



DEPARTMENT OF HEALTH & HUMAN SERVICES

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6700B Rockledge Drive
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Telephone: (301) 496-7163
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DATE: September 12, 2018

TO: Michael M. Gottesman, M.D.
Deputy Director for Intramural Research, NIH

FROM: Director
Division of Compliance Oversight, OLAW

SUBJECT: Animal Welfare Investigation (#010-18) - Animal Welfare Assurance
A4149-01 [Case 12L]

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your September 4, 2018 memo regarding an incident of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the National Human Genome Research Institute (NHGRI). According to the information provided, OLAW understands that on July 16, 2018 a co-PI practiced injecting Cortland's salt solution into 15 zebrafish although an amendment covering this procedure had not yet been fully approved. Four of the 15 fish died immediately, the remaining fish remained healthy. The procedure was repeated in 18 fish on August 6, 2018 although the amendment had still not been fully approved. Over the next three days 11 fish were euthanized and 7 were found dead. The abnormal clinical signs and deaths were reported by the NICHD Facility Veterinarian. On August 14, 2018 the NHGRI APD observed injections by the co-PI on five fish under the NHGRI training protocol. There were no complications.

Corrective and preventive actions included counseling of the PI and co-PI. In addition, several refinements to the injection technique have been made at the recommendation of the NHGRI APD.

The actions taken to resolve the issue and prevent recurrence were appropriate and accepted by OLAW. We appreciate being informed of this matter and find no cause for further action by this office.

Sincerely,

(b) (6)

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

cc: Dr. Stephen Denny
Dr. Richard Wyatt, OAI/OD
David Bodine, Ph.D., Chair, NHGRI ACUC



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

www.nih.gov

September 4, 2018

TO: Brent C. Morse, D.V.M.
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare

FROM: Deputy Director for Intramural Research, NIH

SUBJECT: Animal Welfare Investigations - Assurance A4149-01 (#010-18)

This correspondence conveys the results of an investigation by the National Human Genome Research Institute (NHGRI) Animal Care and Use Committee (ACUC) regarding an adverse event reported to the NIH Office of Animal Care and Use in August 2018. The event involved an investigator conducting unapproved animal procedure training on zebrafish.

As noted in the NHGRI ACUC memorandum, the event was reported to the NHGRI ACUC Chair by an NICHD facility veterinarian on 8 August and subsequently investigated by an NHGRI ACUC Subcommittee. The details of the investigations and the corrective actions taken by the animal care program are addressed in the attached memorandum.

Please contact me or Dr. Stephen Denny, Acting Director, Office of Animal Care and Use, if additional information or clarifications are required.

(b) (6)

Michael M. Gottesman, M.D.

Attachment

cc: Dr. Bodine
Dr. Denny
Dr. Wyatt



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
Bethesda, Maryland 20892

www.nih.gov

Date: August 31, 2018

To: Michael Gottesman, M.D.

From: David Bodine, PhD
NHGRI ACUC Chairperson

Subject: NHGRI Animal Welfare Incident
Final Report

(b) (6)

This letter describes an incident of a co-PI performing unauthorized procedures on zebrafish.

Incident Timeline:

- July 16, 2018: Dr. Erin Jimenez injected Cortland's salt solution IP into 15 fish, in order to gain proficiency in the injection technique. The procedure was performed under hypothermia anesthesia and as described in an amendment dated March 12, 2018 (final approval pending IBC approval).for Burgess protocol G-01-3. Four of the 15 fish died immediately. The remaining 11 fish remained healthy after the injections. Neither OLAM nor the Building 6 staff were aware of the test procedure or the loss of fish.
- August 6, 2018: Dr. Erin Jimenez injected Cortland's salt solution IP into a second group of 18 fish to gain more experience with the procedure. The procedure was performed under hypothermia anesthesia and as described in the amendment listed above(final approval still pending IBC approval). Neither OLAM nor the Building 6 staff were aware of the test procedure
- August 7: Dr. Jimenez euthanized four of the 18 fish for study purposes.
- August 8: Dr. Jimenez euthanized three of the 18 fish for study purposes. Four of the 18 injected fish were found dead by Building 6 staff. Dr. Tannia Clark reported abnormal clinical signs and deaths to OLAM and Drs. Bodine, Burgess, and Jimenez.
- August 9: Three of the 18 injected fish were found dead. Four of the 18 injected fish were euthanized under Dr. Clark's direction due to poor condition.
- August 13: Dr. Linkenhoker returned from leave and spoke with Dr. Jimenez about her practice injections.
- August 14: Dr. Linkenhoker and Stephen Frederickson observed the injection procedure performed by Dr. Jimenez on five fish. This was done under the NHGRI training protocol G-15-3 and under veterinary supervision since no other staff at NIH

has been identified at this time as being proficient in this procedure. The injections were performed with ease and as described in the literature. The fish recovered uneventfully from anesthesia. The fish were returned to routine housing and have been observed by Erin Jimenez, Stephen Frederickson, and Building 6 staff. No complications have been observed since August 14. Dr. Linkenhoker informed OACU about this incident and the following corrective actions.

Corrective Actions:

- Drs. Burgess and Jimenez were reminded that the NHGRI training protocol must be used in cases where an animal user is learning a new technique, unless a training pilot study is approved as part of the research protocol. Also, when an animal user is performing a technique that is new to them, the procedure must be performed under veterinary supervision.
- For the August 14, 2018 injections, the following changes were made at the recommendation of Dr. Linkenhoker.
 - The fish were anesthetized with tricaine instead of hypothermia
 - The angle of injection was reduced
 - Fresh/sterile buffer and sterile needles were used
 - If any of these fish are found dead, they will be submitted to DVR Pathology for evaluation. If this does occur, Drs. Clark and Linkenhoker will work with Dr. Jimenez to determine what other changes will need to be made to prevent mortalities from these injections.
 - Given that tricaine anesthesia was safe and effective for this procedure, an amendment has been submitted to the ACUC to include this as part of the injection procedure.
 - Needles will be autoclaved prior to each set of injections.

At this time, no additional corrective actions are necessary. Any additional injection practice will be done under the NHGRI training protocol, and OLAM staff must be notified of the additional practice in advance.

Discussion of this incident occurred at the August 30, 2018 NHGRI ACUC meeting. Dr. Burgess was in attendance and accepted full responsibility for not coordinating the injection training with OLAM under the training protocol requirements. It was agreed that no additional corrective actions were necessary.

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, September 06, 2018 7:37 AM
To: Denny, Stephen (NIH/OD) [E]; OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: A4149-01 NIH IRP Reportable Event (NHGRI #010-18)

Thank you for this report Dr. Denny. 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

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From: Denny, Stephen (NIH/OD) [E]
Sent: Thursday, September 06, 2018 6:27 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Subject: A4149-01 NIH IRP Reportable Event (NHGRI #010-18)

Dear OLAW/DCO,

Final reports from the NIH Institutional Official and the NIH National Cancer Institute ACUC addressing an animal incident reported to this office on 8 August are attached. The incident involved a principal investigator conducting injection procedure training on zebrafish prior to approval of the animal study proposal.

If you have any questions please contact me via email or the phone number listed below. Thanks, Steve

STEPHEN L DENNY, DVM, MS, DACLAM | Acting Director, Office of Animal Care and Use | National Institutes of Health | Bldg 31-Rm B1C37, 9000 Rockville Pike, Bethesda, MD 20982 | Phone: (301) 496-5424 | <http://oacu.od.nih.gov>