Room #

Secondary Individual

Signature

IOWA STATE UNIVERSITY
OF SCIENCE AND TECHNOLOGY

Office of the Vice President for Research
2610 Beardshear Hall
515 Morrill Road
Ames, IA 50011-2036
515-294-6344
FAX 515-294-6100

October 3, 2017

Secondary Individual
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 ondary Individ

I am writing to share the final report for an incident that occurred at Iowa State University (ISU). Our Animal Welfare Assurance number is: A3236-01.

The grant that supports this work is: R01ES027245.

The goal of this study is to examine the effects of chronic exposure to various neurotoxic pesticides and the impact on the development and progression of Parkinson's disease. Animals are treated with neurotoxic pesticides and undergo a variety of behavioral tests. Per the IACUC-approved protocol, a subcutaneous mini-pump was to be surgically implanted in rats and then deliver 2-3 mg/kg rotenone, daily, for 28 or 56 days. The vehicle solution was dimethylsulfoxide (DMSO) and Miglyol 812; control animals received an equal volume of vehicle.

On July 28, 2017, the PI submitted an Adverse Event form to the IACUC office. The adverse event reported rats who had received repeated subcutaneous injections of rotenone had reacted to the injections. Upon review of the report and comparison to approved protocols, it was determined that the IACUC had not approved repeated subcutaneous injections of rotenone.

The researchers contacted the Laboratory Animal Resources (LAR) veterinarians. Animals who were treated with rotenone were mild to moderately depressed and dehydrated. The LAR veterinarians treated the animals with Lactated Ringer's Solution, and provided moistened feed for 3 days. The animals recovered and were used for the remainder of the study.

The IACUC began an investigation of potential noncompliance; it was determined that a student on the project had misread the protocol to be subcutaneous injections and followed the procedures of a published paper. In sum, the protocol was changed from administering rotenone via a subcutaneously implanted pump to repeated subcutaneous injections. Additionally, the dose was changed from 2-3mg/kg daily for 28 or 56 days to 0.5mg/kg 5 times a week for 3 weeks, 4 days.

The IACUC discussed the noncompliance case at their full committee meeting on September 6, 2017. The committee determined the changes implemented to the protocol prior to IACUC approval constituted minor, non-continuing noncompliance. It was deemed minor because the incident was not fatal, the procedure was

similar to that which was approved, and a lower dose of rotenone was administered. The incident was determined to be non-continuing because this is the first incident of noncompliance with this PI.

The IACUC also recommended the following corrective actions:

1. *Re-training for all students on protocol.* Students included as Key-Personnel on the study must be retrained in all procedures listed in the protocol that they will be involved in carrying out.
2. *Research team institutes "Project Launch" meetings prior to the beginning of new projects.* Research team is to meet to discuss all aspects of the study and the protocol prior to beginning a new study.
3. *Directed post-approval monitoring visits.* The research team will be subject to additional post-approval monitoring visits.
4. *Restrictions on the use of data.* The data collected during the non-IACUC approved portion of the study, in which this incident occurred, may not be used for grant applications or publications.

The researchers will no longer administer rotenone subcutaneously for future approved-replicates of the study; rather, they will administer the rotenone via inter-peroneal injection, which is part of the IACUC-approved protocol.

Please let me know if you have any questions or concerns.

Thank you,

Signature

Dr. Sarah Nusser
Institutional Official
Vice President for Research

Morse, Brent (NIH/OD) [E]

From: OLAW Division of Compliance Oversight (NIH/OD)
Sent: Tuesday, October 10, 2017 3:15 PM
To: Secondary Individual OLAW Division of Compliance Oversight (NIH/OD)
Cc: IACUC Committee; Secondary Individual Secondary Individual econdary Individu Secondary Individual
Subject: RE: Final report - Iowa State University

Thank you for submitting this final report. We will send an official response soon.

Regards, Brent Morse

Brent C. Morse, DVM, DACLAM
Acting Director
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

Please note that this message and any of its attachments are intended for the named recipient(s) only and may contain confidential, protected or privileged information that should not be distributed to unauthorized individuals. If you have received this message in error, please contact the sender.

From: Secondary Individual [mailto:dary Ind@iastate.edu]
Sent: Tuesday, October 10, 2017 12:04 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: IACUC Committee <iacuc@iastate.edu>; Secondary Individual @iastate.edu>; Secondary Individual ondary Indiv@iastate.edu>; Secondary Individual @iastate.edu>
Subject: Final report - Iowa State University

Dear Dr. Morse,

Please find attached to this email the final report for this incident.

Thank you,

Secondary Individua
Director
Office for Responsible Research (ORR)
Iowa State University
2420 Lincoln Way, Room #
Ames, IA 50014
Phone: Phone Number
ndary Indi@iastate.edu
www.compliance.iastate.edu

From: OLAW Division of Compliance Oversight (NIH/OD) [mailto:olawdco@od.nih.gov]
Sent: Tuesday, August 01, 2017 2:22 PM

To: Secondary Individual @iastate.edu>; OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: IACUC Committee <iacuc@iastate.edu>; Secondary Individual @iastate.edu>; Secondary Individual ndary Indiv@iastate.edu>; Secondary Individual @iastate.edu>
Subject: RE: Preliminary report - Iowa State University

Thank you for this preliminary report. We will use this email to open a case file. Please send the final report to this email inbox. Thank you again.

Sincerely, Brent Morse

Brent C. Morse, DVM, DACLAM
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare
National Institutes of Health

From: Secondary Individual [mailto:dary Ind@iastate.edu]
Sent: Tuesday, August 01, 2017 3:19 PM
To: OLAW Division of Compliance Oversight (NIH/OD) <olawdco@od.nih.gov>
Cc: IACUC Committee <iacuc@iastate.edu>; Secondary Individual @iastate.edu>; Secondary Individual ndary Indiv@iastate.edu>; Secondary Individual @iastate.edu>
Subject: Preliminary report - Iowa State University

Dear condary Individ

I am writing to make a preliminary report of an incident that occurred at Iowa State University. Our Animal Welfare Assurance number is: A3236-01. The grant that supports this work is: R01ES027245.

The PI reported an adverse event. Rats were found to be depressed and dehydrated, as well as indication of swelling and scabs around subcutaneous injection sites. We are working with the PI to confirm details and we will submit our formal report upon completion of our investigation.

Thank you,

Secondary Individua
Director
Office for Responsible Research (ORR)
Iowa State University
2420 Lincoln Way, Room #
Ames, IA 50014
Phone: Phone Number
dary Ind@iastate.edu
www.compliance.iastate.edu