



DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

FOR US POSTAL SERVICE DELIVERY:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive – MSC 7982
Bethesda, Maryland 20892-7982
Home Page: <http://grants.nih.gov/grants/olaw/olaw.htm>

FOR EXPRESS MAIL:

Office of Laboratory Animal Welfare
Rockledge One, Suite 360
6705 Rockledge Drive
Bethesda, Maryland 20817
Telephone: (301) 496-7163
Facsimile: (301) 402-7065

June 11, 2018

Re: Animal Welfare Assurance
#A3095-01 (OLAW Case G)

Chris Kevil, Ph.D.
Vice Chancellor for Research and Director
Center for Cardiovascular Diseases and Sciences
Louisiana State University Health Sciences Center Shreveport
1501 Kings Highway
Shreveport, LA 71103

Dear Dr. Kevil,

The Office of Laboratory Animal Welfare (OLAW) acknowledges receipt of your June 4, 2018 letter reporting a series of noncompliance with the PHS Policy on Humane Care and Use of Laboratory Animals at Louisiana State University Health Sciences Center Shreveport, following up on an initial January 25, 2018 telephone notification and March 20, 2018 interim report. According to the information provided, OLAW understands the IACUC suspended two protocols based on several instances of noncompliance including the use animals that weighed less than approved on protocol; exceeding the number of approved animals; failure to adequately describe and follow humane endpoints; inadequate record keeping and documentation of analgesic administration; housing animals in laboratories longer than approved and at unauthorized locations; housing multiple animals in an incubator contrary to the approved protocol; performing surgeries on Fridays and weekends in an attempt to circumvent veterinary oversight and duplicating protocols. The animal activities in question were supported by PHS funds and the funding agency has been notified of the suspensions.

The corrective actions consisted of the following:

- (1) Retraining the Principal Investigator (PI) and laboratory personnel on the recognition and treatment of post-procedural pain, post-surgical record keeping, post-procedural supportive care and humane endpoints.
- (2) Relocating the incubator into the animal facility for enhanced oversight.
- (3) Requiring that surgeries be performed on Mondays with sacrifice scheduled no later than Fridays.
- (4) Maintaining appropriate animal records and laboratory books for subsequent review by veterinary personnel and the IACUC.
- (5) Enhancing communication between the Principal Investigator and the Director and Associate Director of Animal Resources.
- (6) Revising or amending one protocol to avoid duplication and unnecessary use of animals.

- (7) Amending two of the approved protocols to include details on record keeping, surgical procedures, post-operative signs and care, humane endpoints, euthanasia and the use of mouse cages for surgical recovery of individual rats until ambulatory within the incubator.

Based on the information provided, OLAW is satisfied that appropriate actions have been taken to investigate, correct and prevent recurrence of the noncompliance. We appreciate having been informed about this matter and find no cause for further action by this Office.

Sincerely,

(b) (6)

Neera V. Gopee, DVM, PhD, DACLAM, DABT
Animal Welfare Program Specialist
Division of Compliance Oversight
Office of Laboratory Animal Welfare

cc: IACUC Chair



Health Sciences Center

Office of the Vice Chancellor
for Research

Chris Kevill, PhD

1501 Kings Highway
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June 4, 2018

Neera V. Gopee, DVM, DACLAM, DABT
Veterinary Medical Officer
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. Gopee:

The LSU Health Sciences Center-Shreveport, in accordance with Assurance D16-00059 (A3095-01) and PHS Policy IV.F.3., provides this final report of noncompliance regarding suspension of two approved animal protocol.

The noncompliance is a result of a series and continuing incidents involving 2 identical animal use protocols. A preliminary report was provided to you in February, 2018, via telephone call by Dr. V. Hugh Price, DVM, Director, Animal Resources and Attending Veterinarian. A formal report was submitted to you on March 20, 2018, that detailed the events of the non-compliance and included a list of corrective actions.

The project and the animals covered by the protocol are PHS funded, and the funding agency was notified.

Briefly, the investigative subcommittee found a list of infractions that included: using animals that weighed less than stated on the protocol, using more animals than requested on the protocol, experimental endpoints not clear and not adhered to, poor record keeping, keeping animals in the lab longer than approved, poor records of analgesia use, housing multiple animals in an incubator when only approved to house animals one at a time, lack of adherence to humane endpoints, conducting surgery on Fridays and weekends in an apparent attempt to circumvent veterinary monitoring, and duplication protocols.

After receiving a report on the above activities at the January 16, 2018, meeting, the Animal Care and Use Committee (Institutional Animal Care and Use Committee) of the LSU Health Sciences Center Shreveport voted to suspend both protocols, and the Chair appointed a subcommittee to investigate and propose corrective actions.

