



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

February 13, 2019

Re: Animal Welfare Assurance
A3338-01 [OLAW Case Q]

Dr. Vittorio Gallo
Chief Research Officer and Scientific Director
Children's National Medical Center
111 Michigan Avenue NW
Washington, DC 20010

Dear Dr. Gallo,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your February 7, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Children's National Medical Center. According to the information provided, it is understood that on January 2, 2019 your institution became aware that piglet had died in a hypoxia chamber. Although the piglet appeared to be sick before expiring, the Research Animal Facility (RAF) Veterinary team was not notified. This was the first time that an IACUC-approved lower oxygen level was used in an experiment. Placement of pigs in the hypoxia chamber was halted pending outcome of the IACUC investigation. It was noted that this activity was funded by the PHS.

Corrective actions included informing the Principal Investigator (PI) to submit a protocol modification to revise the hypoxia levels in the protocol to those less detrimental to the well-being of the animals. The PI is to ensure that no changes are made (including increased hypoxia time), or procedures performed, without prior review and approval by the IACUC. Also, the PI is to implement appropriate methods of monitoring to ensure that all research team members are following IACUC-approved procedures and regulations. Shipment schedule changes need to be carefully considered by the PI in scheduling procedures with the animals in a timely manner and according to what is approved in the protocol. All individuals listed on the protocol will meet with the AV for retraining. A letter of reprimand was sent to the PI requiring a response to be reviewed by the IACUC.

The prompt consideration of this matter by the Children's National Medical Center was consistent with the philosophy of institutional self-regulation. Similarly, the actions taken to resolve the issue and prevent recurrence were appropriate. 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

Dr. Robert M. Gibbens, USDA, APHIS, AC



111 Michigan Avenue, NW
Washington, DC 20010-2970
ChildrensNational.org

A3338-Q

February 7, 2019

Re: Assurance D16-00219 (A3338-01)

Brent Morse, DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 7982
6705 Rockledge Drive
Bethesda, MD 20892-7982

Dear Dr. Morse:

In accordance with the Guidance on prompt reporting to OLAW under IV.F.3 of the PHS Policy and as the Institutional Official representing the Children's National Medical Center (CNMC), I respectfully submit this letter regarding a recent incident requiring investigation by the CNMC IACUC. Please note that this institution is self-reporting the events that transpired, as well as the actions that we have taken to rectify the problem and to prevent its recurrence.

The investigation was related to the following activities supported by PHS: R01HL128546 and R01HL139712 for protocol #30593, titled, "Brain Protection in Congenital Heart Disease."

The IACUC followed the CNMC IACUC Policy, "Investigating and Reporting Animal Care and Use Concerns by the IACUC" regarding the investigation, and the issues surrounding the investigation were as follows:

- 1/2/2019 The IACUC Office received a report from the Attending Veterinarian (AV) with details of a possible non-compliance incident that occurred in the Research Animal Facility (RAF). The AV's report included a necropsy report of a piglet after it was found expired in a hypoxia chamber by a RAF caretaker and an interview with the Post-Doctoral researcher in charge of the hypoxia experiments. The report indicated that the piglet appeared to be sick prior to expiring and the RAF Veterinary team was not notified of the animals deteriorating health. The AV and Post-Doctoral researcher were in agreement that placement of piglets in the hypoxia chamber would halt temporarily until the investigation was complete. The IACUC office notified the IACUC Chair of the reported incident, and the IO and the PI's Center Director of the impending investigation. After review of the report, the Chair determined that additional information was required and immediately organized a meeting of a subcommittee to address the incident.
- 1/3/2019 The IACUC Office sent an e-mail to the PI notifying him of the impending investigation. The PI was also asked to provide a date and time to meet with the subcommittee for an interview.
- 1/4/2019 The subcommittee interviewed the PI along with the Post-Doctoral Researcher in charge of the Hypoxia studies. The subcommittee submitted their report to the IACUC office and

requested for this incident to be discussed at the next IACUC meeting before submitting their recommendations.

1/8/2019 After review of the report submitted by the subcommittee, the Chair interviewed the RAF personnel in charge of reserving the OR suite for post-hypoxia procedures. This individual was implicated by the PI and the report mentioned him as having provided approval for an extension on the amount of days the piglet spent in the hypoxia chamber. All documents relating to this investigation were sent out to the IACUC members for review and would be discussed at the next monthly meeting taking place in two days.

