VP and Deputy Director
Fred Hutchinson Cancer Research Center
1101 Fairview Avenue North
Seattle, WA 98109-1024

Dear Dr. Applebaum,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter dated September 13, 2021 reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Fred Hutchinson Cancer Research Center. Your letter supplements the information in the prompt telephone preliminary report on August 19, 2021. According to the information provided, OLAW understands that on August 6, 2021, during post-operative monitoring of two cages of mice with left thorax incisions by Comparative Medicine staff, the incisions were fully dehiscenced in one cage (5 mice), and partially in the second cage (5 mice). Standard Surgery/Procedure cage cards were not in place on either cage. The five mice with full incisional dehiscence were immediately euthanized. The other five mice were determined to have only minor appositional gaps and were recovering well at the time of reporting. No additional procedures have been performed since this event. This animal activity was not funded by the PHS.

Corrective and preventive actions: The two research team members that were involved completed the required aseptic training course, along with additional customized training focusing on the importance of labeling post-procedure cages with Surgery/Procedure cage cards, the use of analgesia, and instrument and patient prep. Veterinarians met with the research team members to discuss closure technique and proper placement of tissue glue. Wound clips were recommended for skin closure instead of tissue glue, and it was noted that wound clips are already approved on the IACUC protocol as an alternative closure method. A veterinarian will observe the next planned procedure to ensure proper closure technique and to provide other technical guidance. Additionally, a collaborator that is experienced with the procedure was added to the IACUC protocol to provide support as needed. To improve analgesia, veterinarians recommended either the use of buprenorphine SR (sustained-release) for long-lasting pain relief without the need for repeat dosing, or standard buprenorphine to be dosed every 8 hours over a 24-hour duration. The protocol was amended accordingly.

Based on the information provided, OLAW is satisfied that appropriate actions have been taken by the Fred Hutchinson Cancer Research Center to investigate this incident, provide corrective measures, and prevent recurrence. OLAW concurs that the incident warranted reporting. Although this activity was not PHS funded, the application of the standards of the PHS Policy across the animal care and use program reduces any potential appearance of a double standard. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

Brent C. Morse -S

Digitally signed by Brent C. Morse

-S

Date: 2021.09.16 16:11:29 -04'00'

Brent C. Morse, DVM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC contact



September 13, 2021

Brent Morse, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare (OLAW)
National Institutes of Health
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, MD 20892

RE: Reportable Event

Animal Welfare Assurance Number:	D16-00142 (Legacy #A3226-01)
Name of Institution:	Fred Hutchinson Cancer Research Center
PHS Funding:	No PHS Funding for this project

Dear Dr. Morse:

This letter serves as follow-up to an initial verbal notification made by (b) (6) on August 13, 2021, regarding a reportable event.

The Fred Hutchinson Cancer Research Center (Fred Hutch) Institutional Animal Care and Use Committee (IACUC) reviewed the reportable event at the September 7, 2021 fully convened IACUC meeting. The report was submitted on August 10, 2021 by a Comparative Medicine Veterinarian and described an event involving incisional dehiscence in 10 mice.

On August 6, Comparative Medicine staff performed post-operative monitoring on two cages of mice with left thorax incisions. The post-operative monitoring was requested by the research team. The incisions were fully dehiscence in one cage (5 mice), and partially in the second cage (5 mice). Standard Surgery/Procedure cage cards were not in place on either cage. Upon review of the IACUC protocol, it was determined that the mice had received orthotopic lung injection procedures. The orthotopic lung injection procedure was approved on the IACUC protocol. The 5 mice with full incisional dehiscence were immediately euthanized. The other 5 mice were determined to have only minor appositional gaps and were recovering well at the time of reporting. No additional lung injection procedures have been performed since this event.

On August 10, Comparative Medicine veterinarians discussed the event with the two research team members who performed the lung injection procedure. Several deficiencies were identified and are listed below with their corresponding corrective actions:

1. The research team members did not complete the required Comparative Medicine hands-on training course "Rodent Anesthesia and Aseptic Surgery Technique Training" and did not use Surgery/Procedure cage cards.

Corrective action: The two research team members that were involved completed the required aseptic training course, along with additional customized training focusing on the importance of labeling post-procedure cages with Surgery/Procedure cage cards, the use of analgesia, and instrument and patient prep.

2. The closure technique was inadequate and used too much tissue glue, leading to dehiscence.

Corrective action:

- a) Comparative Medicine veterinarians met with the research team members to discuss closure technique and proper placement of tissue glue. Wound clips were recommended for skin closure instead of tissue glue, and it was noted that wound clips are already approved on the IACUC protocol as an alternative closure method.
 - b) A Comparative Medicine veterinarian will observe the next planned lung injection procedure to ensure proper closure technique and to provide other technical guidance.
 - c) Additionally, a collaborator that is experienced with the orthotopic lung injection procedure was added to the IACUC protocol to provide support as needed.
3. Pain management was insufficient. The analgesia plan approved on the IACUC protocol included optional buprenorphine to be dosed every 8 hours over a 72-hour duration; however, no buprenorphine was administered.

Corrective action: Analgesia is required for all procedures that may cause more than momentary pain or distress unless scientific justification is provided. For the orthotopic lung injection procedure, Comparative Medicine veterinarians recommended either the use of buprenorphine SR (sustained-release) for long-lasting pain relief without the need for repeat dosing, or standard buprenorphine to be dosed every 8 hours over a 24-hour duration. The protocol was amended accordingly, received IACUC review, and was approved on August 31, 2021.

The IACUC determined the corrective and preventive actions were adequate, and no further action was required.

If you have any suggestions for further improvements to our program, please do not hesitate to share them with us. If I can be of any further assistance, please contact me at (b) (6) or fappelba@fredhutch.org.

Sincerely,

(b) (6)

Fred Appelbaum, MD
Executive Vice President & Deputy Director
Fred Hutchinson Cancer Research Center

cc: (b) (6)

A McGarry Houghton, IACUC Chair
Gordon Roble, DVM, Attending Veterinarian
Principal Investigator
Fred Hutch Office of General Counsel

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, September 15, 2021 7:08 AM
To: (b) (6)
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: OLAW reporting letter_ D16-00142-Legacy #A3226-01-Fred Hutchinson Research Center

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

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

From: (b) (6)
Sent: Tuesday, September 14, 2021 1:32 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: OLAW reporting letter_ D16-00142-Legacy #A3226-01-Fred Hutchinson Research Center

Dear Dr. Morse:

Attached please find the final report as follow-up to an initial verbal notification that was provided on August 13, 2021 regarding a reportable event.

If you have any questions, please contact me. We would appreciate a confirmation via email that you have received the attached document.

Sincerely,

(b) (6)

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Initial Report of Noncompliance

By: BCM

Date: 8/19/2021

Time: 3:06

Name of Person reporting: (b) (6)

Telephone #: (b) (6)

Fax #:

Email:

Name of Institution: Fred Hutchinson Cancer Rsch Cen

Assurance number: A3226

Did incident involve PHS funded activity? No

Funding component:

Was funding component contacted (if necessary):

What happened?

10 mice underwent surgery by lab staff. Five had to be euthanized due to wound dehiscence. Found that lab staff did not complete all surgical training. Lacked aseptic technique and wound closure skills and did not administer buprenorphine appropriately.

Species involved: mus musculus

Personnel involved: Researcher

Dates and times: 8/13/20218

Animal deaths: euthanized

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

Vets retrained lab staff.

Projected submission to OLAW of final report from Institutional Official:

< 60 days

OFFICE USE ONLY

Case #