



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) 402-7065

September 5, 2018

Re: Animal Welfare Assurance
A3310-01 [OLAW Case 1P]

Dr. Phillip Cunningham
Associate Vice President for Research
Wayne State University
5700 Cass Ave., (b) (4)
Detroit, MI 48202

Dear Dr. Cunningham,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your August 29, 2018 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Wayne State University. According to the information provided, OLAW understands that a PI's laboratory staff allowed approximately 80, 5-dpf zebrafish larvae to be exposed to cisplatin for 4 hours without IACUC approval. When the PI became aware of the incident, she immediately met with staff and students and explained that procedures not in an approved IACUC protocol should never be performed and she then self-reported the incident to the IACUC.

Corrective and preventive measures in addition to those by the PI included amending the institutional policy which now specifies that zebrafish embryonated eggs PRIOR to hatching (≤ 3 days post-fertilization) do not require a protocol.

The prompt consideration of this matter by the PI and Wayne State University was consistent with the philosophy of institutional self-regulation. Similarly, the actions taken to resolve the issue were appropriate and are expected to be effective. 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: IACUC Contact



A3310-1P

Philip R. Cunningham, Ph.D.
Assoc. Vice President for Research Integrity
Wayne State University
5057 Woodward Avenue, Suite 2317
Detroit, MI 48202

(b) (6)
philc@wayne.edu

Animal Welfare Assurance Number: D16-00198

August 29, 2018

Brent C. Morse, DVM, DACLAM
Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
6700B Rockledge Drive, Suite 2500, MSC 6910
Bethesda, MD 20892
olawdco@mail.nih.gov

Follow-up report of an incident of non-compliance.

Dear Dr. Morse,

I am writing to provide you with a follow-up report of an incident of non-compliance which led to a deviation from the provisions of the *Guide* with respect to the proper care and use of animals in research. [REDACTED] initially reported the incident to you by phone on August 2, 2018.

On May 22, 2018, two WSU Investigators and their research staff met to discuss a potential collaboration using zebrafish to study the effects of cisplatin on hearing. One of the investigators (PI#1) uses zebrafish in environmental toxicology studies and the other investigator (PI#2) uses a mouse model of cisplatin-mediated ototoxicity. During this meeting, exposure of 5-day post-fertilization (dpf) fish to cisplatin was discussed and PI#1 indicated that an amendment should be submitted and approved before proceeding with experiments involving live animals. PI#1 offered to provide PI#2 with surplus zebrafish embryos and/or larvae that had been euthanized to allow optimization of fixing and staining techniques prior to approval.

During an extended absence of PI#1, and before an amendment had been submitted, the staff of both labs exposed approximately 80, 5-dpf larvae to cisplatin for 4 hours. It was reported that all lab staff wore appropriate PPE, no adverse health outcomes were observed from the exposure, and the exposures occurred on larval fish that were going to be euthanized that day.

When PI#1 became aware of the incident, she immediately met with staff and students, explained that procedures not in an approved IACUC protocol should never be performed, and that any doubts or questions regarding such issues must first be discussed with the investigator. PI#1 then self-reported the incident to the IACUC.

The collaborating PI (PI#2) mistakenly believed that other institutions may not consider 5-dpf zebrafish as vertebrates and as such, would not require an IACUC protocol for the treatment of larvae. According

to PI#1 this question had come up in previous meetings with PI#2 and it was made clear that the 5-dpf guideline was "a gray zone" and that PI#1 did not feel comfortable moving forward with live larvae until approval was obtained.

Following discussion of the circumstances surrounding the event at several meetings, the IACUC determined that the incident constituted non-compliance on August 22, 2018. Consistent with the guidance presented on the OLAW website as well as with the advice that you provided to the attending veterinarian during your phone conversation on August 2, this is considered reportable under PHS policy requirements.

The IACUC commended PI#1 for self-reporting the incident and determined that the corrective actions taken by PI#1 upon discovery of the non-compliance, including immediate education of their staff and discussion with PI#2, will prevent future issues of this nature. Additionally, the institutional policy outlining which animals require an approved IACUC protocol has been amended to specify hatched zebrafish >3-dpf (see excerpted policy section below).

Activities that DO NOT require IACUC Approval:

- Research, teaching and/or testing using cadavers or tissues from dead animals UNLESS the cadavers or tissues are to be acquired from animals specifically purchased or euthanized for the activity.
- Activities ordered and/or performed by the Attending Veterinarian or designee that involve only standard veterinary or emergency procedures necessary to ensure animal welfare.
- Activities involving retrieval or use of animal-related data from records.
- Research, teaching and/or testing involving embryonated eggs PRIOR to hatching. For zebrafish, this is considered ≤3 days post-fertilization.
- Any activity involving invertebrate species.
- Non-research, non-teaching, or non-testing activities involving privately owned animals, in which the activity is not an official WSU activity.
- Removal of vertebrate vermin.

Please do not hesitate to contact me if you would like additional information.

Sincerely,

(b) (6)

Philip R. Cunningham, Ph.D.

c.c. Dr. James Swearingen, Global Director, AAALAC International, accredit@AAALAC.org
Dr. Lisa Anne Polin, IACUC Chair, ac8694@wayne.edu

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, August 30, 2018 6:36 AM
To: Philip Cunningham
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Follow-up report of non-compliance

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

Axel Wolff

From: Philip Cunningham [mailto:philc@wayne.edu]
Sent: Wednesday, August 29, 2018 2:22 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: accredit@AAALAC.org; Lisa Polin <ac8694@wayne.edu>; (b) (6)
(b) (6)
Subject: Follow-up report of non-compliance

Please see the attached follow-up report involving an incident of non-compliance. Please contact me if you would like additional information.

Best regards,
Phil

Philip R. Cunningham, Ph.D.
Associate Vice President
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