



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
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FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
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Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

July 6, 2017

Re: Animal Welfare Assurance
A3423-01 [OLAW Case 1Y]

Victoria G. Rivera, MPA
Interim Director, Office of Research Compliance
University of Hawaii
2425 Campus Road, Sinclair 10
Honolulu, Hawaii 96822

Dear Ms. Rivera:

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your June 26, 2017 letter regarding noncompliance with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals at the University of Hawaii. According to the information supplied, OLAW understands that two laboratory mice died in 2015 during an unapproved behavior procedure. An Animal Welfare Program staff member received an animal welfare concern on May 1, 2017 about a student who disclosed animal deaths while presenting at a student research science symposium. The student had completed research as a collaboration between two PIs. Each PI had their own IACUC protocol and the letter indicated that both PIs referenced a third-party protocol assuming that the behavior test was approved on that protocol, but the procedure was not included on any protocol. Additionally, it was discovered that an individual tasked with training others in behavior procedures trained an unapproved individual on the behavior procedure who in-turn trained the student. The animal deaths were not reported to the IACUC after they occurred nor were they reported during either PIs protocol annual renewals.

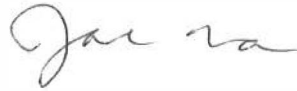
Corrective actions included the following.

- A reprimand letter was sent to both PIs with copies sent to Chancellors, Deans, and Chairs.
- One PI's protocol was inactive because it had expired in 2016, but the other PI's protocol is to be closed out or amended if the behavior procedure will be used in the future.
- Both PIs will receive re-training upon submission of any new protocol or amendments. Re-training will focus on items including ensuring personnel are familiar with approved protocols and ramification of violating Guidelines and Procedures for Conducting Inquiries and Investigations into Noncompliances.
- A signatory assurance statement will be added to the IACUC protocol form to alert PIs to ensure proper training and share SOPs with research personnel listed on IACUC approved protocols.
- References to non-core protocols within protocol applications will no longer be permitted.

Please be advised that OLAW recommends prompt preliminary reporting of noncompliance issues with submission of a final report once corrective action has been taken. Additionally, in future reports, please specify whether the associated animal work was supported by PHS, NSF, or VA funding and include the relevant grant or contract number(s), if applicable. Based on the information provided, OLAW accepts the corrective actions described to reduce the likelihood of recurrence of these noncompliances. We appreciate being informed of these matters and find no cause for further action by this Office.

Page 2 - Ms. Rivera
July 6, 2017
OLAW Case A3423-11

Sincerely,

A handwritten signature in cursive script, appearing to read "Jane Na".

Jane Na, DVM
Veterinary Medical Officer, OLAW
Office of Laboratory Animal Welfare

cc: IACUC Contact



UNIVERSITY
of HAWAII
SYSTEM

Office of Research Compliance
Animal Welfare and Biosafety Programs

June 26 2017

Dr. Axel Wolff
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
RKL1, Suite 1050 (MSC 9782)
6705 Rockledge Drive
Bethesda, Maryland 20892-7982

Re: University of Hawaii Animal Welfare Assurance #A3423-01
Unapproved Activities and Mouse Mortalities; COMM-OLAW-2017-3

Dear Dr. Wolff,

I am writing to inform OLAW of an adverse incident that resulted in the fatalities of two laboratory mice. The death of the animals were a result of an unapproved behavioral procedure that was conducted between January/February-August 2015. The IACUC only recently became aware of the activities while investigating a reported animal welfare concern complaint.

Timeline and Response

On May 01, 2017, an animal welfare concern complaint was received by the University of Hawaii Animal Welfare Program staff. The complainant reported that a graduate student presenting a research project at a student research science symposium, on April 28, 2017, commented that most of the mice in the student's behavior experiment drowned. A total of approximately 24 mice may have been used in the experimental testing. The student's project involved testing mice using a behavioral assay that examined autistic cues when animals are challenged. The behavioral assay referenced as the Forced Swim Test (FST) was the unapproved procedure that was conducted. The FST evaluates the level of depression in mice by their response to swimming in water without the means of support. Drowning is not the endpoint of the experiment.