1/10/2019 The Chair convened the monthly meeting of the IACUC and asked the AV to present information about the incident regarding the protocol involving the death of a piglet during an experiment. The AV explained how the incident came about and the results of the necropsy. The members thoroughly discussed what they viewed to be the major problems in this incident: this was the first time that an IACUC-approved lower Oxygen level was used in an experiment; the researchers failed to report the sick experimental animal to the RAF or AV even though they realized that there was a problem with the animal; the researchers failed to adhere to the approved protocol by extending the number of days the experimental animal spent in the hypoxia chamber. Following a discussion of what the PI had said about the OR scheduling personnel during the investigative interview, the members unanimously determined that he was actually not involved in the incident. The members drew the following conclusions from discussion of the investigation: (1) the AV needs to conduct a training session for the whole group of researchers with animal contact on this protocol, about what is and is not normal when observing/monitoring the animals and the need to contact the RAF immediately if anything seems odd; (2) any shipment schedule changes need to be carefully considered by the PI in scheduling procedures with the animals in a timely manner and according to what is approved in the protocol; (3) the animal most likely experienced pain/distress before it expired; (4) the members decided that the PI should address the following issues to be sent in a letter of reprimand from the Chair:

- a) All individuals listed on this protocol will meet with the AV for retraining on RAF swine monitoring and procedures, and an attendance sheet with dates and signatures of all of the attendees will be sent electronically to the IACUC office.
- b) This protocol will require an amendment to revise the hypoxia levels to those less detrimental to the well-being of the animals.
- c) Once the IACUC office confirms receipt of the attendance sheet and the protocol is modified accordingly, and reviewed and approved by the IACUC, the PI will be notified about resuming hypoxia studies.
- d) Ensure that no changes are made (including increased hypoxia time) or procedures performed without prior review and approval by the IACUC.
- e) Implement appropriate methods of monitoring to ensure that all research team members are following IACUC approved procedures and regulations.

(5) Guidance from the OLAW regarding reportable situations indicates that the IACUC is obligated to report this investigation to the OLAW. The quality of care during research



violated regulations that the CRI is required to comply with, and are promulgated by the Office of Laboratory Animal Welfare (OLAW) of the NIH Public Health Service (PHS) and the USDA. The Chair called for a vote on reporting to the regulatory agencies.

IACUC ACTION: Reportable event to OLAW and USDA. Motion was made, seconded and passed:

For: 8 Against: 0 Abstain: 0 Recused: 0

- 1/16/2019 A letter of reprimand was sent to the PI and a response was required.
- 1/17/2019 The PI responded and addressed the issues presented by the IACUC. The Attending Veterinarian confirmed training had occurred and submitted the training log to show that the PI and all individuals listed on the protocol as having animal contact attended the training.
- 2/1/2019 The modification to increase hypoxia levels received final approval after DMR following FCR. The IACUC Chair verified that the PI had addressed all of the IACUC's requirements and the PI was notified that the IACUC's requirements had been addressed and accepted, so the investigation was completed and the PI could continue with all activities described in the currently approved version of the protocol.

Please accept this report as an indication of our institution's commitment to comply with all PHS policies and regulations on research animal care and to ensure that situations affecting research animal welfare are deliberately addressed and corrected.

Sincerely,

(b) (6)

Vittorio Gallo, PhD
Chief Research Officer, CNHS
Scientific Director, CRI Institutional Official, IACUC

111 Michigan Avenue, NW Washington, D.C. 20010-2970

Tel: (b) (6)

Fax:

Email: vgallo@childrensnational.org

Cc: Y.W. Chen, DVM, PhD Chair, IACUC

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Thursday, February 07, 2019 12:23 PM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: (b) (6) Chen, Yi-Wen; Gallo, Vittorio
Subject: RE: Assurance D16-00219 (A3338-01)

Thank you for providing this report (b) (6) 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: (b) (6)
Sent: Thursday, February 07, 2019 11:12 AM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6) Chen, Yi-Wen <YChen@childrensnational.org>; Gallo, Vittorio <VGallo@childrensnational.org>
Subject: Assurance D16-00219 (A3338-01)

Dear Dr. Morse,

This e-mail is regarding a recent internal investigation of possible non-compliance in the Children's Research Institute of the Children's National Medical Center.

Please find an attached letter of self-reporting from the Institutional Official.

Thank you,

(b) (6)

(b) (6)