The ACUC received the report of the subcommittee at the February 20, 2018, meeting, and vote to require the following corrective actions.

NOTE: A description of the completed corrective action follows each required action.

1. The PI and all laboratory personnel should undergo more training, specifically on how to identify signs of distress in laboratory animals and signs of adequate anesthesia. (NOTE: Following successful training this suspension should be lifted).

Corrective Action Taken: The training was completed on 2/27/2018 and covered recognition and treatment of post-procedural pain, post-procedural record keeping, post-surgical record keeping, diet supplementation in the post-surgical period, and humane endpoints. Training was conducted by the Associate Director, Animal Resources and Clinical Veterinarian. Accordingly, the suspension was lifted.

2. The PI should move the incubator back into the animal facility so that the welfare of the animals can be followed more rigorously.

Corrective Action: The incubator was moved back into the animal facility on 2/23/2018.

3. As there is no scientific justification for performing surgeries on a Friday, and given the serious nature of the extensive list of ANPs, the PI and his personnel need to now perform surgeries on a weekday so that multiple sets of eyes (the PI's group and animal facilities personnel) can check on the welfare of the animals.

Corrective Action: The PI agreed that all surgeries would be performed on Monday with sacrifice no later than Friday. This became effective on 2/27/2018.

4. The PI and all laboratory personnel need to keep a detailed logbook (animal weights, procedures, monitoring, blood pressure, and heart rate) next to the incubator. This will allow multiple sets of eyes (the PI's research group and animal facilities personnel) to observe the animals following surgery and during recovery. These monitoring conditions will be revisited by the IACUC after a period of at least 6 months of active surgery.

Corrective Action: This was an integral part of the training provided by the Associate Director, Animal Resources. This information is being recorded in lab notebooks maintained in the research lab as well as in a binder in the animal room. The binder in the animal room allows the veterinary staff easy

access to the post-procedural and post-surgical monitoring information. This became effective on 2/27/2018.

5. The PI and all laboratory personnel need to keep detailed lab books (separate from the log book) regarding what happens to each animal throughout its life here at LSUHSC-S. This allows complete transparency at every level, e.g. has the animal been used for training or an experiment, was it fasted, was there a problem with surgery, what analgesics were given and when etc. – Good laboratory practice is needed.

Corrective Action: This detailed record keeping was discussed and agreed upon in the training session that was conducted by the Associate Director, Animal Resources. The lab personnel developed forms to aid in keeping the required information and facilitate record keeping. The new forms were implemented on 2/25/2018. This will be monitored during lab visits by the Associate Director, and/or the Director, Animal Resources. In addition, the ACUC subcommittees inspecting labs during the Semi-Annual Inspection and Program Review will conduct a closer inspection of these records.

6. The PI and his personnel AND animal resources should maintain a more transparent dialogue. – It is very apparent to this committee that there has been a breakdown in communication and transparency. This must be resolved as the main concern is always the animal welfare and to ensure this, communication is essential at every level.

Corrective Action: Both the Director, Animal Resources and the Associate Director, Animal Resources make regular visits to the lab to check on progress. The Director, Animal Resources, has always maintained an "open door" policy in regards to PI issues and has encouraged this PI to contact him anytime he feels he has a problem of any nature as it deals with his animals or his animal use protocols.

7. One of the PI's more recent animal protocols needs to be revised or amended to differentiate from previous protocols. This revision should account for experiments previously performed in an earlier protocol with exactly the same procedures to assure no duplication of experiments and unnecessary use of animals.

Corrective Action: One protocol (the older protocol) was terminated. The second newer protocol was retained and modified as described in the next item. A new protocol was submitted that differed from the second remaining protocol.

8. The PI must revise 2 of the approved protocols to specifically include:
a. Detailed record keeping (i.e. documentation on rats "cradle to grave"), including new "records for pain management"

- b. Step by step description of procedure for surgeries
- c. A detailed description of post-operative signs and symptoms.
- d. A step by step procedure for post-op care (currently post-op care as written in the protocol is not being adhered to)
- e. A detailed plan for euthanasia (i.e. identify conditions for immediate euthanasia, and humane endpoints "discolored leg, 2 legs not in use," and conditions to monitor closely)
- f. A modification to enable the use of mouse cages (1 per rat) which are then placed in a human baby incubator until rats are ambulatory. This allows more than 1 rat to be recovered at one time in the incubator and yet keep them separate.

Corrective Action: As noted above, one of the duplicate protocols was closed. A modification detailing the information requested above was submitted on the remaining protocol all of the above points. The modification was reviewed by the entire Animal Care and Use Committee via the Full Committee Review process and approved on 3/27/2018.

