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

June 15, 2021

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

Dr. Elizabeth Boyd
VP for Research Administration
Fred Hutchinson Cancer Research Center
1101 Fairview Avenue North
Seattle, WA 98109-1024

Dear Dr. Boyd,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter dated June 8, 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 January 11, 2021. According to the information provided, OLAW understands that on December 8, 2020, 12 mice received an adenoviral vector intravenous (IV) injection that exceeded the maximum approved volume as stated in the IACUC protocol. The protocol indicated that mice would receive one or two injections of the adenoviral vector, with a maximum volume of 100 ul per injection. The second injection would be given 30 minutes after the first injection (for a maximum volume of 200 ul). However, for the cohort of 12 mice, the volume given was 200 uL for the first injection and 200 ul for the second injection, for a total of 400 uL volume. One mouse died immediately following the second injection. The other 11 mice injected with the viral vector were healthy and did well. The associated animal activity was supported by NIH funding. The event will be reported to the awarding institute.

Corrective and preventive measures included the following:

- A protocol amendment was submitted to remove unclear language regarding the maximum injection volume (i.e. removing reference to the 200 uL volume).
- The adenoviral injection procedure was updated to include pulmonary embolism as a potential complication.
- The IACUC concurred that this event met the criteria for self-reporting and requested that the Principal Investigator confirm that all laboratory members were familiar with IACUC policy regarding the expectation that events that should be reported to the IACUC within five days.

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. 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: 2021.06.15 09:13:06 -04'00'

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

cc: IACUC contact

Elizabeth Boyd, PhD
Vice President for Research Administration and Faculty Affairs
1100 Fairview Ave. N.
Seattle, WA 98109-1024
Tel (b) (6)
eboyd@fredhutch.org

June 8, 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
NIH Funding:	R01 HL147324

Dear Dr. Morse:

This letter serves as follow-up to an initial verbal notification made by Meghan Scott, Director of the Institutional Review office (IRO), on January 8, 2021, regarding a reportable event.

On January 5, February 2, and April 6, 2021, the Fred Hutchinson Cancer Research Center (Fred Hutch) Institutional Animal Care and Use Committee (IACUC) reviewed a Reportable Event submitted on December 17, 2020.

The report described an event that occurred December 8, 2020, wherein 12 mice received an adenoviral vector intravenous (IV) injection that exceeded the maximum approved volume as stated in the IACUC protocol. The protocol indicated that mice would receive one or two injections of the adenoviral vector, with a maximum volume of 100 uL per injection. The second injection would be given 30 minutes after the first injection (for a maximum volume of 200 uL). However, for the cohort of 12 mice, the volume given was 200 uL for the first injection and 200 uL for the second injection, for a total of 400 uL volume.

The source of the confusion came from different maximum volumes approved for different procedures on the same protocol, all involving IV injection. The research team member involved thought the same maximum volume was approved for the adenoviral vector injection. Additionally, the adenoviral vector procedure listed a maximum volume of 200 uL injection in two places (which could have led to misunderstanding for the cohort that was to receive two injections).

A follow-up report from the research team, submitted February 1, 2021, clarified that one mouse died immediately following the second injection. The other 11 mice injected with the viral vector were healthy and doing well. The IACUC noted that a possible cause of death could have been pulmonary

embolism (a known complication of IV injection). However, the IACUC was not able to determine if injection of the approved 100 uL (rather than 200 uL) would have resulted in the same outcome.

The initial corrective action plan indicated the Principal Investigator would submit a protocol amendment to clarify the maximum IV injection volume. Additionally, the IACUC determined that the corrective action plan should involve the following:

- A protocol amendment should be submitted to remove unclear language regarding the maximum injection volume (i.e. removing reference to the 200 uL volume). The amendment should state the maximum volume for the adenoviral administration injection is 100 uL, and that up to two injections would be given.
- The adenoviral injection procedure should be updated to include pulmonary embolism as a potential complication.
- The IACUC concurred that this event met the criteria for self-reporting and requested that the Principal Investigator confirm that all laboratory members were familiar with the IACUC Policy 18.0, *IACUC Noncompliance and Reportable Events* and the expectation that events that should be reported to the IACUC within 5 days.

The requested protocol amendment was approved by the IACUC on February 19, 2021. At the convened IACUC meeting on April 4, 2021 the IACUC reviewed the final PI response, confirming all corrective and preventive action steps had been completed. The IACUC determined no further action was required. As noted above, the event was supported by NIH funding. The event will be reported to the awarding institute.

If you have any suggestions for further improvements to our program, please do not hesitate to share them with us.

Sincerely,

(b) (6)

Elizabeth Boyd, PhD
Vice President for Research Administration and Faculty Affairs
Fred Hutchinson Cancer Research Center

cc: Meghan Scott, Director, Institutional Review Office
Bruce Busby, IACUC Chair
Gordon Roble, DVM, Attending Veterinarian
Office of General Counsel, Fred Hutch

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Friday, June 11, 2021 7:07 AM
To: Scott, Meghan K
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: OLAW Reporting Letter_D16-00142 Legacy #A3226-01 Fred Hutchinson Cancer Research Center

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

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

From: Scott, Meghan K <mscott@fredhutch.org>
Sent: Wednesday, June 9, 2021 4:58 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: OLAW Reporting Letter_D16-00142 Legacy #A3226-01 Fred Hutchinson Cancer Research Center

Dear Dr. Morse:

Attached please find the final report as follow-up to an initial verbal notification that was provided on January 8, 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,

Meghan Scott
Pronouns: she/her/hers
Director
Institutional Review Office
O (b) (6)
mscott@fredhutch.org

Fred Hutchinson Cancer Research Center
1100 Fairview Ave. N., Mail Stop J2-100
Seattle, WA 98109
fredhutch.org

COVID-19 related FAQs: IRB here - Clinical Research Support here.

A3226 – 2P

Initial Report of Noncompliance

By: BCM

Date: **1/11/2021** Time: 12:06

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? yes
Funding component: _____
Was funding component contacted (if necessary): _____

What happened?

12 mice administered IV injections of 2 x 200 microliters instead of protocol approved 2 x 100.
One mouse died

Species involved: mus musculus
Personnel involved: Researcher
Dates and times: ?
Animal deaths: yes, one mouse

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

Early in investigation

Projected submission to OLAW of final report from Institutional Official:

< 60 days

OFFICE USE ONLY
Case #_____