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

October 25, 2019

Re: Animal Welfare Assurance
A3011-01 [OLAW Case 1P]

Dr. Richard Reeder
Vice President for Research
State University of New York-Stony Brook
(b) (4) Melville Library
Stony Brook, NY 11794-3368

Dear Dr. Reeder,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your letter dated October 1, 2019 regarding noncompliance with the Public Health Service (PHS) Policy on Humane Care and Use of Laboratory Animals at Stony Brook University. This letter had not been preceded by a preliminary report to OLAW.

According to the information provided, our office understands that a laboratory failed to adhere to an IACUC approved protocol, performed inadequate recordkeeping, and insufficiently monitored mice post procedurally. As a result, there was a rise in morbidity and mortality, with six mice dying and eleven requiring euthanasia. The mice were part of an NIH funded activity.

Corrective measures included evaluation of the treatment article to rule out contamination, and submission of an amendment that included a plan and schedule for weighing animals, adjustments in analgesia and supportive care, and a plan for recordkeeping of health assessments and administration of analgesia. The IACUC approved the submitted amendment on September 17, 2019. An additional corrective measure entails post approval monitoring that will be conducted by the clinical veterinarian for this activity.

Based on its assessment of this explanation, OLAW understands that measures have been taken to prevent recurrence of this problem. OLAW concurs with the actions taken by your institution to comply with the PHS Policy on Humane Care and Use of Laboratory Animals. We appreciate having been informed of this matter and at this time find no cause for further action by this office. Please note that reports of noncompliance to OLAW should include dates of occurrence when describing the incident. Please include this information in future submissions. Also, please be aware that results obtained from activities without IACUC approval may encounter obstacles with publication.

Sincerely,

(b) (6)

Nicolette Petervary, VMD, DACAW
Animal Welfare Policy Specialist
Office of Laboratory Animal Welfare

cc: IACUC contact

A3011-1P

Stony Brook University

OLAW Reportable Event
[per PHS Policy at Section IV.F.3]
Animal Welfare Assurance # D-16-00006(A3011-01)

Type of Report:

☐ Follow-up to prior report dated
☐ First report, with intent to follow-up with OLAW
☒ First and final report to OLAW 10.1.19

IACUC # or PIs lab: HH Lab, IACUC # 1039478; Molecular Mechanisms of Regulation of Bone Remodeling and Orthodontic Tooth Movement by Vascular Endothelial Growth Factor

Species: Mouse **Funding:** NIH

Description of reportable incident: Failure to adhere to IACUC approved protocol and failure to monitor animals post-procedurally as necessary to ensure well-being.

Details: A sudden increase in the morbidity/mortality of the animals was noted after the approved procedure. Post-approval monitoring was initiated. The attending veterinarian noted that the Principal Investigator (PI) was not monitoring the animals daily post-procedurally, as per protocol. Examination of records show that although lab records were being kept, animal health records were not: the records did not show daily weight measurements, or notations for need to provide analgesic. Moreover, there was no notation that the PI had administered analgesic in the drinking water 24 hours in advance of the procedure as per protocol. At the request of the veterinarian, body weight was taken at day 7 for the remaining animals. Some of them were euthanized due to low body weight.

Background: The overall goal of the project is to observe the effects of VEGF (submucosal injection at the buccal region of the maxillary first molar) on alveolar bone remodeling, osteoclast differentiation and bone resorption in an orthodontic tooth movement mouse model. PI has IACUC approval for submucosal injection in 12 different groups of animals.

The first three groups were completed with no significant adverse effects. In the 4th group the VEGFR-2 antibody (1µl (10µg/µl) per side per mouse) injections were performed. The amount of VEGFR-2 injected was based on a previous publication (Kohno et al. 2004). Five days following appliance implantation and submucosal injections, PI reported that no sick animals were observed. Starting on the 6th day, three mice were found dead and eight were reported

sick to the veterinary staff. The following day three more mice were found dead and 11 were euthanized. 7 mice were allowed to remain on the study.

PI thought perhaps the batch of VEGFR-2 was responsible and the supplying company (R&D Systems, Minneapolis, MN) was immediately contacted via phone calls and emails. An endotoxin level test report for the lot was provided showing less than 0.0186EU/µg and based on this, the amount of endotoxin injected was less than 0.372EU per mouse. No other information has been provided by the company.

Corrective Actions:

- The PI immediately took responsibility and, after consultation with the clinical veterinarian, submitted an amendment stating that they will:
- Notify the DLAR vet when starting the next study.
- Weigh the animals before the procedure and then every day following procedure until day 14.
- Remove pre-procedure acetaminophen since this was not being given, nor was it considered by the veterinary staff to have contributed, or would it have prevented this outcome.
- Add a gel diet to the protocol starting a few days before the procedure to acclimate the animals to the diet.
- Administer supplemental fluids as needed if signs of dehydration are observed.
- Euthanize animals at 15% weight loss.
- Monitor daily and include written reporting on the welfare (appearance of the animals, signs of dehydration, weight etc.) and provision of analgesics.
- Administer subcutaneous buprenorphine, as needed for signs of pain and record such assessment.

This amendment was approved by the full IACUC on 9/17/19.

Careful post approval monitoring will be continue to be conducted by the clinical veterinarian to prevent a recurrence of animal loss.

Form completed by:

(b) (6)

Stony Brook University | The State University of New York

October 1, 2019

Brent Morse, D.V.M.
Acting Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360, MSC 9782
6705 Rockledge Drive
Bethesda, MD 20892-7982

Re: Assurance # A3011-01; D16-00006

Dear Dr. Morse;

Enclosed please find an event that Stony Brook University has deemed reportable to your office in accordance with PHS Policy, IV.F.3.

Please contact (b) (6) should you have any questions, or require additional information.

Sincerely,

(b) (6)

Richard J. Reeder, PhD
Vice President for Research and Institutional Official

Xc: Stella Tsirka, PhD, IACUC Chair
(b) (6)