If additional information is needed, please do not hesitate to contact me.

Sincerely,

(b) (6)



Chris Kevil, PhD
Vice Chancellor for Research
Dean, School of Graduate Studies
Institutional Official

Gopee, Neera (NIH/OD) [E]

From: Gopee, Neera (NIH/OD) [E]
Sent: Friday, June 01, 2018 12:58 PM
To: (b) (6)
Cc: Price, Hugh; (b) (6)
Subject: RE: Lin Final Report letter

Thank you for this final report (b) (6) We will send an official response soon.

Best Regards,
Neera

Neera V. Gopee, DVM, PhD, DACLAM, DABT
Veterinary Medical Officer
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: (b) (6)@lsuhsc.edu]
Sent: Thursday, May 31, 2018 4:46 PM
To: Gopee, Neera (NIH/OD) [E] <neera.gopee@nih.gov>
Cc: Price, Hugh <HPrice@lsuhsc.edu>; (b) (6)@lsuhsc.edu>
Subject: (b) (6) Final Report letter

Hello Dr. Gopee,

Attached is the Final Report letter concerning (b) (6)

Thank you,

(b) (6)

LSU Health
SHREVEPORT

Gopee, Neera (NIH/OD) [E]

From: Gopee, Neera (NIH/OD) [E]
Sent: Friday, March 23, 2018 11:24 AM
To: 'Price, Hugh'
Cc: Kevil, Christopher; (b) (6) Woolard, Matthew D.; OLAW Division of Compliance Oversight (NIH/OD)
Subject: RE: Initial Report of Non-Compliance

Thank you for this preliminary report, Dr. Price. We will start a new case file and look forward to receiving the final report from the IO after has completed all requested correction actions.

Best Regards,
 Neera

Neera V. Gopee, DVM, PhD, DACLAM, DABT
 Veterinary Medical Officer
 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: Price, Hugh [mailto:HPrice@lsuhsc.edu]
Sent: Tuesday, March 20, 2018 5:31 PM
To: Gopee, Neera (NIH/OD) [E] <neera.gopee@nih.gov>
Cc: Kevil, Christopher <CKevil@lsuhsc.edu>; (b) (6)@lsuhsc.edu; Woolard, Matthew D. <mwoola@lsuhsc.edu>
Subject: Initial Report of Non-Compliance

Dr. Gopee,

Attached is the initial report of a non-compliance action that began with a protocol suspension at the January Meeting of the Animal Care and Use Committee of the LSU Health Sciences Center Shreveport. The investigative subcommittee reported its findings and suggested corrective actions at the February meeting of the full committee, and the committee voted to accept the report including the corrective actions.

The PI is in the process of completing all corrective actions, and a follow-up letter will be sent shortly.

Thank you for your assistance in this matter.

V. Hugh Price, Jr., DVM
 Director, Animal Resources and Attending Veterinarian

March 20, 2018

Health Sciences Center

Office of the Vice Chancellor
for Research

Chris Kevll, PhD

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Bethesda, MD 20892

Dear Dr. Gopee,

The LSU Health Sciences Center Shreveport, in accordance with Assurance D-16-00059 (A3095-01) and PHS Policy IV.F.3., provides this report of non-compliance regarding suspension of two Animal Care and Use Committee (ACUC)(this institution's name for the Institutional Animal Care and Use Committee)-approved animal protocols.

The protocols in question were suspended by vote of the ACUC at its regularly scheduled monthly meeting on January 16, 2018. Both protocols were exactly the same.

The suspension resulted from a number of issues that had been reported over the period of several months:

1. Animals are being used at weights smaller than requested in the protocols.
2. In some cases, more animals have been ordered than are on the animal protocol.
3. Animal endpoints are not adequately discussed in the protocol, nor are they being adhered to.
4. Record keeping is not consistent with what has been written in the protocols (e.g. weights recorded daily during diet restriction).
5. When records are kept they are not accurate and not possible to follow, e.g. old University of Miami forms are used which do not accurately reflect the "pain" criteria of these rats (the mention of tumors was included on the sheet). Pain scores were marked from 1-3 (i.e. 3=mortality), yet the sheet stated that they should be 1-5. Personnel were also unclear as to what the pain score meant.
6. Record keeping following surgery is not adequate, e.g. it is not possible to determine what has happened to the rat, whether it has been administered anything and when euthanasia/sac took place.
7. It is not possible to track what has happened to every animal once it arrives into the facility, e.g. has it been used for training or an experiment, was it fasted, was there a problem with surgery, what analgesics were given and when etc. – Good laboratory practice is needed.
8. It is unclear as to whether more than one rat is being housed in a mouse cage in the incubator during recovery.
9. Recovery time is longer than that stated in the protocol, e.g. 48 hours.
10. The PI's lab members need more information on how 1) to identify laboratory animals in distress and 2) identify when animals are under adequate anesthesia.

