



DEPARTMENT OF HEALTH & HUMAN SERVICES

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Office of Laboratory Animal Welfare  
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Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

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6700B Rockledge Drive, Suite 2500  
Bethesda, Maryland 20817  
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DATE: October 17, 2018

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

FROM: Deputy Director, Office of Laboratory Animal Welfare

SUBJECT: Animal Welfare Investigation (#012-18) - Animal Welfare Assurance  
A4149-01 [Case 12 O]

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your October 9, 2018 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the National Institute of Neurological Disorders and Stroke, NIH. According to the information provided, OLAW understands that imaging studies were performed over two days in two live mice without prior review and approval by the Animal Care and Use Committee. Specifically, two mice were anesthetized, imaged, and recovered although the protocol had not been amended to include this activity. The mice were also housed in the Mouse Imaging Facility without approval.

The corrective actions consisted of counseling and retraining the responsible investigators on relevant policies and procedures of animal care and use.

Based on its assessment of this explanation, OLAW understands that measures have been implemented to correct and prevent recurrence of this problem. OLAW concurs with the actions taken by the institution to comply with the PHS Policy.

(b) (6)

Axel Wolff, M.S., D.V.M.

cc: Dr. Richard Wyatt  
Dr. Stephen Denny  
Dr. Alfonso Silva



## DEPARTMENT OF HEALTH &amp; HUMAN SERVICES

Public Health Service

National Institutes of Health  
Bethesda, Maryland 20892[www.nih.gov](http://www.nih.gov)

October 9, 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 (#012-18)

This correspondence conveys the results of an investigation by the National Institute of Neurological Disorders and Stroke (NINDS), in accordance with Assurance A4149-01 and PHS Policy IV.F.3. The adverse event involved conducting animal activities without appropriate IACUC review and approval.

As noted in the attached NINDS ACUC memorandum, the event was first reported to the NIH Office of Animal Care and Use by the NINDS ACUC Chair on September 14, 2018. 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. Silva  
Dr. Denny  
Dr. Wyatt



**DEPARTMENT OF HEALTH & HUMAN SERVICES**

**National Institutes of Health  
National Institute of Neurological  
Disorders and Stroke**

49 Convent Drive MSC 4478  
Building 49 Room 3A72  
Bethesda MD 20892-4478

Date: October 11, 2018

From: Afonso C. Silva, Ph.D., Chair, NINDS/NIDCD/NCCIH ACUC

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

Subject: Reportable incident involving conduct of animal activities without appropriate IACUC review and approval

The following is a summary of a reportable incident involving the conduct of animal activities without appropriate IACUC review and approval, the investigative steps taken, and a description of the resolutions of the matter.

**Summary of the Incident:**

On Tuesday September 4, 2018, the veterinarian of the Mouse Imaging Facility (MIF) became aware that optical imaging experiments were being conducted in live mice in the MIF without appropriate IACUC review and approval. The veterinarian also became aware that the mice were being housed all week in the MIF. Upon this discovery, the veterinarian informed the Chair of the NINDS/NIDCD/NCCIH ACUC, and the Animal Program Director of the NINDS.

**Summary of the Investigative Steps Taken:**

The Chair received an email about the incident from the veterinarian of the MIF. The Chair contacted the postdoctoral fellow involved in conducting the experiments. Both him and a graduate student also associated with the study admitted that they've conducted experiments in two live mice without submitting an amendment to their Animal Study Proposal to the NINDS/NIDCD/NCCIH ACUC. The experiments were carried out in two female C57Bl6 mice, which were imaged in two consecutive days in the MIF with the optical imaging system. On the first day (Wednesday, August 29, 2018), the animals were anesthetized with isoflurane, imaged for about two minutes in the optical imaging system, recovered from anesthesia and returned to their temporary home cage in the MIF. On the second day (Thursday, August 30, 2018) September the animals were again anesthetized with isoflurane, and were injected with 100 µl of a contrast agent into the tail vein. After 5 minutes the animals were placed in the optical imaging system and imaged again. The mice were recovered from anesthesia and returned to their home cages, and were kept there over the weekend. On Tuesday September 4, 2018, the investigators brought the animals back to the MIF and asked one of the facility technicians how to depilate the mice all

over. That's when the veterinarian became aware that experiments that were not covered by an approved ASP were being carried out, and informed the Chair and the Animal Program Director. In his interview with the Chair, the postdoctoral fellow informed the Chair that he was instructed by his advisor, who is also an investigator in the protocol, to conduct the experiments, even though the advisor knew that the experiments needed to first be approved by the ACUC. The Chair contacted the Principal Investigator of the ASP, who was not aware that these experiments were being conducted. The PI contacted the investigator involved (advisor to the post-doctoral fellow and to the graduate student), and he apologized, stating that "in his enthusiasm for the development of their exciting and potentially groundbreaking new technology, he let his exuberance get ahead of their documented protocols". The Chair informed the investigator and the PI that the incident constituted a serious violation the ACUC Policies and Regulations on the Laboratory Use of Animals, which may be subject to disciplinary action.

#### Summary of Corrective Actions Taken:

The Chair discussed the incident with the PI of the protocol and with the ACUC, and the ACUC suggested to retrain the three investigators involved in the procedures and policies involving the conduction of experiments in live animals at the NIH. The three investigators must take the training courses that are available from the Animal Health Care Section of the NINDS. The Principal Investigator discussed the case with the three investigators and stated clearly the seriousness of the situation. The three investigators took full responsibility for the incident, and promised to adhere to the procedures and policies from now on.

#### Resolutions of the Matter:

A full report of the incident was presented, discussed, and approved by our ACUC at the September 12, 2018 meeting. At this point, the ACUC feels that appropriate actions were taken to make the PI and his investigators aware of the problem. The PI has no history of protocol noncompliance, and the ACUC feels that similar future incidents are unlikely to occur. Therefore, the ACUC feels that this incident can be closed.

(b) (6)



Afonso C. Silva, Ph. D.

**Wolff, Axel (NIH/OD) [E]**

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**From:** OLAW Division of Compliance Oversight (NIH/OD)  
**Sent:** Wednesday, October 10, 2018 10:23 AM  
**To:** Denny, Stephen (NIH/OD) [E]  
**Cc:** OLAW Division of Compliance Oversight (NIH/OD)  
**Subject:** RE: A4149-01 NIH Animal Incident Report (NINDS #012-18)

Thank you for this report, Dr. Denny. We will respond soon.  
Axel Wolff

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**From:** Denny, Stephen (NIH/OD) [E]  
**Sent:** Wednesday, October 10, 2018 9:53 AM  
**To:** OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>  
**Subject:** A4149-01 NIH Animal Incident Report (NINDS #012-18)

Dear OLAW/DCO,

Final reports from the NIH Institutional Official and the NIH National Institute of Neurological Disorders and Stroke ACUC addressing an animal incident reported to this office on 14 September are attached. The incident involved a principal investigator conducting mouse imaging activities without appropriate IACUC review and approval.

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>