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 3, 2019

Re: Animal Welfare Assurance
A3544-01 [OLAW Case L]

Dr. Dennis Durbin
Chief Scientific Officer
Nationwide Children's Hospital
700 Children's Drive – (b) (4)
Columbus, Ohio 43205-2696

Dear Dr. Durbin,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your August 27, 2019 letter reporting an instance of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at the Research Institute at Nationwide Children's Hospital, following up on an initial telephone report on July 10, 2019. According to the information provided, OLAW understands that ten rats failed to receive post-operative analgesic and nine rats received expired analgesic. This was determined by examining the inconsistency between the surgical records and pharmacy logs.

The corrective actions consisted of revoking the animal use privileges for the investigator responsible. The supervising investigator was directed to develop a rigorous oversight process for all animal activities and the laboratory was placed under enhanced post-approval monitoring by the Institutional Animal Care and Use Committee (IACUC). The NIH grant was not charged for any unauthorized animal activities and the funding component was notified about the matter.

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

Sincerely,

(b) (6)

Axel V. Wolff, M.S., D.V.M.
Deputy Director
Office of Laboratory Animal Welfare

cc: IACUC Chair

A3544

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.℠

August 27, 2019

Axel Wolff. DVM
Director, Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health
Rockledge 1, Suite 360
6705 Rockledge Drive
Bethesda, MD 20892

Dear Dr. Wolff:

The Research Institute at Nationwide Children's Hospital, in accordance with Assurance D16-00331 and PHS Policy IV.F.3., provides this report of noncompliance involving an approved protocol entitled "Production of Tissue Engineered Small Intestine" . This incident was first reported to you on July 10, 2019 via a telephone call. As detailed below, an IACUC investigation found inadequate record keeping supporting buprenorphine treatment of rats for post-operative pain relief as required by the IACUC protocol. Use of expired buprenorphine was also documented.

The research is funded by NIH Grant: NIH/NIDDK 2R42DK107168-02 entitled "Tissue Engineered Intestine: STTR- PHASE-II (Nanofiber Solutions)". Billing charges related to the procurement, care and use of rats between January 1, 2018 and July 1, 2019 have been identified and will be invoiced to and paid from a non-federal source. The NIH funding agency will be notified.

Details of the IACUC investigation and findings are as follows:

Post approval monitoring of animal procedures and record keeping was increased for a researcher involved in a recent IACUC protocol violation (OLAW A3544-01 Case J).

A different IACUC protocol (AR12-0001) required post-operative treatment of rats with 1 dose of buprenorphine for pain relief; additional doses could be given twice daily as needed for signs and symptoms of pain for the next 3 days. A single stock vial of buprenorphine was provided by the NCH pharmacy to the investigator in January 2018 for this protocol. Buprenorphine treatment must be documented in Surgical Records *and* Pharmacy Drug Use Logs.

Monitoring of these records revealed irregularities in delivery of post-operative buprenorphine. The IACUC investigative committee reported two findings:

1. Surgical Records and Pharmacy Drug Use Logs are inconsistent with buprenorphine treatment of all animals as required by the protocol.

- Records were reviewed for 25 rats with individual ID numbers.
- 15 rats treated with one or more doses of buprenorphine were identified in Surgical Records and Pharmacy Drug Use Logs provided by laboratory staff. In total, 30 doses of buprenorphine were administered. This is the maximum number of doses contained in the single stock vial of buprenorphine provided to the investigator by the Pharmacy.
- According to Surgical Records, buprenorphine was administered to 10 additional animals with unique ID numbers. The Pharmacy Drug Use Log contains no corresponding record of

buprenorphine treatment for these animals (rat ID numbers, date, time, and dose of drug are absent). As noted above, all 30 available doses were used to treat the other 15 animals accounted for in both the Surgical and Drug Use Log records. Buprenorphine for the 10 additional animals was therefore not prepared from the single available vial associated with this protocol. Another source vial of buprenorphine was not found in a search of Pharmacy, laboratory, and ARC records.

2. Buprenorphine was delivered to some rats after the expiration date.

- Buprenorphine from the stock vial was appropriately diluted for treatment of rats. Diluted solutions have a 30 day expiration as detailed in IACUC and Pharmacy standard operating procedures. Expired diluted buprenorphine solution was administered to 9 animals. In some instances, the diluted drug was 1-3 months past expiration.

The following corrective action plan was implemented after the incident:

1. Researcher access to the ARC was revoked on June 24, 2019 pending completion of the IACUC investigation and consideration of the findings by the full IACUC committee.

2. Immediate permanent revocation of the privilege to conduct animal research is recommended for the researcher directly responsible for these violations.

3. The investigator who supervised this researcher must establish a rigorous process for oversight of animal research, including regular internal audits of surgical and post-operative care, analgesic records and procedures for all protocols.

4. IACUC post-approval monitoring (PAM) of all protocols held by the responsible investigator will be undertaken to ensure compliance with approved procedures and record keeping, including surgical and post-operative care and analgesic use records.

The protocol is not suspended as the non-compliant activity was carried out by the researcher who acted without informing the Investigator or other study staff. The Investigator agreed with all IACUC findings and recommendations.

At the IACUC meeting on August 5, 2019, the IACUC reviewed and accepted the corrective action plan. The IACUC determined that this was an isolated incident and not a programmatic failure.

Please do not hesitate to contact me if you require further information.

With regards,
(b) (6)

Dennis Durbin, MD
Institutional Official
Chief Scientific Officer

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, September 03, 2019 7:38 AM
To: (b) (6) OLAW Division of Compliance Oversight (NIH/OD)
Cc: (b) (6) Durbin, Dennis
Subject: RE: Final report from D16-00331

Thank you for providing this final 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

From: (b) (6)
Sent: Friday, August 30, 2019 2:59 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6) Durbin, Dennis <Dennis.Durbin@nationwidechildrens.org>
Subject: Final report from D16-00331

Please see the attached Final Report.

The Research Institute at Nationwide Children's Hospital, in accordance with Assurance D16-00331 and PHS Policy IV.F.3., provides this report of noncompliance involving an approved protocol entitled "Production of Tissue Engineered Small Intestine" . This incident was first reported to you on July 10, 2019 via a telephone call. As detailed below, an IACUC investigation found inadequate record keeping supporting buprenorphine treatment of rats for post-operative pain relief as required by the IACUC protocol. Use of expired buprenorphine was also documented. At that time, a written final report was requested. The full IACUC met on August 5, 2019 and approved the attached report.

If you need any additional information, please let me know.

(b) (6)

NATIONWIDE CHILDREN'S
When your child needs a hospital, everything matters.

A3544-L

Office of Laboratory Animal Welfare

OLAW

Initial Report of Noncompliance

By: aw

Date: 7/10/19 Time: 11:45

Name of Person reporting: Denis Dubin
Telephone #: (b) (6)
Fax #:
Email:

Name of Institution: Nationwide Children's Hospital
Assurance number: A3544

Did incident involve PHS funded activity? NIH
Funding component: NIDDK
Was funding component contacted (if necessary): _____

What happened?

Discrepancy between records regarding giving analgesics
10 rats didn't get buprenorphine, 9 got approved drug

Species involved: Rat
Personnel involved:
Dates and times:
Animal deaths:

Projected plan and schedule for correction/prevention (if known): _____

Investigator was fined, PI under enhanced post-approval monitoring

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY
Case #_____