The student's research was a collaborative effort between two principal investigators (PIs A and B). PI A was responsible for development of mice by breeding or assisted reproduction techniques, maintaining the mice and reproductive tissue collection. The student that presented the results of the study at the symposium reported to PI A. PI B was responsible for brain collection and genomic/epigenomic analyses. Both PIs had their own animal research IACUC approved protocols but wrongly assumed that the FST was approved on their protocols. The student misinformed the symposia audience by overstating the animal fatalities, when in actuality two mice died. These unexpected animal deaths were not reported to the IACUC when the incident occurred nor during the renewal of the PI's protocols. Because necropsies were not conducted, drowning was not definitively determined to be the cause of death.

Preliminary information for an investigation was gathered and an IACUC subcommittee formed. The subcommittee met several times during May and June to discuss the investigative procedure and to formulate interview questions. Interviews were conducted with the PIs and key research personnel on May 18, 2017 and May 26, 2017, respectively.

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Summary of Findings

From the information gathered and interviews conducted, the following was clear:

- Both PIs referenced a third party protocol, assuming that the FST was IACUC approved on that protocol. The FST was not approved on any animal use protocol.
- A key individual in PI B's lab, tasked with training personnel on behavioral testing, trained an unapproved student on the FST, who in-turn trained the graduate student that conducted the FST that presented the research at the symposium.
- The graduate student was not supervised by the key individual nor student's faculty advisor (PI A).
- The animal deaths were not reported at the time of the adverse incident nor at the annual renewals of the PI's protocols. PI B was unaware that animal fatalities occurred.
- A manuscript was submitted for publication.

IACUC Action

The protocol assigned to PI B is inactive and expired in October 2016. PI A transferred all animals to another protocol. Therefore, the IACUC did not suspend the research activities previously covered by the PI's protocols as the applications are inactive.

The subcommittee provided a report to the full committee to consider. The report was accepted and approved by the IACUC at its June 15, 2017 business meeting.

- Reprimand letters are being sent to both PI A and B, with copies to Chancellors, Deans, and Chairs.
- PI A is required to close out the protocol in question or amend it to include the FST if the procedure will be used for future experimentation.
- PI B is required to provide the IACUC a report to reflect the mice fatalities and explain the oversight given that the PI was unaware of the deaths.
- Both PIs are required to receive and document additional training upon submission of any new protocols/amendments. Retraining will focus on but not be limited to:
 - Ensuring research personnel are familiar with approved protocols and have access to project information.
 - Policies regarding accessing and filming in the vivarium.
 - Ramification of violating UH IACUC Policy 9 *Guidelines and Procedures for Conducting Inquiries and Investigations into Non-compliances, Deviations, and Cases of Animal Misuse or Abuse*.
- A letter is being forwarded to the Dean of Graduate Students detailing the graduate student's involvement with the FST procedure, joint authorship of a publication referencing the unapproved IACUC procedure and possible inclusion of unapproved protocols and research data in a submitted thesis.
- A letter is being forwarded to the UH Research Integrity Program (RIP) informing that office of the submission of a manuscript containing unapproved procedures (FST) and research data. Suggest that the RIP confirm with the PIs whether any other grants and/or abstracts contain the unapproved procedure and/or data derived from the student's research.

- A signatory assurance statement will be added to the IACUC protocol form. The rationale for this corrective measure is to alert PIs to share and ensure proper training of all approved procedures and SOPs with research personnel listed on IACUC approved protocols.
- PIs past practice of referencing of non-core protocols will no longer be permitted on animal use protocol applications.

Please contact me at Phone Number or riveravg@hawaii.edu with any questions.

Sincerely,



Victoria G. Rivera, MPA
Interim Director, Office of Research Compliance

c: Manuel G. Himenes, Jr., Chair, UH IACUC
Secondary Individual Program Manager, Animal Welfare and Biosafety Programs

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, June 28, 2017 7:26 AM
To: Secondary Individual
Subject: RE: University of Hawaii IACUC Investigates Animal Use Complaint

Thank you for this report, Secondary Individual. We will send a response soon.
Axel Wolff

From: Secondary Individual [mailto:Secondary Individual@hawaii.edu]
Sent: Tuesday, June 27, 2017 8:44 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: Victoria Rivera <riveravg@hawaii.edu>
Subject: University of Hawaii IACUC Investigates Animal Use Complaint

Good Morning Dr. Wolff:

On behalf of Ms. Victoria Rivera, Interim Director for Research Compliance, Institutional Official for the UH Animal Welfare Program, please find the attached report.

Sincerely,

Secondary Individual
Manager, Animal Welfare and Biosafety Programs
Office of Research Compliance