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) 480-3387

April 22, 2020

Re: Animal Welfare Assurance
A3377-01 [OLAW Case 7B]

Dr. David P. Norton
Vice President for Research
University of Florida
(b) (4) Grinter Hall
Gainesville, FL 32611-5500

Dear Dr. Norton,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your April 3, 2020 letter reporting an incident of non-compliance with the PHS Policy on Humane Care and Use of Laboratory Animals within the animal care and use program at the University of Florida. According to the information provided, OLAW understands that a mistake in the reconstitution of pyridostigmine bromide led to toxicity in rats requiring euthanasia. The animals involved in this incident were not on a study funded by the PHS.

Corrective and preventive actions included mixing a new solution of pyridostigmine. Also, staff will double check the volume of pyridostigmine and the lab will develop a dilution SOP and retrain lab members.

OLAW believes that the actions taken by the University of Florida are consistent with the provisions of the PHS Policy on Humane Care and Use of Laboratory Animals for institutional self-monitoring and self-reporting. Although this activity was not PHS funded, the application of the expectations of the PHS Policy across the animal care and use program reduces any potential appearance of a double standard. OLAW appreciates being informed of this issue and finds 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

A3377-7B

UF UNIVERSITY of FLORIDA

Office of the Vice President for Research

223 Grinter Hall
PO Box 115500
Gainesville, FL 32611-5500
352-392-1582

April 3, 2020

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 University of Florida, in accordance with Assurance D16-00244 (A3377-01) and PHS Policy IV.F.3., provides this report of an adverse event regarding animal death due to improper drug reconstitution.

In February 2020, rats received four different insecticides/repellants as described in the IACUC approved protocol. Within an hour of administration, rats showed signs of toxicity – salivation, lacrimation, tremors, weakness, and immobility. Several rats died that afternoon. All the remaining animals were euthanized immediately by the laboratory staff. The lab and Animal Care Services (ACS) vet staff worked closely together to discover the cause of the unexpected outcome. Initial investigation into the four agents administered found no significant differences from previous agents used in the past. In order to determine which agent was responsible, a trial was conducted on 4 rats using single agent sequential exposures. After two treatments it was determined that pyridostigmine bromide was responsible for the adverse clinical signs observed in the exposed rats. Further investigation into this formulation revealed that it was reconstituted incorrectly. This lead to an increased concentration and ultimately an increased dose (3 fold) that was inadvertently administered to the rats.

The following corrective actions were implemented by the laboratory following the incident:

1. There was nothing in the dilution procedure for pyridostigmine that was different from that used in the last 8 years. This is the first instance of an untoward outcome during the exposure. It is not clear what went wrong, but it was clear that the total volume of the remaining pyridostigmine stock was well short of the 150 ml that should have been present after ~10 exposure doses. Staff will double check total volumes in the future.

2. On March 4, 2020, a fresh solution of pyridostigmine was mixed and administered to animals without adverse effects.

The IACUC full committee voted on March 10, 2020 that this incident was an adverse event and was reportable through the IO to regulatory agencies. In addition to the above corrective actions the Committee requested that the laboratory develop a dilution SOP as it pertains to this work and retrain all laboratory members.

This study is supported by the following grants:

1. W81XWH-15-1-0515: Department of Defense
2. W81XWH-19-1-0657: Department of Defense

The funding components have been notified of the adverse event.

The University of Florida is committed to protecting the welfare of animals used in research and appreciates the guidance and assistance provided by OLAW in this regard. Should you have any questions regarding this report, please contact Daniel R. Brown, Ph.D., IACUC Chair.

Thank you for your consideration of this matter.

Sincerely,

(b) (6)

David Norton, Ph.D.
Vice President for Research
Institutional Official

(b) (6)

Wolff, Axel (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Wednesday, April 15, 2020 8:42 AM
To: Mahoney,Michael P
Cc: OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Reportable adverse event (00793798)

Thank you. We will respond soon.
Axel Wolff

From: Mahoney,Michael P <mmahoney@ufl.edu>
Sent: Monday, April 13, 2020 4:42 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: (b) (6)
Subject: Reportable adverse event (00793798)

Dr. Morse,

I am sending the attached report of an adverse event from the University of Florida. UF did not send a preliminary report for this event.

The protocol involved in this adverse event is funded by DOD and I have cc'd the applicable Program Officials on this email.

Please acknowledge receipt and let me know if you have any issues.

-Michael

Michael Mahoney
Director of Research Operations and Services
University of Florida | UF Research | PO Box 115500
Grinter (b) (4) PH: (b) (6) | http://research.ufl.edu