11. Rats are kept in rooms/locations not designated, despite written warning.
12. It is unclear as to when the PI and the lab group can handle vs. perform a procedure on a rat.
13. No scientific justification was given for performing procedures on a Friday, which means post-op over the weekend.
14. The most recent of the two identical protocols appears to be a duplication of an earlier protocol (approximately 2 years older), and, as such, animals are being used for the same experiments twice.

The IACUC discussed the findings of the investigative subcommittee at the regularly scheduled monthly meeting on February 20, 2018, and voted to require the following corrective actions from the PI:

1. The PI and all laboratory personnel should undergo more training, specifically on how to identify signs of distress in laboratory animals and signs of adequate anesthesia. (NOTE: Following successful training this suspension should be lifted).
2. The PI should move the incubator back into the animal facility so that the welfare of the animals can be followed more rigorously.
3. As there is no scientific justification for performing surgeries on a Friday, and given the serious nature of the extensive list of ANPs, the PI and his personnel need to now perform surgeries on a weekday so that multiple sets of eyes (the PI's group and animal facilities personnel) can check on the welfare of the animals.
4. The PI and all laboratory personnel need to keep a detailed logbook (animal weights, procedures, monitoring, blood pressure, and heart rate) next to the incubator. This will allow multiple sets of eyes (the PI's research group and animal facilities personnel) to observe the animals following surgery and during recovery. These monitoring conditions will be revisited by the IACUC after a period of at least 6 months of active surgery.
5. The PI and all laboratory personnel need to keep detailed lab books (separate from the log book) regarding what happens to each animal throughout its life here at LSUHSC-S. This allows complete transparency at every level, e.g. has the animal been used for training or an experiment, was it fasted, was there a problem with surgery, what analgesics were given and when etc. – Good laboratory practice is needed.
6. The PI and his personnel AND animal resources should maintain a more transparent dialogue. – It is very apparent to this committee that there has been a breakdown in communication and transparency. This must be resolved as the main concern is always the animal welfare and to ensure this, communication is essential at every level.
7. One of the PI's more recent animal protocols needs to be revised or amended to differentiate from previous protocols. This revision should account for experiments previously performed in an earlier protocol with exactly the same procedures to assure no duplication of experiments and unnecessary use of animals.
8. The PI must revise 2 of the approved protocols to specifically include:
 - a. Detailed record keeping (i.e. documentation on rats "cradle to grave"), including new "records for pain management"
 - b. Step by step description of procedure for surgeries
 - c. A detailed description of post-operative signs and symptoms.
 - d. A step by step procedure for post-op care (currently post-op care as written in the protocol is not being adhered to)

- e. A detailed plan for euthanasia (i.e. identify conditions for immediate euthanasia, and humane endpoints "discolored leg, 2 legs not in use," and conditions to monitor closely)
- f. A modification to enable the use of mouse cages (1 per rat) which are then placed in a human baby incubator until rats are ambulatory. This allows more than 1 rat to be recovered at one time in the incubator and yet keep them separate.

As of the date of this letter, the PI has completed the first corrective action. Therefore, as stated in that corrective action, the protocol suspension has been lifted.

Currently, the PI is working with the Attending Veterinarian and the Chairman, Animal Care and Use Committee to implement the remainder of the corrective actions. Progress/updates on the remaining corrective corrections will be provided to the ACUC and recorded in the meeting minutes.

The LSU health Sciences Center Shreveport is committed to protecting the welfare of animals use din research at this institution and appreciates the guidance and assistance provided by OLAW in this regard. Should you have any questions regarding this report, please contact Matthew Woolard, Ph.D., ACUC Chairman (mwoola@lsuhc.edu) or myself (ckevil@lsuhsc.edu).

Thank you for your consideration in this matter.

Sincerely,

(b) (6)



Chris Kevil, PhD
Vice Chancellor for Research
Dean, School of Graduate Studies
Institutional Official
LSU Health Sciences Center Shreveport



Initial Report of Noncompliance

By: Neera Gopee

Date: 1-25-18

Time: 5:15pm

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

Name of Institution: LSU
 Assurance number: A3095-01

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

What happened?

Rats were housed at satellite location in laboratory for longer than what was approved by IACUC. Diet was noncompliant with protocol. Protocol has been suspended until IACUC investigates and animals have been placed on a holding protocol.

Species involved: rats
 Personnel involved: PI
 Dates and times:
 Animal deaths:

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

Projected submission to OLAW of final report from Institutional Official:

OFFICE USE ONLY
 Case # _____